

Risk Factors Comparison 2025-02-28 to 2024-02-29 Form: 10-K

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In evaluating the Company and our business, careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the SEC. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occur, our business, prospects, financial condition, results of operations and cash flow could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition, results of operations or cash flow. Risks Related to the Clinical Development and Manufacturing of our Product Candidate Risks Related to Clinical Development Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control, including difficulties in identifying patients with MASH, significant competition for recruiting such patients in clinical trials, and restrictions on patients and investigators related to outbreaks of infectious diseases or public health crises. Identifying and qualifying patients to participate in clinical trials is critical to our success. We may **encounter delays in enrolling or** be unable to **enroll or** retain a sufficient number of patients **in our** ~~to successfully complete the long-term follow-up portion of the ongoing Phase 2b SYMMETRY study, and may encounter delays in enrolling or be unable to enroll or retain a sufficient number of patients in our planned~~ Phase 3 SYNCHRONY studies or any other future clinical trials. In particular, as a result of the inherent difficulties in diagnosing MASH and the significant competition for recruiting patients with MASH in clinical trials, there may be delays in enrolling the patients we need to complete clinical trials on a timely basis, or at all. In addition, enrollment in Phase 3 clinical trials may be adversely affected by **the March 2024** marketing approval **of Rezdifra™ or the potential marketing approvals** for one or more investigational MASH drugs. Factors that may generally affect patient enrollment include: • the size and nature of the patient population; • the number and location of clinical sites we enroll; • the impact of geopolitical tensions, such as the ~~ongoing armed conflict in Israel and the Gaza Strip~~ **Middle East**, on clinical trial sites, such as those in Turkey and Israel, where **clinical we are currently planning to activate sites have been activated to participate** in our Phase 3 SYNCHRONY program; • the ability of our clinical sites to maintain adequate personnel; • competition with other companies for clinical sites or patients; • the eligibility and exclusion criteria for the trial; • the design of the clinical trial; • inability to obtain and maintain patient consents; • risk that enrolled participants will drop out before completion; • the availability of marketed therapies; and • clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. In addition, if any significant adverse events or other side effects are observed in any of our ~~future~~ clinical trials, it may make it more difficult for us to recruit patients to our clinical trials and patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of one or more product candidates altogether. Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays, which would increase our costs and have an adverse effect on our company. We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than us. The biotechnology industry is intensely competitive and subject to rapid and significant technological change. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions. We understand that a number of pharmaceutical companies, including AstraZeneca PLC / MedImmune LLC, Boehringer Ingelheim AG, ~~Inc.~~, Eisai, Inc., Eli Lilly **and Company**, GSK plc, ~~and Company~~, Johnson & Johnson, Merck & Co., Inc., Novo Nordisk A / S, Pfizer Inc., Roche Holding AG, and Takeda Pharmaceutical Company Limited, as well as large and small biotechnology companies such as **Aligos Therapeutics, Inc.**, Alnylam Pharmaceuticals, Inc., Altimmune, Inc., Amgen, Inc., Arrowhead Pharmaceuticals, Inc., Boston Pharmaceuticals, Inc., Cirius Therapeutics, Inc., ~~CohBar, Inc.~~, Concept Therapeutics, Inc., ~~89bio~~, D & D Pharmatech, Inc., **Eccogene Co., Ltd.**, **89bio**, Galactin Therapeutics Inc., Galmed Pharmaceuticals, ~~Ltd.~~, ~~Gilead Sciences, Inc.~~, Hanmi Pharmaceutical Company, Ltd., HighTide Therapeutics, **Inc.**, Inventiva Pharma SA, Ionis Pharmaceuticals, Inc., Madrigal Pharmaceuticals, Inc., MediciNova, Inc., NeuroBo Pharmaceuticals, Inc., North Sea Pharmaceuticals, **OrsoBio, Inc., Poxel SA,** Regeneron Pharmaceuticals, Inc., ~~Poxel SA~~, Sagimet Biosciences, Inc., **Sciwind Biosciences Co., Ltd.**, Terns Pharmaceuticals, Inc., Viking Therapeutics, Inc. and Zhejiang Doer Biologics Co. Ltd. are or may be pursuing the development or marketing of pharmaceuticals that target MASH. It is also probable that the number of companies seeking to develop products and therapies for the treatment of serious metabolic diseases, such as MASH, will increase. Many of our competitors have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market technologically superior products. In addition, many of these competitors have significantly greater experience than we have in undertaking nonclinical studies and human clinical trials of new pharmaceutical products and in obtaining regulatory approvals of human therapeutic products. Accordingly, our competitors may succeed in obtaining FDA approval for superior products. In addition, many competitors have greater name recognition and more extensive collaborative relationships. Smaller and earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidate or any future product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than we

are in manufacturing and marketing their products. If we are unable to compete effectively against these companies, then we may not be able to commercialize our product candidate or any future product candidates or achieve a competitive position in the market. This would adversely affect our ability to generate revenue. Our competitors also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Failures or delays in the commencement or completion of, or ambiguous or negative results from our planned clinical trials of our product candidates could result in increased costs to us and could delay, prevent, or limit our ability to generate revenue and continue our business. We do not know whether the ~~long-term follow-up portion of the SYMMETRY study will be completed or the~~ Phase 3 SYNCHRONY program or any future clinical trials will enroll or be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including, among others: • the FDA or comparable foreign regulatory authorities may not authorize us or our investigators to commence our planned clinical trials or any other clinical trials we may initiate, or may suspend our clinical trials, for example, through imposition of a clinical hold, and may request additional data to permit allowance of our **Investigational New Drug Application (“IND”)**; • delays in filing or receiving allowance of additional INDs that may be required; • lack of adequate funding to continue our clinical trials and nonclinical studies; • negative results from our ongoing nonclinical studies; • delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and study sites; • inadequate quantity or quality of a product candidate or other materials necessary to conduct clinical trials, for example delays in the manufacturing of sufficient supply of finished drug product; • difficulties obtaining ethics committee or Institutional Review Board (**“IRB”**) approval to conduct a clinical study at a prospective site or sites; • challenges in recruiting and enrolling subjects to participate in clinical trials, the proximity of subjects to study sites, eligibility criteria for the clinical study, the nature of the clinical study protocol, the availability of approved effective treatments for the relevant disease, and competition from other clinical study programs for similar indications; • challenges and delays in activating planned clinical trial sites globally due to the impact of geopolitical tensions, including the **escalating ongoing armed conflict in Israel and the Gaza Strip Middle East**; • severe or unexpected drug-related side effects experienced by subjects in a clinical trial; • we may decide, or regulatory authorities may require us, to conduct additional nonclinical or clinical trials or abandon product development programs; • delays in validating, or inability to validate, any endpoints utilized in a clinical trial; • the FDA or comparable foreign regulatory authorities may disagree with our clinical study design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials; and • difficulties retaining subjects who have enrolled in a clinical trial but may be prone to withdrawal due to rigors of the clinical trials, lack of efficacy, side effects, personal issues, or loss of interest. Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical study may be suspended or terminated by us, the FDA or comparable foreign regulatory authorities, the IRBs at the sites where the IRBs are overseeing a clinical study, a data and safety monitoring board (**“DSMB”**) overseeing the clinical study at issue or other regulatory authorities due to a number of factors, including, among others: • failure to conduct the clinical study in accordance with regulatory requirements or our clinical protocols; • inspection of the clinical study operations or study sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including in response to the imposition of a clinical hold; • unforeseen safety issues or safety signals, including any that could be identified in our ongoing nonclinical studies or clinical trials, adverse side effects or lack of effectiveness; • changes in government regulations or administrative actions; • problems with clinical supply materials; and • lack of adequate funding to continue clinical trials. Any inability to successfully complete nonclinical and clinical development could result in additional costs to us or impair our ability to generate revenue. In addition, if we make changes to a product candidate, such as the drug product-device combination **being that we plan to use used** in the Phase 3 SYNCHRONY program, we may need to conduct additional nonclinical studies or clinical trials to bridge or demonstrate the comparability of our modified product candidate to earlier versions, which could delay our clinical development plan or marketing approval for our current product candidate and any future product candidates. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Clinical development is uncertain and our clinical trials for EFX and any future product candidates may experience delays, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business. We cannot be sure that we will be able to continue development of EFX or submit INDs or similar applications for any future product candidates, on the timelines we expect, if at all. To proceed with our development plans and ultimately commercialization, we may need to conduct and meet regulatory requirements for additional preclinical studies and clinical trials. We cannot be certain of the timely completion or outcomes of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical programs or if the outcomes of our preclinical studies and clinical trials will enable any future clinical trials to begin under a proposed protocol. We rely and will continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates. We depend and will continue to depend upon third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs and trial sites, which may result in delays to our development timelines and increased costs. We rely heavily on third parties over the course of our clinical trials, and, as a result, have limited control over the clinical investigators and limited visibility into their day-to-day activities, including with respect to their compliance with ~~the approved clinical~~ **trial protocol protocols**. Nevertheless, our

reliance on third parties does not relieve us of our regulatory responsibilities and we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. We and these third parties are required to comply with **good clinical practice (“GCP”)** requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional nonclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. In addition, our clinical trials must be conducted with products produced under current good manufacturing practice (“cGMP”) requirements and may require a large number of patients. Our failure or any failure by these third parties to comply with these applicable regulations or to recruit a sufficient number of patients may require us to repeat 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. The third parties who conduct our clinical trials are not our employees and, except for remedies that may be available to us under our agreements with those third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing nonclinical and clinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. 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 clinical protocols or regulatory requirements or for other reasons, our 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 a timely manner or at all. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed. If any of our relationships with these third- party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure (including by clinical sites or investigators) to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenues could be delayed significantly.

Risks Related to the Manufacturing of our Product Candidate

The manufacture of our product candidates is complex and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure. The processes involved in manufacturing our product candidates, including pre- filled, dual- chamber syringe presentations of our product candidates, are complex, expensive, highly regulated, and subject to multiple risks. Further, as product candidates are developed through nonclinical studies to late- stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. In addition, the manufacturing process for any products that we may develop is subject to FDA and other comparable foreign regulatory authority approval processes and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA and foreign regulatory authority requirements, including, for example, complying with cGMP, applicable product tracking and tracing requirements and applicable **Quality System Regulation (“QSRs”)**, on an ongoing basis. If we or our third- party manufacturers are unable to reliably produce products to specifications acceptable to the FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our contract manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging or comparability nonclinical or clinical trials or the repetition of one or more clinical trials, increase clinical study costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations, and growth prospects. We are subject to many manufacturing risks, any of which could substantially increase our costs, delay clinical programs and limit supply of our product candidates. We have contracted with a third- party manufacturer, Boehringer Ingelheim, to make EFX drug substance (active pharmaceutical ingredient (“API”)) and with another third- party manufacturer, Vetter Pharma International GmbH, or Vetter, to manufacture EFX drug product (“DP”) including a DP- device combination **for**

to be used ~~use~~ in Phase 3 studies. We have successfully manufactured API and a DP- device combination under GMP conditions, ~~each of~~ which have both been released for ~~use in our ongoing~~ Phase 3 ~~clinical use~~ **SYNCHRONY program**. ~~The~~ We plan to enter into new commercial supply agreements with each of Boehringer Ingelheim and Vetter at the appropriate time. For Phase 3 clinical studies, the formulation used for API manufacture has been modified to enable production of a lyophilized DP rather than the frozen liquid used in Phase 2b studies. This change improves long- term pharmaceutical stability of the DP, making it suitable as the potential commercial presentation. A program of pharmaceutical and clinical studies has shown that the DP- device presentation ~~being to be~~ used in Phase 3 studies is comparable to that used for Phase 2b studies. **We have begun negotiating terms for commercial supply with each of Boehringer Ingelheim and Vetter and expect to enter into final agreements prior to readout of the Phase 3 SYNCHRONY Histology study**. The process of manufacturing our product candidates is complex, highly regulated and subject to several risks, including:

- the manufacturing process is susceptible to product loss due to contamination by adventitious microorganisms, equipment failure, improper installation or operation of equipment, vendor or operator error and improper storage conditions. Even minor deviations from normal manufacturing processes could result in reduced production yields and quality as well as other supply disruptions. If microbial, viral, or other contaminants are discovered in our products or in the manufacturing facilities in which our products are made, the manufacturing facilities may need to be closed for an extended period of time to investigate and eliminate the contamination;
- the manufacturing facilities in which our products are made could be adversely affected by equipment failures, labor and raw material shortages, pandemics, epidemics, or outbreaks of infectious disease, financial difficulties of our contract manufacturers, natural disasters, power failures, local political unrest and numerous other factors; and
- any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls or other interruptions in the supply of our products. We may also have to record inventory write- offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more expensive manufacturing alternatives. The manufacture of EFX requires significant expertise and capital investment, including the development of advanced manufacturing techniques and in- process controls. Manufacturers of these products sometimes encounter difficulties in production, especially during scale- up from the manufacturing process used for early clinical trials to a validated and qualified process needed for pivotal clinical trials and commercial launch. These problems include failure to meet target production costs and yields, failure to meet product release specifications, including stability of the product, quality assurance system failures, operator error and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. We cannot assure you that any product quality issues relating to the manufacture of our product candidate or any future product candidates will not occur in the future. We do not have, and we do not currently plan to acquire or build the facilities or internal capabilities to manufacture bulk drug substance, finished drug product or delivery device for use in clinical trials or commercialization. To a large extent, that makes us dependent on the goodwill of our contract manufacturing partners to quickly fix deviations that will inevitably occur during the manufacturing of our product and to manufacture API and / or the DP- device combination in sufficient quantities to meet commercial demand, if approved for marketing. Any delay or interruption in the supply of clinical trial materials on our contract manufacturing partners, could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials altogether. A new lyophilized EFX DP- device combination product for commercial use is being evaluated in the Phase 3 SYNCHRONY program. We contract with third parties for the manufacture of EFX and the delivery device utilized for EFX and expect to continue to do so for future clinical trials and for commercialization of EFX as well as for any future product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of EFX, or the delivery devices utilized for EFX, or any future product candidates or medicines or that such supply will not be available to us at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third- party manufacturers for the manufacture of EFX, delivery devices utilized for EFX or any future product candidates for nonclinical and clinical testing and for commercial supply of any of these product candidates for which we obtain marketing approval. Reliance on third- party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. To the extent any issues arise with our third- party manufacturers, we may be unable to establish any agreements with any other third- party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including:
- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance and safety and pharmacovigilance reporting. Third- party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. For our product candidates that are biologic- device combination products, third- party manufacturers may not be able to comply with cGMP regulatory requirements applicable to biologic- device combination products, including applicable provisions of the FDA' s drug product cGMP regulations, device cGMP requirements embodied in the FDA' s **Quality System Regulation ("QSR")** or similar regulatory requirements outside the United States. Our failure, or the failure of third- party manufacturers, 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 medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations. If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills

required to manufacture our product candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing-an analytical comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our product candidate that such CMO owns independently. This would increase our reliance on such CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our product candidates. In addition, in the case of CMOs that supply our product candidate, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply of bulk drug substance or for the manufacture of our drug product- delivery device combination. If any one of our current contract manufacturers cannot perform as agreed **to support our ongoing clinical trials or as needed to meet potential commercial demand if EFX is approved**, we may be required to replace that manufacturer. Although we believe that there potentially are alternative manufacturers who could manufacture our drug substance or drug product- delivery device combination or any future product candidates, we may incur added costs and delays in identifying and qualifying any such replacement. Our current and anticipated future dependence upon others for the manufacture of EFX or any future product candidates or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

Risks Related to Our Business, Industry and Intellectual Property Risks Related to Business Development We are heavily dependent on the success of EFX, our only product candidate. We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next several years will be devoted to EFX, which is currently our only product candidate. Accordingly, our business currently depends heavily on the successful development, regulatory approval, and commercialization of EFX. We cannot be certain that EFX will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of EFX or if EFX does not receive regulatory approval or fails to achieve significant market acceptance, we would be delayed by many years in our ability to achieve profitability, if ever. The research, testing, manufacturing, safety, efficacy, labeling, approval, sale, marketing, and distribution of EFX is, and will remain, subject to comprehensive regulation by the FDA and foreign regulatory authorities. Failure to obtain regulatory approval for EFX in the United States, Europe, Japan or other jurisdictions will prevent us from commercializing and marketing EFX in such jurisdictions. Clinical development of EFX prior to the BALANCED study was conducted by Amgen, Inc. (“Amgen”) in patients with type 2 diabetes. We did not conduct any of the development of EFX related to clinical trials in patients with T2D, and we have relied on Amgen to have conducted such research and development in accordance with the applicable protocol, legal, regulatory, and scientific standards, have accurately reported the results of all nonclinical studies and clinical trials conducted prior to our license of EFX, and have correctly collected and interpreted the data from these studies and trials. To the extent any of the foregoing has not occurred, our expected development time and development costs for EFX may be increased. Even if we were to successfully obtain approval from the FDA and foreign regulatory authorities for EFX, any approval might contain significant limitations related to use, including limitations on the stage of disease EFX is approved to treat, as well as restrictions for specified age groups, warnings, precautions or contraindications. Furthermore, even if we obtain regulatory approval for EFX, we will still need to develop a commercial infrastructure or develop relationships with collaborators to commercialize, establish a commercially viable pricing structure and obtain coverage and adequate reimbursement from third-party payors, including government healthcare programs. If we, or any future collaborators, are unable to successfully commercialize EFX, we may not be able to generate sufficient revenue to continue our business. We have expended and will continue to expend our limited resources to pursue a particular therapeutic candidate or indication, such as our focus on developing EFX for the treatment of MASH, and may fail to capitalize on therapeutic candidates or indications that may be more profitable or for which there is a greater likelihood of success. We have focused our extensive research and development efforts on EFX for the treatment of MASH. Therefore, we have, and in the future may, forego or delay pursuit of opportunities with other therapeutic candidates or for other indications that later prove to have greater commercial potential. We are highly dependent on the success of the future clinical trials of EFX, the outcomes of which are uncertain. Because EFX is our first and only therapeutic candidate, if it encounters safety, efficacy, supply or manufacturing problems, developmental delays, regulatory or commercialization issues or other problems, the value of our platform could be greatly diminished and our development plans could be curtailed and our business would be significantly harmed. 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 and EFX for the treatment of MASH may not yield any commercially viable therapeutic candidates. If we do not accurately evaluate the commercial potential or target market for a particular therapeutic candidate or misread trends in the biopharmaceutical industry, in particular for serious metabolic diseases, we may relinquish valuable rights to that therapeutic 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 therapeutic candidate. At any time and for any reason, we may determine that one or more of our discovery programs or pre-clinical or clinical therapeutic candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or therapeutic candidate. Accordingly, we may choose not to develop a potential therapeutic candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical or clinical therapeutic candidates or programs. Suspending, deprioritizing or terminating a program or therapeutic candidate in which we have invested significant resources, means we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or therapeutic candidates. If we fail to develop and successfully commercialize other product candidates, our business and future prospects may be harmed and our business will be more vulnerable to any problems that we encounter in developing and commercializing our product candidate. Our product candidate and any future product candidates must undergo rigorous clinical trials and regulatory approvals, and success in nonclinical studies or earlier-stage clinical trials may not be indicative of results in future clinical trials. EFX and any future product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and similar regulatory bodies in other jurisdictions. The approval process is typically lengthy and expensive, and approval is never certain. As a company, our only experience with clinical trials is our completed **Phase 2 BALANCED study**, ~~our HARMONY study, for which we have reported week 24 results, and our ongoing SYMMETRY studies study, for which we have reported Week 36 results,~~ and we have not yet completed the clinical trials required to obtain regulatory approval. We may not be able to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants or begin or successfully complete clinical trials in a timely fashion, if at all. Our anticipated clinical trials, including our **ongoing SYNCHRONY Phase 3 trials**, ~~of for~~ **of for** which we dosed the first patients in ~~December~~ **the fourth quarter of** 2023, may be insufficient to demonstrate that our potential products will be safe or effective. Additional clinical trials may be required if clinical trial results are negative or inconclusive, which will require us to incur additional costs and significant delays. Success in nonclinical studies and earlier-stage clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the effectiveness and safety of a product candidate. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial to support regulatory approval for a MASH therapy. In addition, there is a high failure rate for drugs and products proceeding through clinical trials. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in nonclinical studies and earlier-stage clinical trials. Similarly, the outcome of nonclinical studies may not predict the success of clinical trials. Moreover, data obtained from nonclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product development. Additionally, we are developing a pre-filled, dual-chamber syringe presentation of EFX that is considered to be a biologic-device combination product by the FDA, and any **BLA biologics license application** for EFX will require review and coordination by FDA's drug and device centers prior to approval. Any such delays could negatively impact our business, financial condition, results of operations and prospects. From time to time, we may publish interim 'top-line' or preliminary data from our clinical trials. Preliminary or interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business and financial prospects. In addition, certain of our hypotheses regarding the potential clinical and therapeutic benefit of EFX compared to other candidates in development for MASH are based on cross-trial comparisons of results that were not derived from head-to-head preclinical studies or clinical trials. These observations, which do not reflect robust comparative analyses, may suggest misleading similarities or differences due to differences in study protocols, conditions and patient populations, and may not be reliable predictors of the relative efficacy or other benefits of EFX compared to other product candidates that are in development for the treatment of MASH. We may develop EFX, and potentially future product candidates, in combination with other therapies, which exposes us to additional risks. We may develop EFX and future product candidates in combination with one or more approved therapies. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially. We may also evaluate EFX or any other future product candidates in combination with one or more other therapies that have not yet been approved for marketing by the FDA or similar regulatory authorities outside of the United States. We will not be able to market and sell EFX or any product candidate we develop in combination with any such unapproved therapies that do not ultimately obtain marketing approval. If the FDA or similar regulatory authorities outside of the United States do not approve these other drugs or revoke their approval, or if safety, efficacy, manufacturing, or supply issues arise with the drugs we choose to evaluate in combination with EFX or any other product candidate we develop, we may be unable to obtain approval of or market EFX or any other product candidate we develop. If we are not successful in discovering, developing, receiving regulatory approval for and commercializing EFX and any future product candidates, our ability to expand our business and achieve our strategic objectives would be impaired. Although we plan to devote a majority of our resources to the continued nonclinical and clinical testing and

potential approval of EFX for the treatment of patients with MASH, another key element of our strategy is to discover, develop and commercialize a portfolio of products. We are seeking to do so through the identification and potential development of additional pipeline programs, but our resources are limited, and those that we have are geared towards nonclinical and clinical testing and seeking regulatory approval of EFX for the treatment of patients with MASH. We may also explore strategic collaborations for the development or acquisition of new product candidates, but we may not be successful in entering into such relationships. EFX is our only product candidate in clinical stages of development. Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- an approved product may not be accepted as safe and effective by trial participants, the medical community or third-party payors; and
- intellectual property or other proprietary rights of third parties for product candidates we develop may potentially block our entry into certain markets or make such entry economically impracticable.

Risks Related to our License and Third- Parties We may be required to make significant payments under our license agreement for EFX. We acquired worldwide, exclusive rights to EFX pursuant to our license agreement with Amgen, which we refer to as the Amgen Agreement. Under the Amgen Agreement, in consideration for the license, we made an upfront payment of \$ 5. 0 million to Amgen and also issued 2, 653, 333 shares of our Series A convertible preferred stock to Amgen at the time of the initial closing of our Series A Preferred Stock financing in June 2018, with a subsequent 3, 205, 128 shares of our Series A convertible preferred stock issued at the time of the second closing of the Series A Preferred Stock financing in November 2018. On July 2, 2019, we announced the dosing of the first patient in the BALANCED study of EFX, which resulted in a \$ 2. 5 million milestone obligation under the Amgen Agreement. Additionally, we paid Amgen \$ 7. 5 million in December 2023 in connection with dosing the first patient in our Phase 3 SYNCHRONY program. As additional consideration for the license, we are required to pay Amgen up to \$ 30. 0 million in connection with marketing approvals and aggregate milestone payments of up to \$ 75. 0 million upon the achievement of specified commercial milestones. Commencing on the first commercial sale of licensed products, we are obligated to pay tiered royalties of low to high single-digit percentages on annual net sales of the products covered by the license. If milestone or other non-royalty obligations become due, we may not have sufficient funds available to meet our obligations, which will materially adversely affect our business operations and financial condition. If we breach our license agreement with Amgen related to EFX, we could lose the ability to continue the development and commercialization of EFX. We are dependent on patents, know-how and proprietary technology in-licensed from Amgen. Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidate or any future product candidates and use our and our licensor's proprietary technologies without infringing the proprietary rights of third parties. Amgen may have the right to terminate the license agreement in full in the event we materially breach or default in the performance of any of the obligations under the license agreement. A termination of the license agreement with Amgen could result in the loss of significant rights and could harm our ability to commercialize our product candidates. Disputes may also arise between us and Amgen, as well as any future potential 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 patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidate and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. In addition, the Amgen Agreement under which we currently license intellectual property is complex, and certain provisions may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property, or increase what we believe to be our financial or other obligations under the Amgen Agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangement on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer. We may seek to establish collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans. We may pursue collaborations in order to develop and commercialize EFX and any future product candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the

costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products and the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborators may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our product candidate or any future product candidates or bring them to market and generate product revenue.

Risks Related to Employee Matters and Growth We must attract and retain highly skilled employees in order to succeed. If we are not able to retain our current senior management team and our scientific advisors or continue to attract and retain qualified scientific, technical and business personnel, our business will suffer. To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel and we face significant competition for experienced personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. We are dependent on the members of our management team and our scientific advisors for our business success. We do not maintain “key person” insurance for any of our key personnel. An important element of our strategy is to take advantage of the research and development expertise of our current management and to utilize the expertise of our scientific advisors in the MASH field. We currently have employment agreements with all of our executive officers. Our employment agreements with our executive officers are terminable by them without notice and some provide for severance and change in control benefits. The loss of any one of our executive officers or key scientific consultants could result in a significant loss in the knowledge and experience that we, as an organization, possess and could cause significant delays, or outright failure, in the development and further commercialization of our product candidate or any future product candidates. There is intense competition for qualified personnel, including management, in the technical fields in which we operate, and we may not be able to attract and retain qualified personnel necessary for the successful research, development and commercialization of EFX or any future product candidates. In particular, we have experienced a very competitive hiring environment in the San Francisco Bay Area, where we are headquartered. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success with which we can discover and develop product candidates and our business will be limited. Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors, or collaborators that would violate the law or regulation, including, without limitation, healthcare, employment, foreign corrupt practices, environmental, competition, and patient privacy and other privacy laws and regulations. Such improper actions could subject us to civil or criminal investigations, and monetary and injunctive penalties, and could adversely impact our ability to conduct business, operating results, and reputation. We are exposed to the risk of employee fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and / or negligent conduct that fails to comply with the laws enforced by the FDA and other similar foreign regulatory bodies, fails to provide true, complete and accurate information to the FDA and other similar foreign regulatory bodies, fails to comply with manufacturing standards we have established, fails to comply with healthcare fraud and abuse laws in the United States and similar foreign laws, or fails to report financial information or data accurately or to disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the United States, our potential exposure under these laws will increase significantly, and our costs associated with compliance with these laws are also likely to increase. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. These laws may impact, among other things, our current activities with principal investigators and research patients, as well as proposed and future sales, marketing and education programs. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and

Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations. We may encounter difficulties in managing our growth, which could adversely affect our operations. As of February 23-14, 2024-2025, we had 55-63 full-time employees and one part-time employee. As we continue development and pursue the potential commercialization of EFX and other product candidates, as well as function as a public company, we will need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Our future financial performance and our ability to develop and commercialize our product candidate and to compete effectively will depend, in part, on our ability to manage any future growth effectively. We may acquire additional technology and complementary businesses in the future. Acquisitions involve many risks, any of which could materially harm our business, including the diversion of management's attention from core business concerns, failure to effectively exploit acquired technologies, failure to successfully integrate the acquired business or realize expected synergies or the loss of key employees from either our business or the acquired businesses. Risks Related to Protecting Our Intellectual Property Our success depends upon our ability to obtain and maintain intellectual property protection for our products and technologies. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection. Our success will depend in significant part on our and our current or future licensors', licensees' or collaborators' ability to establish and maintain adequate protection of our intellectual property covering the product candidates we plan to develop, and the ability to develop these product candidates and commercialize the products resulting therefrom, without infringing the intellectual property rights of others. We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use, and any other inventions that are important to the development of our business. In addition to taking other steps to protect our intellectual property, we have applied for, and intend to continue to apply for, patents with claims covering our technologies, processes and product candidates when and where we deem it appropriate to do so. Our in-licensed patents and patent applications in both United States and certain foreign jurisdictions relate to EFX and related Fc-fusion polypeptides. There can be no assurance that the claims of our patents or any patent application that issues as a patent, will exclude others from making, using or selling our product candidate or any future product candidates or products that are substantially similar to our product candidate or any future product candidates. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. In countries where we have not and do not seek patent protection, third parties may be able to manufacture and sell our product candidate or any future product candidates without our permission, and we may not be able to stop them from doing so. With respect to patent rights, we do not know whether any of the pending patent applications for our product candidate or any future product candidates will result in the issuance of patents that effectively protect our technologies, processes and product candidates, or if any of our issued patents or our current or future licensors', licensees' or collaborators' issued patents will effectively prevent others from commercializing competitive technologies, processes and products. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or in some cases not at all, until they are issued as a patent. Therefore, we cannot be certain that we or our current or future licensors, licensees or collaborators were the first to make or file on the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our current or future licensors, licensees or collaborators were the first to file for patent protection of such inventions. There is also no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which could be used by a third party to challenge the validity of our patents, should they issue, or prevent a patent from issuing from a pending patent application. Any of the foregoing could harm our competitive position, business, financial condition, results of operations, and prospects. Any changes we make to our product candidate or any future product candidates, including formulations that may be required for commercialization, or that cause them to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new applications and / or seek other forms of protection for any such altered product candidates. The patent landscape surrounding the technology underlying our product candidate or any future product candidates is crowded, and there can be no assurance that we would be able to secure patent protection that would adequately cover an alternative to our product candidate or any future product candidates. The patent prosecution process is expensive and time-consuming, and we and our current or future licensors, licensees or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current or future licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from or license to third parties and may be reliant on our current or future licensors, licensees or collaborators to perform these activities, which means that these patent applications may not be prosecuted, and these patents enforced, in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaborators fail to establish, maintain, protect or enforce such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current or future licensors, licensees or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, which in recent years have been the subject of much litigation, and, therefore, the issuance, scope, validity, enforceability, and commercial value of any patent claims that we have rights or may obtain cannot be predicted with certainty. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. Changes in either the patent laws or interpretation of the patent laws in the

United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our current or future licensors', licensees' or collaborators' pending and future patent applications may not result in patents being issued that protect our technology or product candidates, or products resulting therefrom, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our current or future licensors, licensees or collaborators to narrow the scope of the claims of pending and future patent applications, which would limit the scope of patent protection that is obtained, if any. Our and our current or future licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology that is currently claimed in such applications unless and until a patent issues from such applications, and then only to the extent the claims that issue are broad enough to cover the technology being practiced by third parties. Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after the resulting products are commercialized. As a result, our owned and in-licensed patents may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We expect to seek extensions of patent terms for our issued patents, where available. This includes in the United States under the Hatch- Waxman Act, which permits a patent term extension of up to five years beyond the original expiration date of the patent as compensation for regulatory delays. However, such a patent term extension cannot lengthen the remaining term of a patent beyond a total of 14 years from the product's approval date. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of product approval. During the period of patent term extension, the claims of a patent are not enforceable for their full scope but are instead limited to the scope of the approved product. In addition, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. In addition, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to the expiration of relevant patents or otherwise failing to satisfy applicable requirements. If this occurs, any period during which we have the right to exclusively market our product will be shorter than we would otherwise expect, and our competitors may obtain approval of and launch products earlier than might otherwise be the case. Patent terms may be inadequate to protect our competitive position on our product candidate or any future 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 U. S. non- provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. A number of U. S. patents directed to various aspects of EFX will expire in 2029; we currently anticipate that a composition of matter patent will be eligible for patent term extension to 2034. Even if patents covering our product candidate or any future product candidate are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidate or any future product candidate might expire before or shortly after we or our partners commercialize those candidates. 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. We may not be able to protect our intellectual property rights throughout the world. The legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective or effective as that in the United States and we may, therefore, be unable to acquire and enforce intellectual property rights outside the United States to the same extent as in the United States. Whether filed in the United States or abroad, our patent applications may be challenged or may fail to result in issued patents. In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing or commercializing competing products. Furthermore, others may independently develop or commercialize similar or alternative technologies or drugs, or design around our patents. Our patents may be challenged, invalidated, circumvented or narrowed, or fail to provide us with any competitive advantages. In many foreign countries, patent applications and / or issued patents, or parts thereof, must be translated into the native language. If our patent applications or issued patents are translated incorrectly, they may not adequately cover our technologies; in some countries, it may not be possible to rectify an incorrect translation, which may result in patent protection that does not adequately cover our technologies in those countries. Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States are less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and certain state laws in the United States. Consequently, we and our licensor may not be able to prevent third parties from practicing our and our licensor's inventions in all countries outside the United States, or from selling or importing products made using our and our licensor's inventions in and into the United States or other jurisdictions. For example, the complexity and uncertainty of European patent laws have increased in recent years. In Europe, the new unitary patent system that came into effect in 2023 would significantly impact European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court, or ("UPC"). As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC- based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long- term effects of any potential changes. Competitors may use our and our licensor's technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we and our licensor have patent protection,

but enforcement is not as strong as that in the United States. These products may compete with our product candidate or any future product candidates and our and our licensor's patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biotechnology. This could make it difficult for us and our licensor to stop the infringement of our and our licensor's patents or the marketing of competing products in violation of our and our licensor's proprietary rights, generally. Proceedings to enforce our and our licensor's patent rights in foreign jurisdictions could result in substantial costs and divert our and our licensor's efforts and attention from other aspects of our business, could put our and our licensor's patents at risk of being invalidated or interpreted narrowly, could place our and our licensor's patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensor. We or our licensor may not prevail in any lawsuits that we or our licensor initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. The requirements for patentability differ in certain countries, particularly developing countries. For example, China has a heightened requirement for patentability and, specifically, requires a detailed description of medical uses of a claimed drug. In addition, India, certain countries in Europe and certain developing countries, including Thailand, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensor may have limited remedies if patents are infringed or if we or our licensor are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. Accordingly, our and our licensor's efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements. Periodic maintenance and annuity fees on issued United States patents and most foreign patent applications and patents must be paid to the U. S. Patent and Trademark Office ("USPTO") and foreign patent agencies, respectively, in order to maintain such patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application, examination and issuance processes. While an inadvertent lapse can, in some 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 failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensor fail to maintain the patents and patent applications covering our product candidate or any future product candidates, our competitors might be able to enter the market with similar or identical products or technology, which would have a material adverse effect on our business, financial condition and results of operations. We may be unable to obtain intellectual property rights or technology necessary to develop and commercialize EFX or any future product candidates. Several third parties are actively researching and seeking and obtaining patent protection in the MASH field, and there are issued third-party patents and published third-party patent applications in these fields. However, we may not be aware of all third-party intellectual property rights potentially relating to our product candidate or any future product candidates and technologies. Depending on what patent claims ultimately issue and how courts construe the issued patent claims, as well as depending on the ultimate formulation and method of use of our product candidate or any future product candidates, we may need to obtain a license under such patents. There can be no assurance that such licenses will be available on commercially reasonable terms, or at all. If a third party does not offer us a necessary license or offers a license only on terms that are unattractive or unacceptable to us, we might be unable to develop and commercialize one or more of our product candidate or any future product candidates, which would have a material adverse effect on our business, financial condition and results of operations. Moreover, even if we obtain licenses to such intellectual property, but subsequently fail to meet our obligations under our license agreements, or such license agreements are terminated for any other reasons, we may lose our rights to in-licensed technologies. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several 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, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects. Our inability to protect our confidential information and trade secrets would harm our business and competitive position. In addition to seeking patents for some of our technology and products, in our activities we also rely substantially on trade secrets, including unpatented know-how, technology and other proprietary materials and information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, these steps may be inadequate, we may fail to enter into agreements with all such

parties or any of these parties may breach the agreements and disclose our proprietary information and there may be no adequate remedy available for such breach of an agreement. We cannot assure you that our proprietary information will not be disclosed or that we can meaningfully protect our trade secrets. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing, or unwilling, to protect trade secrets. If a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Risks Related to Intellectual Property Litigation We may become involved in lawsuits or other proceedings to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of our business. Third parties may infringe our or our licensor's patents or misappropriate or otherwise violate our or our licensor's intellectual property rights. In the future, we or our licensor may initiate legal proceedings to enforce or defend our or our licensor's intellectual property rights, to protect our or our licensor's trade secrets or to determine the validity or scope of intellectual property rights we own or control. Also, third parties may initiate legal proceedings against us or our licensor to challenge the validity or scope of intellectual property rights we own, control or to which we have rights. For example, generic or biosimilar drug manufacturers or other competitors or third parties may challenge the scope, validity or enforceability of our or our licensor's patents, requiring us or our licensor to engage in complex, lengthy and costly litigation or other proceedings. These proceedings can be expensive and time-consuming and many of our or our licensor's adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Moreover, the outcome following legal assertions of invalidity and unenforceability is unpredictable. Accordingly, despite our or our licensor's efforts, we or our licensor may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own, control or have rights to, particularly in countries where the laws may not protect those rights as fully as in the United States. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, if we or our licensor initiated legal proceedings against a third party to enforce a patent covering a product candidate, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. In an infringement or declaratory judgment proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our or our licensor's patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our or our licensor's patents at risk of being invalidated, narrowed, held unenforceable or interpreted in such a manner that would not preclude third parties from entering the market with competing products. Third-party pre-issuance submission of prior art to the USPTO, or opposition, derivation, revocation, reexamination, inter partes review or interference proceedings, or other pre-issuance or post-grant proceedings or other patent office proceedings or litigation in the United States or other jurisdictions provoked by third parties or brought by us or our licensor, may be necessary to determine the inventorship, priority, patentability or validity of inventions with respect to our or our licensor's patents or patent applications. An unfavorable outcome could leave our technology or product candidates without patent protection, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or could require us or our licensor to obtain license rights from the prevailing party in order to be able to manufacture or commercialize our product candidate or any future product candidates without infringing third-party patent rights. Our business could be harmed if the prevailing party does not offer us or our licensor a license on commercially reasonable terms, or at all. Even if we or our licensor obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensor. In addition, if the breadth or strength of protection provided by our or our licensor's patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or any future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and it may distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into collaborations. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, many foreign jurisdictions have rules of discovery that are different than those in the United States and which may make defending or enforcing our or our licensor's patents extremely difficult. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability to develop, manufacture, market and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Third parties may initiate legal proceedings against us or our licensor alleging that we or our licensor infringe their intellectual property rights or we or our licensor may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property

rights controlled by third parties, including in oppositions, interferences, revocations, reexaminations, inter partes review or derivation proceedings before the USPTO or its counterparts in other jurisdictions. These proceedings can be expensive and time-consuming and many of our or our licensor's adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensor can. An unfavorable outcome in any such proceeding could require us or our licensor to cease using the related technology or developing or commercializing our product candidate or any future product candidates, or to attempt to license rights to it from the prevailing party, which may not be available on commercially reasonable terms, or at all. We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidate or any future product candidates or force us to cease some of our business operations, which could materially harm our business. We perform searches of patent and scientific databases in order to identify documents that may be of potential relevance to the freedom-to-operate and/or patentability of our product candidate or any future product candidates. In general, such searches are conducted based on keywords, sequences, inventors/authors and assignees/entities to capture U. S. and European patents and patent applications, PCT publications and scientific journal articles. The patent landscape around our EFX product candidate is complex, and we may not be aware of all third-party intellectual property rights potentially relating to our product candidate or any future product candidates and technologies. Moreover, it is possible that we are or may become aware of patents or pending patent applications that we think do not relate to our product candidate or any future product candidates or that we believe are invalid or unenforceable, but that may nevertheless be interpreted to encompass our product candidate or any future product candidates and to be valid and enforceable. As to pending third-party applications, we cannot predict with any certainty which claims will issue, if any, or the scope of such issued claims. If any third-party intellectual property claims are asserted against us, even if we believe the claims are without merit, there is no assurance that a court would find in our favor, e. g., on questions of infringement, validity, enforceability or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability and the ability of our licensor to commercialize any product candidates we may develop, and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U. S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U. S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U. S. patent. If any such third-party patents (including those that may issue from such applications) were successfully asserted against us or our licensor or other commercialization partners and we were unable to successfully challenge the validity or enforceability of any such asserted patents, then we or our licensor and other commercialization partners may be prevented from commercializing our product candidate or any future product candidates, or may be required to pay significant damages, including treble damages and attorneys' fees if we are found to willfully infringe the asserted patents, or obtain a license to such patents, which may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. Any of the foregoing would have a material adverse effect on our business, financial condition and operating results. We may be subject to claims by third parties asserting that our employees or we have misappropriated a third party's intellectual property, or claiming ownership of what we regard as our own intellectual property. Many of our employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. We may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer, or that third parties have an interest in our patents as an inventor or co-inventor. Litigation may be necessary to defend against these claims. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain other damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms, or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations and prospects. Intellectual property rights do not necessarily address all potential threats. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to make products that are similar to any product candidates we may develop or utilize similar technology but that are not covered by the claims of the

patents that we license or may own in the future; • we, or our current or future collaborators, might not have been the first to make the inventions covered by the issued patents and pending patent applications that we license or may own in the future; • we, or our current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights; • it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents; • issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; • the patents of others may harm our business; and • we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property. Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects. Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or the USPTO. If we or our licensing partner initiate legal proceedings against a third party to enforce a patent covering our product candidate or any future product candidates, the defendant could counterclaim that the patent covering our product candidate, as applicable, is invalid and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include inter partes review, post grant review, and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. A loss of patent protection for our product candidates could have a material adverse impact on our ability to commercialize or license our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations. Likewise, patents directed to our proprietary technologies and our product candidates may expire before or soon after our first product achieves marketing approval in the United States or foreign jurisdictions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, financial condition, prospects and results of operations. A number of U. S. patents directed to various aspects of EFX will expire in 2029; we currently anticipate that a composition of matter patent will be eligible for patent term extension to 2034. Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidate or any future product candidates. As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves technological and legal complexity, and obtaining and enforcing biotechnology patents is costly, time-consuming and inherently uncertain. The U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances, weakening the rights of patent owners in certain situations or ruling that certain subject matter is not eligible for patent protection. In addition to increasing uncertainty with regard to our and our licensor's ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts, the USPTO and equivalent bodies in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our and our licensor's ability to obtain new patents or to enforce existing patents and patents we and our licensor may obtain in the future. Patent reform laws, such as the Leahy-Smith America Invents Act ("~~the Leahy-Smith Act~~") as well as changes in how patent laws are interpreted, could increase the uncertainties and costs surrounding the prosecution of our and our licensor's patent applications and the enforcement or defense of our or our licensor's issued patents, all of which could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Government Regulation

Risks Related to Obtaining Regulatory Approval

We have limited experience in conducting clinical trials and have never obtained approval for any product candidates, and may be unable to do so successfully. As a company, other than the completed BALANCED, study and our ongoing HARMONY and SYMMETRY studies, we have no experience in designing, conducting or completing clinical trials and have never progressed a product candidate through to regulatory approval. In part because of this lack of experience, our clinical trials may require more time and incur greater costs than we anticipate. We cannot be certain that our planned clinical trials, including the ongoing SYNCHRONY Phase 3 trials, will begin or conclude on time, if at all. Large-scale trials will require significant additional financial and management resources. Any performance failure on the part of such third parties could delay the clinical development of our product candidate or any future product candidates or delay or prevent us from obtaining regulatory approval or commercializing our current or any future product candidates, depriving us of potential product revenue and resulting in additional losses. The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. Our inability to obtain regulatory approval for EFX or any future product candidate would substantially harm our business. The time required to obtain approval from the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of nonclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may

change during the course of a product candidate's development and may vary among jurisdictions. **The FDA and comparable regulatory authorities may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials. Further, the FDA or comparable regulatory authorities may disagree with our interpretation of data from clinical trials.** EFX or our future product candidates could fail to receive regulatory approval from the FDA or a comparable foreign regulatory authority for many reasons, including: • disagreement with the design or implementation of our clinical trials; • failure to demonstrate that a product candidate is safe and effective for its proposed indication; • failure of clinical trials to meet the level of statistical significance required for approval; • failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks; • disagreement with our interpretation of data from nonclinical studies or clinical trials; • the insufficiency of data collected from clinical trials of EFX or any future product candidates to obtain regulatory approval; • failure to obtain approval of the manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies; or • changes in the approval policies or regulations that render our nonclinical and clinical data insufficient for approval. The FDA or a comparable foreign regulatory authority may require more information, including additional nonclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program for other reasons. If we were to obtain approval, regulatory authorities may approve EFX or any future product candidates for fewer or more limited indications than we request, may require labeling or a Risk Evaluation and Mitigation Strategy ("REMS") that includes significant use or distribution restrictions or safety warnings, precautions, or contraindications, 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. **The U. S. Supreme Court's June 2024 decision in Loper Bright Enterprises v. Raimondo overturned the longstanding Chevron doctrine, under which courts were to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the Loper decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action or as a result of legal challenges, 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, our business could be materially harmed. The U. S. Congress, the Trump administration, or any new administration may make substantial changes to fiscal, tax, and other federal policies that may adversely affect our business. In 2017, the U. S. Congress and the Trump administration made substantial changes to U. S. policies, which included comprehensive corporate and individual tax reform. In addition, the Trump administration called for significant changes to U. S. trade, healthcare, immigration and government regulatory policy. With the transition to the Biden administration in early 2021, changes to U. S. policy occurred and since the start of the Trump Administration in 2025, U. S. policy changes have been implemented at a rapid pace and additional changes are likely. Changes to U. S. policy implemented by the U. S. Congress, the Trump administration or any new administration have impacted and may in the future impact, among other things, the U. S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U. S. regulatory environment, inflation and other areas. Although we cannot predict the impact, if any, of these changes to our business, they could adversely affect our business. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them.** Additional time may be required to obtain regulatory approval for our product candidates because they are combination products. EFX is being developed, and future product candidates may be developed, as combination products that require coordination within the FDA and similar foreign regulatory agencies for review of their device and drug / biologic components. Medical products containing a combination of new drugs, biological products or medical devices may be regulated as "combination products" in the United States and **Europe EU**. A combination product generally is defined as a product comprised of components from two or more regulatory categories (e. g., drug / device, device / biologic, drug / biologic). Each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a new drug, biologic or device. In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of the overall product based upon a determination by the FDA of the primary mode of action of the combination product. Where approval of the drug or biologic and device is sought under a single application, there could be delays in the approval process due to the increased complexity of the review process and the lack of a well-established review process and criteria. The EMA has a parallel review process in place for combination products, the potential effects of which in terms of approval and timing could independently affect our ability to market our combination products in **Europe the EU**. While we intend to seek designations for our product candidates with the FDA and comparable other regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations. The FDA and comparable other regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. Despite these designations, there can be no assurance that we will successfully obtain these or

other designations for any of our other product candidates. In addition, while such designations could expedite the development or review process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our product candidates, there can be no assurance that we will realize their intended benefits. For example, we have received a Breakthrough Therapy designation for EFX for the treatment of MASH and we may seek a Breakthrough Therapy designation for some of our product candidates in the future. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in control regimens. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for designation. In addition, in October 2021, the FDA granted Fast Track designation for EFX for the treatment of MASH, and we may seek Fast Track Designation for some of our future product candidates. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, as we have for EFX for the treatment of MASH, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track Designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Biologics designated as breakthrough therapies or granted Fast Track designation by the FDA may also be eligible for other expedited approval programs, including accelerated approval. A product candidate may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of accelerated approval, the FDA may require that a sponsor of a product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence. Under the Food and Drug Omnibus Reform Act of 2022, ~~or ("FDORA"),~~ the FDA is permitted to require, ~~as appropriate,~~ that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. In addition, FDORA gives the FDA increased authority to withdraw accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. The FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. Accelerated approval may also be withdrawn if, among other things, a confirmatory trial required to verify the predicted clinical benefit of the product fails to verify such benefit or if such trial is not conducted with due diligence. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway, we may not be able to obtain accelerated approval and, even if we do, we may not experience a faster development, regulatory review or approval process for that product. In addition, receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to full marketing approval. We may seek priority review designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process. If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not result in expedited development and does not necessarily result in expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all. Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing EFX or any future product candidates outside the United States. We intend to market any approved products in the United States, the **EU European Union**, Japan and other foreign jurisdictions. Even if our products are approved for marketing in the United States, in order to market and sell our products in other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks

associated with obtaining FDA approval. In addition, in many countries outside the United States, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country. For example, even if EFX is approved in the United States, the EMA may require more information, including additional nonclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans in the **EU-European Union**. Moreover, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for our product candidate or any future product candidates may be withdrawn if we fail to comply with regulatory requirements, if problems occur after the product candidate reaches the market or for other reasons. If we fail to comply with the regulatory requirements in international markets and fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidate or any future product candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions. Approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. If we fail to obtain approval of our product candidate or any future product candidates by regulatory authorities in another country, we will be unable to commercialize our product in that country, and the commercial prospects of that product candidate and our business prospects could decline.

Risks Related to Ongoing Regulatory Obligations Even if we are able to obtain regulatory approvals for our product candidate or any future product candidates, if they exhibit harmful side effects after approval, our regulatory approvals could be revoked or otherwise negatively impacted, and we could be subject to costly and damaging product liability claims. Clinical trials are conducted in representative samples of the potential patient population which may have significant variability. Even if we receive regulatory approval for EFX or any of our future product candidates, we will have tested them in only a small number of patients during our clinical trials. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, may a more complete safety profile be identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. If our applications for marketing are approved and more patients begin to use our product, new risks and side effects associated with our products may be discovered. There have been other products that have been approved by the regulatory authorities but for which safety concerns have been uncovered following approval. Such safety concerns have led to labelling changes or withdrawal of products from the market, and any of our product candidates may be subject to similar risks. Additionally, we may be required to conduct additional nonclinical and clinical trials, require additional warnings on the label of our product candidate, reformulate our product or make changes, create a medication guide outlining the risks of such side effects for distribution to patients and obtain new approvals for our and our suppliers' manufacturing facilities for EFX and any future product candidates. We might have to withdraw or recall our products from the marketplace. We may also experience a significant drop in the potential sales of our product if and when regulatory approvals for such product are obtained, experience harm to our reputation in the marketplace or become subject to lawsuits, including class actions. Any of these results could decrease or prevent any sales of our approved product or substantially increase the costs and expenses of commercializing and marketing our product. Even if our current product candidate or any future product candidates receive regulatory approval, they will remain subject to extensive regulatory scrutiny and may still face future development and regulatory difficulties. Even if we obtained regulatory approval for a product candidate, regulatory authorities may still impose significant restrictions on our product candidates, including their indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies. For example, if EFX is approved by the FDA based on a surrogate endpoint pursuant to accelerated approval regulations (also referred to as Subpart E regulations), we will be required to conduct additional confirmatory clinical trials demonstrating the clinical benefit on the ultimate outcome of MASH. Further, even if we obtained regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of our product candidate or any future product candidates, they may require labeling changes or establishment of a risk evaluation and mitigation strategy or similar strategy, impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. In addition, manufacturers of our products, if approved, and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP and applicable QSRs, regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency 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. If we, EFX, or any future product candidates or the manufacturing facilities for EFX, the delivery device used for EFX, or any future product candidates fail to comply with applicable regulatory requirements, or undesirable side effects caused by such products are identified, a regulatory agency may:

- issue safety alerts, Dear

Healthcare Provider letters, press releases or other communications containing warnings about such product; • mandate modifications to instructions for use; • mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners; • require that we conduct post- marketing studies; • require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance; • seek an injunction or impose civil or criminal penalties or monetary fines; • suspend marketing of, withdraw regulatory approval of or recall such product; • suspend any ongoing clinical trials; • refuse to approve pending applications or supplements to applications filed by us; • suspend or impose restrictions on operations, including costly new manufacturing requirements; or • seize or detain products, refuse to permit the import or export of products or require us to initiate a product recall. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product and generate revenue. Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, the Department of Health and Human Services’ (“HHS”) Office of Inspector General, state attorneys general, members of Congress and the public. Violations, including promotion of our products for unapproved (or off- label) uses, are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the government. Additionally, comparable foreign regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval outside of the United States. In the United States, engaging in the impermissible promotion of our products for off- label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these federal False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements regarding certain sales practices promoting off- label drug uses involving fines in excess of \$ 1 billion. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations and be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations. The FDA’s policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidate or any future product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability. Risks Related to Healthcare Regulation The advancement of healthcare reform may negatively impact our ability to profitably sell our product candidate or any future product candidates, if approved. The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidate or any future product candidates, restrict or regulate post- approval activities and affect our ability to profitably sell any product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record- keeping requirements. **For more information on healthcare laws and regulations that may impact our company, see the section titled “Business — Government regulation — Healthcare reform ” included in this annual report on Form 10- K.** In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (, or collectively, the “Affordable Care Act ” or “ACA ”), was enacted, which includes measures that have significantly changed the way health care is financed by both governmental and private insurers. Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court’s decision, President Biden issued an Executive Order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the ~~Biden~~ **Trump** ~~administrations-~~ **Administration** or other efforts, if any, to challenge repeal or replace the ACA, will impact our business. In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. The U. S. Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation’s automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, 2 % per fiscal year through 2031 unless Congress takes additional action. ~~Due to the Statutory Pay- As- You- Go Act of 2010, estimated budget deficit increases resulting from the American Rescure Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation.~~ The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period

for the government to recover overpayments to providers from three to five years. **The Centers for Medicare & Medicaid Services (“CMS”)** has published a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U. S. congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. In addition, **at a federal level, President Trump reversed some of President Biden’s** ~~has issued multiple executive orders that have sought to reduce~~ **including rescinding Executive Order 14087 entitled “Lowering Prescription Drug Costs for Americans”**. **President Trump may** ~~In February 2023, HHS also issued~~ **issue new** ~~a proposal in response to an October 2022 executive order orders designed to impact~~ **issued by President Biden that includes a proposed prescription drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through FDA’s accelerated approval pathway.** ~~A~~ **Although a** ~~number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden Administration may reverse or otherwise change these measures, both the Biden Administration and the U. S. Congress~~ **and the Trump administration** ~~have indicated that they will continue to seek new legislative measures to control drug costs. In August 2022, the Inflation Reduction Act of 2022 (the “IRA”) was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries from \$ 7, 050 to \$ 2, 000 starting in 2025, thereby effectively eliminating the coverage gap, allow the U. S. government to negotiate Medicare Part B and Part D pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay until January 1, 2032 the implementation of the HHS rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, if they have one rare disease designation and the only approved indication is for that rare disease. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA’s Medicare drug price negotiation program. The effect of IRA on our business and the healthcare industry in general is not yet known. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and / or impose price controls may adversely affect:~~

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability. ~~Although a number of these, and other proposed measures may require additional authorization to become effective, and the Biden- Trump administration~~ **Administration** ~~may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative and / or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party payors. There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates. Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings. Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, and if approved, market, sell and distribute our products. Restrictions under applicable federal and state healthcare laws and regulations, include the following:~~

- the federal Anti-Kickback Statute prohibits persons from, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for the furnishing or arranging for the furnishing, or the purchase, lease or order, or arranging for or recommending purchase, lease or order, of any good or service for which payment may be made under a federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-

Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act; • federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions, prohibit individuals or entities from, among other things knowingly presenting, or causing to be presented, to the federal government or a government contractor, grantee, or other recipient of federal funds, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “ cause ” the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a “ whistleblower ” to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery; • the federal Health Insurance Portability and Accountability Act of 1996 (“ HIPAA ”) imposes criminal liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense or knowingly and willfully making false statements relating to healthcare matters; similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation; • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“ HITECH ”) and their implementing regulations, including the Final Omnibus Rule published in January 2013, imposes obligations on certain healthcare providers, health plans and healthcare clearinghouses, known as covered entities, as well as their business associates, which are individuals and entities that perform certain services involving the creation, maintenance, receipt, use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non- U. S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; • federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and / or discounts on approved products; • federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; • the federal Open Payments program, created under Section 6002 of the Affordable Care Act and its implementing regulations, requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’ s Health Insurance Program (with certain exceptions) to report annually to CMS information related to “ payments or other transfers of value ” made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians (as defined above) and their immediate family members. As of January 1, 2022, these reporting obligations have now extended to include transfers of value made to certain non- physician providers such as physician assistants and nurse practitioners; and • analogous state, local, and foreign laws and regulations, such as state anti- kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third- party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry’ s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug prices; state and local laws that require the registration of pharmaceutical sales representatives; several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales representatives. State and foreign laws, including for example the EU General Data Protection Regulation, which became effective May 2018 also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and state and foreign laws that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions,

including exclusions from government funded healthcare programs. Failure to comply with health and, data protection, and national security laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and / or adverse publicity and could negatively affect our operating results and business. We and any potential collaborators may be subject to federal, state, and foreign data protection and national security laws and regulations (i. e., laws and regulations that address privacy and, data security, and national security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e. g., Section 5 of the Federal Trade Commission Act) and the CCPA, that govern the collection, use, disclosure and protection of health- related and other personal information could apply to our operations or the operations of our collaborators. The CCPA and similar consumer has been characterized as the first “GDPR- like” privacy laws statute to be enacted in the other United States states provide because it mirrors a number of the key provisions of the GDPR (discussed below in the European Data Collection subsection). Specifically, the act established a comprehensive privacy framework for covered businesses by creating an expanded a broad definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA, as amended by HITECH. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA and other state consumer privacy laws may impact some of our business activities. Further, the CCPA was amended by the California Privacy Rights Act (" CPRA") which entered into force on January 1, 2023. The amendments introduced by the CPRA create additional obligations with respect to processing and storing personal information. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the U. S., which could increase our potential liability and adversely affect our business. Already, in the United States are continuing to , we have witnessed significant developments at the state level with numerous other states passing comprehensive privacy laws that incorporate many similar concepts of the CCPA. A number of other states have proposed- propose new privacy laws, some of which are similar to the above discussed recently passed laws and other proposals differ dramatically. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and / or changes in business practices and policies. There are also states that are specifically regulating health information. For example, Washington state recently passed a 's WA MHMDA applies robust protections similar to, or more stringent than, the requirements of the CCPA, for the collection, use, and disclosure of consumer health data. The WA MHMDA provides privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and / or passed legislation that regulates the privacy and / or security of certain specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically. These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there is discussion in the U. S. Congress of a new comprehensive federal data privacy law to which we may likely become subject, if enacted. In addition, the federal government has begun to regulate certain disclosures of personal information under national security and trade regulation frameworks. For example, Executive Order 14117 on Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government- Related Data by Countries of Concern, as implemented by Department of Justice regulations issued in December 2024, prohibits certain transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict investment agreements, employment agreements and vendor agreements involving such data and countries of concern. Actual or alleged violations of these regulations may be punishable by criminal and / or civil sanctions, and may result in exclusion from participation in federal and state programs. Compliance with U. S. and international data protection laws and regulations, including the General Data Protection Regulation (" GDPR ") and other European Economic Area (" EEA ") and United Kingdom (" UK ") data protection laws could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and / or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time- consuming to defend and could result in adverse publicity that could harm our business. Where we collect and otherwise process personal data regarding Europe, including in the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data, including personal health data regarding (i) individuals in the European Economic Area (" EEA ") and United Kingdom (" UK ") and / or (ii) carried out in the context of the activities of an establishment in the EEA and UK, is subject to the EU General Data Protection Regulation (" EU GDPR "), and similarly, processing of personal data regarding individuals in the UK is subject to the GDPR, as well as other supplementary national data

protection legislation in force in the EEA member states and the UK (including the UK Data Protection Act 2018). The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements related to having a legal basis for processing personal data, stricter requirements related to processing of sensitive data (including health data), obtaining consent of the individuals to whom the personal data relates or ensuring another appropriate legal basis or condition applies to the processing of personal data, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, requiring data protection impact assessments for high risk processing and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA / UK, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to € 20 million (£ 17.5 million under UK GDPR) or 4 % of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers of personal data to countries outside the EEA / UK that are not considered by the European Commission and UK government as providing “adequate” protection to personal data (“third countries”), including the United States. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. To enable the transfer of personal data outside of the EEA or the UK, adequate safeguards (for example, the European Commission approved Standard Contractual Clauses (“SCCs”) must be implemented in compliance with European and UK data protection laws. In addition, transfers made pursuant to the SCCs (and other similar appropriate transfer safeguards) need to be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular regarding applicable surveillance laws and relevant rights of individuals with respect to the transferred personal data, to ensure an “essentially equivalent” level of protection to that guaranteed in the EEA in the jurisdiction where the data imported is based (“Transfer Impact Assessment”). On June 4, 2021, the EC issued new forms of standard contractual clauses for data transfers from controllers or processors in the EU / EEA (or otherwise subject to the GDPR) to controllers or processors established outside the EU / EEA. The UK is not subject to the EC’s standard contractual clauses but has published its own transfer mechanism, the International Data Transfer Agreement and International Data Transfer Addendum (“IDTA”), which will enable transfers from the UK, and has also implemented a similar Transfer Impact Assessment requirement. Further, the EU European Union and United States have adopted its adequacy decision for the EU- U. S. Data Privacy Framework (“Framework”), which entered into force on July 11, 2023. This Framework provides that the protection of personal data transferred between the EU European Union and the United States is comparable to that offered in the EU European Union. This provides a further avenue to ensuring transfers to the United States are carried out in line with GDPR. There has been an extension to the Framework to cover UK transfers to the United States. The Framework could be challenged like its predecessor frameworks. We will be required to implement these new safeguards and carry out Transfer Impact Assessments when conducting restricted data transfers under the GDPR and doing so will require significant effort and cost, and may result in us needing to make strategic considerations around where EEA or UK personal data is stored and transferred, and which service providers we can utilize for the processing of EEA / UK personal data. Although the UK is regarded as a third country under the EU GDPR, the European Commission has issued a decision recognizing the UK as providing adequate protection under the EU GDPR (“Adequacy Decision”) and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK Government has also now introduced a Data Protection and Digital Information Bill (“UK Bill”) into the UK legislative process which will introduce changes to the UK GDPR. This may lead to additional compliance costs and could increase our overall risk. The lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of European personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the EEA. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. In addition, EEA Member States have adopted national laws to implement the EU GDPR that may partially deviate from the EU GDPR and competent authorities in the EEA Member States may interpret the EU GDPR obligations slightly differently from country to country. Therefore, we do not expect to operate in a uniform legal landscape in the EEA. Compliance with the above and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, reputation, financial condition and results of operations. Artificial intelligence presents risks and challenges that can impact our business, including by posing security risks to our confidential information, proprietary information and personal data. Issues in the development and use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability, or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. We may adopt and integrate generative artificial intelligence tools into our systems for specific use cases reviewed by legal and information security. **A growing number of legislators and regulators are adopting laws and regulations and have focused enforcement efforts on the adoption of artificial intelligence, and use of such technologies in compliance with ethical standards and societal expectations. For example, the EU’s Artificial Intelligence Act (“AI Act**

) imposes significant obligations on providers and deployers of artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. Likewise, in the U. S., several states, including Colorado and California, passed laws to regulate various uses of artificial intelligence, including to make consequential decisions. In addition, various federal regulators have issued guidance and focused enforcement efforts on the use of artificial intelligence in regulated sectors. The FDA, for example, issued guidance on the use of artificial intelligence in medical devices, requiring detailed risk management and review processes to obtain approvals. If we develop or use artificial intelligence systems governed by these laws or regulations, we will need to apply significant resources to design, develop, test and maintain such systems in accordance with applicable law and regulation, with the potential for significant enforcement or litigation in the event of any perceived non-compliance. Our vendors may **also** incorporate generative artificial intelligence tools into their offerings ~~without disclosing this use to us,~~ and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If we, our vendors, or our third- party partners experience an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information, and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business. Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any. In some countries, particularly the countries of the **EU-European Union**, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. 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. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our drug candidate to other available procedures. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially. Healthcare insurance coverage and reimbursement may be limited or unavailable for our product candidate, if approved, which could make it difficult for us to sell our product candidate or other therapies profitably. The success of our product candidate, if approved, depends on the availability of coverage and adequate reimbursement from third- party payors including governmental healthcare programs, such as Medicare and Medicaid, commercial payors, and health maintenance organizations. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop. **For more information on healthcare laws and regulations that may impact our company, see the section titled "Business — Government regulation — Coverage, pricing, and reimbursement" included in this annual report on Form 10- K.** Patients who are provided medical treatment for their conditions generally rely on third- party payors to reimburse all or part of the costs associated with their treatment. Coverage and adequate reimbursement from third- party payors are critical to new product acceptance. Third- party payors decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third- party payor may depend upon a number of factors, including the third- party payor's determination that use of a product is: • a covered benefit under its health plan; • safe, effective and medically necessary; • appropriate for the specific patient; • cost- effective; and • neither experimental nor investigational. In the United States, no uniform policy of coverage and reimbursement for products exists among third- party payors. As a result, obtaining coverage and reimbursement approval of a product from a third- party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost effectiveness data for the use of our products on a payor- by- payor basis, with no assurance that coverage and adequate reimbursement will be obtained. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by CMS, an agency within HHS, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private third- party payors tend to follow Medicare coverage and reimbursement limitations to a substantial degree, but also have their own methods and approval process apart from Medicare determinations. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co- payments that patients find unacceptably high. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price ("**ASP**") and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. Our activities in the United States subject us to various laws relating to foreign investment and the export of certain technologies, and our failure to comply with these laws or adequately monitor the compliance of our suppliers and others we do business with could subject us to substantial fines, penalties and even injunctions, the imposition of which on us could have a material adverse effect on the success of our business. Because we have substantial operations in the

United States, we are subject to U. S. laws that regulate foreign investments in U. S. businesses and access by foreign persons to technology developed and produced in the United States. These laws include Section 721 of the Defense Production Act of 1950, as amended by the Foreign Investment Risk Review Modernization Act of 2018, and the regulations at 31 C. F. R. Parts 800 and 801, as amended, administered by the Committee on Foreign Investment in the United States; and the Export Control Reform Act of 2018, which is being implemented in part through Commerce Department rulemakings to impose new export control restrictions on “ emerging and foundational technologies ” yet to be fully identified. Application of these laws, including as they are implemented through regulations being developed, may negatively impact our business in various ways, including by restricting our access to capital and markets; limiting the collaborations we may pursue; regulating the export our products, services, and technology from the United States and abroad; increasing our costs and the time necessary to obtain required authorizations and to ensure compliance; and threatening monetary fines and other penalties if we do not. 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. Compliance with these legal standards could impair our ability to compete in domestic and international markets. 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, (“FCPA”), the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act, the USA PATRIOT 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 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. Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies’ operations, could hinder their ability to hire and retain key **personnel, and substantial changes in leadership, and other personnel, and policy could** prevent new or existing product candidates from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, **including substantial leadership, personnel, and policy changes,** may also slow the time necessary for new drug candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns **or substantial leadership, personnel, and policy changes** could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. Risks Related to Our Financial Condition and Need for Additional Capital We have incurred significant losses since our inception and we expect to incur losses for the foreseeable future. We have no products approved for commercial sale and have not generated any revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred significant losses in each period since our inception in January 2017. For the years ended December 31, **2024, 2023, and 2022 and 2021**, we reported net losses of \$ **252.1 million, \$ 151.8 million, and \$ 112.0 million and \$ 100.8 million**, respectively. As of December 31, **2023-2024**, we had an accumulated deficit of \$ **574.826.12** million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidate. We anticipate that our expenses will increase substantially if, and as, we: • **conduct continue larger- large-** scale clinical trials for our product candidate, EFX, and any future product candidates; • discover and develop new product candidates, and conduct nonclinical studies and clinical trials; • incur any disruption or delays to the supply of our product candidate; • manufacture, or have manufactured, clinical and commercial supplies of our product candidates; • seek regulatory approvals for EFX or any future product candidates; • commercialize EFX or any future product candidates, if approved; • attempt to transition from a company with a development focus to a company capable of supporting commercial activities, including establishing sales, marketing and distribution infrastructure; • hire additional clinical, scientific, and management personnel; • add operational, financial, and management information systems and personnel; • identify additional compounds or product candidates and acquire rights from third parties to those compounds or product candidates through licenses; and • incur additional costs associated with operating as a public company. Even if we succeed in commercializing EFX or any future product candidates, we may continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our

business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. We currently have a limited operating history, have not generated any revenue to date, and may never become profitable. We are a clinical- stage biotechnology company with a limited operating history. Our operations to date have been limited to organizing and staffing our company, acquiring, developing and securing our technology and product candidate, EFX, and conducting nonclinical studies and clinical trials of EFX. We have not yet demonstrated our ability to complete late- stage clinical trials, obtain regulatory approval, formulate and manufacture a commercial- scale product, or conduct sales and marketing activities necessary for successful product commercialization. Investment in biotechnology product development is highly speculative because it entails substantial upfront expenditures in clinical research organizations and contract manufacturing organizations and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. Consequently, any predictions you may make about our future success or viability may not be as accurate as they could be if we had a longer operating history. Though Phase 3 clinical development of EFX has been initiated, we do not expect to receive revenue from EFX for a number of years, if ever. To date, we have not generated any revenue and we will not be able to generate product revenue unless and until EFX, or any future product candidate, successfully completes clinical trials, receives regulatory approval, and is commercialized. We may seek to obtain revenue from collaboration or licensing agreements with third parties. Our ability to generate future product revenue from EFX or any future product candidates also depends on a number of additional factors, including our, or our current and future contractors' and collaborators', ability to:

- successfully complete nonclinical studies and clinical trials for EFX and any future product candidates;
- seek and obtain marketing approvals for any product candidates that complete clinical development;
- establish and maintain supply and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of bulk drug substances and drug products to maintain that supply;
- launch and commercialize any product candidates for which we obtain marketing approval, and, if launched independently, successfully establish a sales, marketing and distribution infrastructure;
- demonstrate the necessary safety data post- approval to ensure continued regulatory approval;
- obtain coverage and adequate product reimbursement from third- party payors, including government payors;
- achieve market acceptance for any approved products;
- address any competing technological and market developments;
- maintain our rights under our existing license agreement with Amgen and any similar agreements we may enter into in the future;
- negotiate favorable terms in any collaboration, licensing or other arrangements into which we may enter in the future and performing our obligations in such collaborations;
- establish, maintain, protect and enforce our intellectual property rights; and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with biotechnology product development, including that our product candidate may not advance through development or achieve the endpoints of applicable clinical trials, we are unable to predict the timing or amount of increased expenses, or if or when we will achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide, or are required by the FDA or foreign regulatory authorities, to perform nonclinical studies or clinical trials in addition to those that we currently anticipate. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing any approved product. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment. We will require additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of our product candidate or develop any future product candidates. As a research and development company, our operations have consumed substantial amounts of cash since inception. We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance EFX into later- stage clinical development. As of December 31, ~~2023~~ **2024**, we had \$ ~~569,797~~ **3.8** million of cash, cash equivalents ~~;~~ **and** short- term and long- term marketable securities. We raised gross proceeds of \$ 105. 8 million from our initial public offering in June 2019 and \$ 216. 4 million from a follow- on public offering in July 2020. We also raised gross proceeds of \$ 25. 0 million from Pfizer through a registered direct common stock offering and borrowed \$ 10. 0 million from Hercules under a term loan in June 2022. In September 2022, we raised gross proceeds of \$ 230. 0 million from a follow- on public offering. In March 2023, we borrowed \$ 15. 0 million from Hercules under our term loan facility. In April and May 2023, we raised gross proceeds of \$ 127. 4 million from sales of common stock under an ATM offering and gross proceeds of \$ 220. 0 million from sales of common stock through an underwritten registered direct offering. **In February 2024, we raised gross proceeds of \$ 10. 9 million from sales of common stock under an ATM offering and borrowed \$ 10. 0 million from Hercules under our term loan facility. In March 2024, we raised gross proceeds of \$ 366. 9 million from a follow- on public offering. We raised gross proceeds of \$ 69. 4 million from the sales of common shares under an ATM offering during November and December of 2024, and an additional \$ 10. 6 million under the same offering during January of 2025. In January 2025, we raised gross proceeds of \$ 402. 5 million from a follow- on public offering of our common stock and, in lieu of common stock to certain investors, pre- funded warrants to purchase shares of our common stock.** Any forecast of the period of time through which our financial resources will adequately support our operations is a forward- looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "**Risk Factors**" section. The assumptions underlying any estimate may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both short and long- term, will depend on many factors, including, but not limited to:

- the initiation, progress, timing, costs and results of nonclinical studies and clinical trials for our product candidate or any future product candidates we may develop;
- the cost and timing of manufacturing our product

candidate for use in clinical trials or, if approved by the FDA, for commercial use; • our ability to maintain our license to EFX from Amgen; • the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more nonclinical studies or clinical trials than those that we currently expect or change their requirements on studies that had previously been agreed to; • the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights; • the effect of competing technological and market developments; • market acceptance of any approved product candidates, including product pricing, as well as product coverage and the adequacy of reimbursement by third- party payors; • the cost of acquiring, licensing or investing in additional businesses, products, product candidates and technologies; • the cost and timing of selecting, auditing and potentially validating a manufacturing site for commercial scale manufacturing; • the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval and that we determine to commercialize; and • our need to implement additional internal systems and infrastructure, including financial and reporting systems. We do not have any committed external source of funds or other support for our development efforts and we cannot be certain that additional funding will be available on acceptable terms, or at all. Until we can generate sufficient revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and other marketing or distribution arrangements. If we raise additional funds through public or private equity offerings, the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Further, to the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, your ownership interest will be diluted. If we raise additional capital through debt financing, we could be subject to fixed payment obligations and may be subject to 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 capital through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. We also could be required to seek collaborators for one or more of our current or any future product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our products or product candidates or one or more of our other research and development initiatives. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Risks Related to Our Indebtedness Our operating activities may be restricted as a result of covenants related to our term loan obligation, which we may be required to repay in an event of default, which could have a materially adverse effect on our business. On June 15, 2022, we entered into a Loan and Security Agreement (the "Loan Agreement") with Hercules Capital, Inc. (the "Hercules"), for an aggregate principal amount of up to \$100.0 million (the "Term Loan"). Until we have repaid such indebtedness, the Loan Agreement subjects us to various customary covenants, including requirements as to financial reporting and insurance, and restrictions on our ability to dispose of our business or property, to change our line of business, to liquidate or dissolve, to merge or consolidate with any other entity or to acquire all or substantially all the capital stock or property of another entity, to incur additional indebtedness, to incur liens on our property, to pay any dividends or other distributions on capital stock other than dividends payable solely in capital stock, to redeem capital stock, to enter into licensing agreements, to engage in transactions with affiliates, or to encumber our intellectual property. ~~Additionally, there is a financial covenant requiring us to maintain a minimum cash balance in relation to the outstanding principal balance of the Term Loan.~~ Our business may be adversely affected by these restrictions on our ability to operate our business. Additionally, we may be required to repay the outstanding indebtedness under the Term Loan if an event of default occurs under the Loan Agreement. Under the Loan Agreement, an event of default will occur if, among other things: we fail to make payments under the Loan Agreement; we breach any of our covenants under the Loan Agreement, subject to specified cure periods with respect to certain breaches; the Lender determines that a material adverse change has occurred; we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings; we are unable to pay our debts as they become due; or we default on contracts with third parties which would permit the holder of indebtedness to accelerate the maturity of such indebtedness or that could have a material adverse change on us. As a result of the occurrence of an event of default, Hercules could accelerate all of the amounts due. In the event of an acceleration of amounts due under the Term Loan, we may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time any such event of default occurs. In this case, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events. Our level of indebtedness and debt service obligations could adversely affect our financial condition and may make it more difficult for us to fund our operations. The Term Loan with Hercules provides up to \$100.0 million of debt financing and has interest- only payments through July 1, 2024, which may be extended based on achievement of certain milestones, until January 1, 2026. Thereafter, we are obligated to make payments that will include installments of principal and interest through the maturity date of January 1, 2027. This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have important negative consequences, including the fact that: • we will need to repay our indebtedness by making payments of

interest and principal, which will reduce the amount of money available to finance our operations, our research and development efforts and other general corporate activities; and • our failure to comply with the restrictive covenants in the Term Loan could result in an event of default that, if not cured or waived, would accelerate our obligation to repay this indebtedness, and Hercules could seek to enforce our security interest in the assets securing such indebtedness.

Risks Related to Commercialization and Market Acceptance Even if we commercialize EFX or any future product candidates, if approved, these products may become subject to unfavorable pricing regulations, third- party reimbursement practices or healthcare reform initiatives, which could harm our business. The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay or limit our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenue we generate from the sale of the product in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidate or any future product candidates obtain marketing approval. Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third- party payors such as government health administration authorities, private health insurers and other organizations. Third- party payors determine which medications they will cover and establish reimbursement levels. Third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval, if any. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which marketing approval is obtained, if any. There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third- party payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize future product candidates, and our ability to generate revenue will be materially impaired. We could be adversely affected by several significant administrative law cases decided by the U. S. Supreme Court in 2024. In *Loper Bright Enterprises v. Raimondo*, for example, the court overruled *Chevron U. S. A., Inc. v. Natural Resources Defense Council, Inc.*, which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U. S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act (APA). Additionally, in *Corner Post, Inc. v. Board of Governors of the Federal Reserve System*, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, *Securities and Exchange Commission v. Jarkesy*, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations. Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA's approval of another company's drug product. In April 2023, the U. S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product originally approved in 2000 whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti-abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district

court in Texas challenging FDA's actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation. Finally, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and could materially adversely impact our business and prospects.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop. We face an inherent risk of product liability exposure related to the testing of our product candidate or any future product candidates in human clinical trials and will face an even greater risk if we commercialize any resulting products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, their family members, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidate or any future product candidates or products that we may develop caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidates or products that we may develop; • termination of clinical trial sites or entire trial programs; • injury to our reputation and significant negative media attention; • withdrawal of clinical trial participants; • significant costs to defend the related litigation; • substantial monetary awards to trial subjects or patients; • loss of revenue; • diversion of management and scientific resources from our business operations; • the inability to commercialize any products that we may develop; and • a decline in our stock price. Our clinical trial liability insurance coverage may not adequately cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Our inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or delay the commercialization of any products or product candidates that we develop. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our product candidate or any future product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in lawsuits based on drugs that had unanticipated side effects. If we are sued for any injury caused by our products, product candidates or processes, our liability could exceed our product liability insurance coverage and our total assets. Claims against us, regardless of their merit or potential outcome, may also generate negative publicity or hurt our ability to obtain physician adoption of our product or expand our business. Risks Related to Market Acceptance If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved. We do not currently have an infrastructure for the sales, marketing, and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory body, we must build our sales, marketing, managerial, and other non-technical capabilities, or make arrangements with third parties to perform these services. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel. If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively and they could expose our company to regulatory enforcement and legal risk in the execution of their sales and commercialization activities. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved. If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition, and prospects will be materially adversely affected. Our product candidate or any future product candidates may not achieve adequate market acceptance among physicians, patients, third-party payors and others in the medical community necessary for commercial success. Even if our product candidate or any future product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, third-party payors, pharmaceutical companies and others in the medical community. Demonstrating the safety and efficacy of our product candidate or any future product candidates and obtaining regulatory approvals will not guarantee future revenue. Our commercial success also depends on coverage and adequate reimbursement of our product candidate or any future product candidates by third-party payors, including government payors and private insurers, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our products. Third-party payors closely examine medical products to determine whether they should be covered by reimbursement and, if so, the level of reimbursement that will apply. We cannot be certain that third-party payors will sufficiently reimburse sales of our product or enable us to sell our product at a profitable price. Similar concerns could also limit the reimbursement amounts

that health insurers or government agencies in other countries are prepared to pay for our products. In many regions, including Europe, Japan and Canada, where we may market our products, the pricing of prescription drugs is controlled by the government or regulatory agencies. Regulatory agencies in these countries could determine that the pricing for our products should be based on prices of other commercially available drugs for the same disease, rather than allowing us to market our products at a premium as new drugs. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile of the product candidate as demonstrated in clinical trials;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which the product candidate is approved;
- acceptance of the product candidate as a safe and effective treatment by clinics and patients;
- the potential and perceived advantages of the product candidate over alternative treatments, including any similar generic treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement and pricing by third- party payors;
- the relative convenience and ease of administration;
- the frequency and severity of adverse events;
- the effectiveness of sales and marketing efforts; and
- unfavorable publicity relating to our product candidate or any future product candidates.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost effective as compared with competing treatments. If any 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.

Risks Related to Our Operations We incur significant costs and expend significant time and effort, as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices. We incur significant legal, accounting and other expenses, and expend significant time and effort by management and other personnel, to comply with the rules applicable to us as a public company. We are subject to the reporting requirements of Nasdaq and of the ~~Securities Exchange Act of 1934, as amended~~, which require, among other things, that we file with the ~~Securities and Exchange Commission (SEC)~~, annual, quarterly, and current reports with respect to our business and financial condition and that we establish and maintain effective disclosure controls, procedures and corporate governance practices. We must also comply with the Sarbanes- Oxley Act of 2002 (the "Sarbanes- Oxley Act"), and specifically Section 404 of the Sarbanes- Oxley Act, which requires that we establish and maintain effective internal controls over financial reporting. In order to maintain compliance with the SEC's rules that implement Section 404 of the Sarbanes- Oxley Act, we are required to make a formal assessment of the effectiveness of our internal control over financial reporting, to certify financial and other information in our quarterly and annual reports and to provide an annual management report on the effectiveness of our internal control over financial reporting, which includes the disclosure of any material weaknesses and associated remediation activities. Also, as a large accelerated filer, we incur additional significant costs to meet the requirement to provide an attestation report on our internal control over financial reporting from our independent registered public accounting firm. We will need to continue to dedicate significant internal resources and outside consultants in order to complete management's annual assessment and to prepare for when we are no longer a smaller reporting company. Despite these efforts, there is no guarantee that we will be able to conclude that our internal controls over financial reporting remain effective. Further, in July 2010, the Dodd- Frank Wall Street Reform and Consumer Protection Act (the "Dodd- Frank Act") was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd- Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as "say on pay" and proxy access. 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 the manner in which we operate our business in ways we cannot currently anticipate. We expect the rules and regulations applicable to public companies, and the additional compliance requirements that we will be subject to when we are no longer a smaller reporting company, to substantially increase our legal and financial compliance costs and to make some activities more time- consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition, and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain key financial or management personnel. If we fail to maintain an effective system of internal controls over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock. Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is 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 control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could harm our business and

have a negative effect on the trading price of our stock. If material weaknesses or significant deficiencies in our internal control over financial reporting are identified in the future, we may not detect or remediate errors on a timely basis and our consolidated financial statements may be materially misstated. We, or our independent registered public accounting firm, may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from ~~NASDAQ~~ Nasdaq or other adverse consequences that would materially harm our business. **If our information technology systems or those of third parties upon which we rely, or our data, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm and other adverse consequences. We, like other organizations in our industry, have experienced and expect to continue to experience cyber threats and incidents. We and the third parties upon which we rely are subject to a variety of evolving threats, including but not limited to social- engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial- of- service attacks, credential stuffing attacks, credential harvesting, personnel misconduct or error, ransomware attacks, supply- chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, attacks enhanced or facilitated by AI, and other similar threats. These threats are growing in complexity and frequency, making them increasingly difficult to detect and address, potentially leading to data loss, operational interruptions, reputational harm, and financial losses. Our business and operations depend heavily on third party service providers for critical functions, including cloud- based infrastructure, data centers, encryption and authentication technologies, employee email, clinical research and development, manufacturing, and other functions. We have limited control over these providers' security practices, and they may not have adequate information security measures in place. Consequently, a security incident affecting our providers could severely impact our operations and reputation. While we may be entitled to damages if our third- party service providers fail to satisfy their data 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 or deficiencies have increased in our or related frequency and severity, and we cannot guarantee that third parties' cyber infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. Security - Given incidents could result in unauthorized access to sensitive information, data loss or limited corruption, operating operational history disruptions, we are still in the process of and increased costs and efforts to recover data. They may also lead to regulatory fines and legal liabilities. Despite our implementing implementation of our internal security measures, no system is entirely secure. We cannot guarantee that our efforts will detect all vulnerabilities or prevent all incidents. Our internal computer preventative measures include monitoring and updating security protocols. The potential financial impact of these incidents, including increased costs and potential legal liabilities, is a significant concern. For example, the loss of clinical trial data from completed or future clinical trials could have significant implications. It could lead to delays in regulatory approval efforts, necessitating costly remediation measures such as liability for stolen assets or information, repairs to damaged systems, and those of current and future incentives to maintain relationships with business partners post- attack. Moreover, investigation costs may arise, including expenses related to notifying data subjects, regulators, or others, as well as engaging third parties - party forensic investigators and experts. This could further entail increased expenditures on which we rely may fail cybersecurity protections, such as organizational changes, additional personnel, advanced technologies, employee training, and are vulnerable to consultations with external experts. Additionally, higher insurance premiums might be incurred, while reputational damage from computer viruses could undermine customer and investor confidence unauthorized access. Geopolitical instability, including Russia impacting the company 's invasion of Ukraine may increase cyber competitiveness, stock price, and long - attacks term shareholder value. Additionally- Lastly, cyberattacks there could be substantial costs associated with recovering or reproducing the lost data. Certain data privacy and security obligations may require us to notify relevant stakeholders, include including industrial espionage affected individuals, wire fraud customers, regulators, and investors, of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences, such as government enforcement actions (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; diversion of management attention; interruptions in our operations (including availability of data); financial loss; and other forms similar harms. Our contracts may not contain limitations of liability cyber fraud- and even where they do deployment of harmful malware, including ransomware, denial- of- service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, our- or efforts will prevent information claims related to our data privacy and security obligations breaches that would result in business, legal, financial, or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Our insurance policies information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A**

successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. We may not be able **adequate** to anticipate all types of **compensate us for the potential losses arising from any such disruption, failure, or security threats breach. In addition**, and we **such insurance** may not be able **available** to implement preventive measures effective **us in the future on economically reasonable terms or at all. Further, our insurance may not cover all claims made** against us all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and **could** can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. While we have **high deductibles in** not, to our knowledge, experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, **and defending a suit, regardless of its merit** could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in the following, which could be **costly** material: • delays in our regulatory approval efforts; • remediation costs, such as liability for stolen assets or information, repairs of system damage, and incentives to business partners in an **and divert management attention** effort to maintain relationships after an attack; • investigation costs, including costs associated with potential notification of the attack to data subjects, regulators or others and costs to engage third party forensic investigators and other experts; • increased cybersecurity protection costs, which may include the costs of making organizational changes, deploying additional personnel and protection technologies, training employees, and engaging third party experts and consultants; • increased insurance premiums; • reputational damage that adversely affects customer or investor confidence; • damage to the company's competitiveness, stock price, and long-term shareholder value; and • significantly increase our costs to recover or reproduce the data. Likewise, we currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidate or any future product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. We rely on these third parties to implement effective security measures and identify and correct for any failures, deficiencies or breaches. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidate or any future product candidates could be hindered or delayed. We use and generate materials that may expose us to material liability. Our research programs involve the use of hazardous materials and chemicals, which are currently only handled by third parties. We are subject to foreign, federal, state and local environmental and health and safety laws and regulations governing, among other matters, the use, manufacture, handling, storage and disposal of hazardous materials and waste products. We may incur significant costs to comply with these current or future environmental and health and safety laws and regulations. In addition, we cannot completely eliminate the risk of contamination or injury from hazardous materials and may incur material liability as a result of such contamination or injury. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our workers' compensation, property and business interruption insurance and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims. General Risk Factors Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by economic and political changes in the location in which we, or our suppliers and vendors, maintain operations. For example, our business may be generally exposed to the impact of political or civil unrest or military action. While we do not have direct exposure to Ukraine or Russia, we do have third-party manufacturing partners with locations in Europe, which may be affected by the ongoing conflict between Russia and Ukraine. In addition, we **have** currently plan to activate **activated** sites for our SYNCHRONY trials in Israel and Turkey **in 2024**. These **plans sites** may be materially impacted or delayed by the ongoing Israel-Hamas war **conflict in the Middle East** and could result in difficulties **securing necessary clearance from regulatory authorities, activating clinical trial sites, and** screening and enrolling patients in such areas on schedule. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. Our business is affected by macroeconomic conditions, including rising inflation, interest rates **and**, supply chain constraints **and significant political, trade, or regulatory developments**. Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates and overall economic conditions and uncertainties such as those resulting from the current and future conditions in the global financial markets. For instance, rising interest rates have impacted the Company's net income. Recent supply chain constraints have led to higher inflation, which if sustained could have a negative impact on the Company's product development and operations. If inflation or other factors were to significantly increase our business costs, our ability to develop our current pipeline and new therapeutic products may be negatively affected. Interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the operation of our business and our ability to raise capital on favorable terms, or at all, in order to fund our operations. Similarly, these macroeconomic factors could affect the ability of our third-party suppliers and manufacturers to manufacture clinical trial materials for our product candidates. **Additionally, significant political, trade, or regulatory developments, such as those stemming from the change in U. S. federal administration, are difficult to predict and could give rise to circumstances outside our control that could have negative impacts on our business operations. For example, on February 1, 2025, the U. S. imposed a 25 % tariff on imports from Canada and Mexico, which were subsequently suspended for a period of one month, and a 10 % additional tariff on imports from China. Historically, tariffs have led to increased trade and political tensions. In response to tariffs, other countries have implemented retaliatory tariffs on U. S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and**

other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. Any changes in political, trade, regulatory, and economic conditions, including U. S. trade policies, in jurisdictions where our third- party suppliers and manufacturers operate, could have a material adverse effect on our financial condition or results of operations. Certain raw materials or other products necessary for the manufacture and formulation of our marketed products and product candidates, some of which are difficult to source, are provided by single- source unaffiliated third- party suppliers. In addition, we rely on certain third parties or our collaborators to perform filling, finishing, distribution, laboratory testing, and other services related to the manufacture of our marketed products and product candidates, and to supply various raw materials and other products. We would be unable to obtain these raw materials, other products, or services for an indeterminate period of time if any of these third parties were to cease or interrupt production or otherwise fail to supply these materials, products, or services to us for any reason, including due to regulatory requirements or actions (including recalls), adverse financial developments at or affecting the supplier, failure by the supplier to comply with cGMPs, contaminations, business interruptions, or labor shortages or disputes (in each case, including as a result of the armed conflict between Russia and Ukraine or public health outbreaks, epidemics, or pandemics or other geopolitical developments). Regional or single- source dependencies may in some cases accentuate these risks. For example, the pharmaceutical industry generally, and in some instances our Company or our collaborators or other third parties on which we rely, depend on China- based suppliers or service providers for certain raw materials, products and services, or other activities. Our ability or the ability of our collaborators or such other third parties to continue to engage these China- based suppliers or service providers for certain preclinical research programs and clinical development programs could be restricted due to geopolitical developments between the United States and China, including as a result of the escalation of tariffs or other trade restrictions or if the previously proposed federal legislation known as the BIOSECURE Act or a similar law were to be enacted. In any such circumstances, we may not be able to engage a backup or alternative supplier or service provider in a timely manner or at all. This, in turn, could materially and adversely affect our or our collaborators' ability to manufacture or supply marketed products and product candidates or advance our or our collaborators' preclinical research or clinical development programs, which could materially and adversely affect our business and future prospects.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non- performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and its financial condition and results of operations. Adverse developments that affect financial institutions, such as events involving liquidity that are rumored or actual, have in the past and may in the future lead to market- wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation as receiver. Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements, for example through our loan with Hercules, in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that us, the financial institutions with which we have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. We are a "large accelerated filer" as defined by the SEC, and the reduced disclosure requirements previously available to us no longer apply. As of June 30, 2023-2024, the market value of our common stock that was held by non- affiliates exceeded \$ 700 million, and as a result, we now continue to qualify as a "large accelerated filer". As such, we incur significant additional expenses in complying with the Sarbanes- Oxley Act of 2002 and rules implemented by the SEC. As a large accelerated filer, we are subject to certain disclosure requirements that are applicable to other public companies that were not applicable to us as a smaller reporting company. These requirements include: • compliance with the auditor attestation requirements of Section 404; • compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements; • full disclosure obligations regarding executive compensation; and • compliance with the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. If we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources. Additionally, we expect that our loss of "smaller reporting company" status will require additional attention from management and will result in increased costs to us, which could include higher legal fees, accounting fees and fees associated with investor relations activities, among others. Risks Related to an Investment in Our Securities The market price of our stock may be volatile, and you could lose all or part of your investment. Because of potential volatility in our trading price and trading volume, we may incur significant costs from class action securities litigation. The trading price of our common stock is likely to be volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. For example, between January 1, 2023-2024 and December 31, 2023-2024, our stock price has ranged from \$ 11-17. 25-76 to \$ 58-35. 38-28. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10- K, these factors include: • developments associated with our license with Amgen, including any termination or other change in our relationship with Amgen; • the success of competitive products or technologies; • regulatory actions with respect to our product candidate or any future product candidates or our competitors' product candidates or products; • results of clinical trials of our product candidate or any future product candidates

or those of our competitors; • actual or anticipated changes in our growth rate relative to our competitors; • announcements by us or our competitors or collaborators of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments; • regulatory, legal or payor developments in the United States and other countries; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to any of our product candidate or any future product candidates or clinical development programs; • the results of our efforts to in- license or acquire additional product candidates or products; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • variations in our financial results or those of companies that are perceived to be similar to us; • fluctuations in the valuation of companies perceived by investors to be comparable to us; • share price and volume fluctuations attributable to inconsistent trading volume levels of our shares; • announcement or expectation of additional financing efforts; • sales of our common stock by us, our insiders or our other stockholders; • changes in the structure of healthcare payment systems; • general economic, industry and market conditions; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad (such as the ongoing conflict between Ukraine and Russia, including the sanctions imposed by the United States, the **EU European Union** and others on Russia and other related parties); • market conditions in the pharmaceutical and biotechnology sectors; and • general economic, industry and market conditions. In addition, the stock market in general, and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Although the markets recovered, market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to inflation, rising interest rates, may significantly reduce the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this “ Risk Factors ” section, could have a dramatic and material adverse impact on the market price of our common stock. Holders of stock in companies that have a volatile stock price frequently bring securities class action litigation against the company that issued the stock. We **have been and may in the future** be the target of this type of litigation **in the future**. **The outcome of such pending and potential litigation is uncertain**. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. **A stockholder lawsuit claims cannot be predicted with certainty, defending against such claims could be costly** also divert the time and attention of our management. **Securities litigation against us could result in substantial costs** and divert our management’s attention from other business concerns, which could seriously harm our business. **Any litigation to which we become a party may result in an onerous or unfavorable judgment, or may be resolved with a monetary payment**. We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well- conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline. The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company or if they cease to cover our company, the trading price for our stock would likely be negatively impacted. In the event that securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline. Risks Related to Our Charter and Bylaws Anti- takeover provisions under our organizational documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management. Our fourth amended and restated certificate of incorporation and second amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include: • a board of directors divided into three classes serving staggered three- year terms, such that not all members of the board will be elected at one time; • a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders; • a requirement that special meetings of the stockholders may be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office, and special meetings of stockholders may not be called by any other person or persons; • advance notice requirements for stockholder proposals and nominations for election to our board of directors; • a requirement that no member of our board of directors may be removed

from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds (2 / 3) of all outstanding shares of our voting stock then entitled to vote in the election of directors; • a requirement of approval of not less than a majority of all outstanding shares of our voting stock to amend any bylaws by stockholder action and not less than two-thirds (2 / 3) of all outstanding shares of our voting stock to amend specific provisions of our certificate of incorporation; and • the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval, which preferred stock may include rights superior to the rights of the holders of common stock. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15 % or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our fourth amended and restated certificate of incorporation and second amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline. Our amended and restated bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees. Our amended and restated 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 state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our second amended and restated bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim that is governed by the internal affairs doctrine (the "Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Exchange Act. Our amended and restated bylaws further provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U. S. federal securities laws and the rules and regulations thereunder. The Delaware Forum Provision and the Federal Forum Provision in our bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage the filing of lawsuits against us and our directors, officers and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders. Risks Related to Income Taxes Changes in tax laws could adversely affect our business and 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 us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards. As of December 31, ~~2023~~ **2024**, we had U. S. federal and state net operating loss, or NOL, carryforwards of \$ ~~284,333,300~~ **300** million and \$ ~~413,660,280~~ **280** million, respectively and federal and state research and development tax credit carryforwards of \$ ~~14,260,400~~ **14,260,400** million and \$ ~~2,300,000~~ **2,300,000** million, respectively. If not utilized, such NOL carryforwards (other than federal NOL carryforwards arising in taxable years beginning after December 31, 2017) and research and development credits will expire at various dates beginning in 2033. Our ability to use our U. S. federal and state NOL and tax credit carryforwards to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. These NOL and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the current law, federal NOL carryforwards generated in tax years beginning after December 31, 2017, are not subject to expiration. However, any such NOL carryforwards may only offset 80 % of our annual taxable income in taxable years beginning after December 31, 2020. In

addition, under Sections 382 and 383 of the Code, the amount of benefits from our NOL carryforwards may be impaired or limited if we incur a cumulative ownership change of more than 50 percentage points by certain stockholders, as interpreted by the U. S. Internal Revenue Service, over a three- year period. We experienced such ownership changes on March 24, 2017, June 7, 2018 ~~and~~, July 8, 2020, **and May 31, 2024**. We may experience ownership changes again in the future, some of which may be outside our control. No ownership change occurred in 2022 ~~and or~~ 2023. As a result, our use of federal NOL and tax credit carryforwards could be limited. State NOL carryforwards may be similarly limited. Any such disallowances may result in greater tax liabilities than we would incur in the absence of such a limitation and any increased liabilities could adversely affect our business, results of operations, financial position and cash flows. **98**