Risk Factors Comparison 2025-02-26 to 2024-02-28 Form: 10-K

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You should carefully consider the risks described below, together with all of the other information included in or incorporated by reference into this **Annual** ~~report~~ **Report and in other documents we file with the SEC**, before making an investment decision. The risks and uncertainties described below are not **intended to be exhaustive and are not** the only ~~ones~~ **risks and uncertainties** we face. Additional risks and uncertainties not presently known to us or that we do not currently believe are ~~important~~ **material** to an investor may also harm our business **, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations**. If any of the events, contingencies, circumstances or conditions described in the following ~~risks~~ **risk factors** actually occur, our business, financial condition or our results of operations could be **materially and adversely affected** ~~seriously harmed. If that happens~~, **which may cause** the trading price of our common stock ~~could~~ **to** decline and you may lose part or all of the value of any of our shares **that** ~~held by~~ you **hold**. Risks ~~Relating~~ **Related** to **the Commercialization and Continued Approval of Rezdiffra** Our ~~Business We have limited operating history~~ **prospects are highly dependent on the success of our only approved product**, ~~we have incurred significant operating losses since inception and we expect to incur significant operating losses~~ **Rezdiffra, which was approved in the United States under the Subpart H accelerated approval pathway** for **new drugs** ~~the foreseeable future. We may never become profitable or, if profitability is achieved, we may be unable to sustain profitability. We have incurred significant operating losses since our inception and expect to incur significant losses~~ for **serious** ~~the foreseeable future as we continue our~~ **or life- threatening illnesses** ~~clinical trial and development programs for resmetirom and other future product candidates. As of December 31, 2023, we had an accumulated deficit of approximately $ 1, 336. 3 million. Losses have principally resulted from costs incurred in our preclinical and clinical trials, research and development programs and from our general and administrative expenses. As of December 31, 2023, we had cash, cash equivalents and marketable securities of approximately $ 634. 1 million. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance and, if resmetirom or other future product candidates are approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring further significant losses for the foreseeable future. We currently generate no revenue from product sales, and we may never be able to commercialize resmetirom or other future product candidates. We do not currently have the required approvals to market resmetirom or any other future product candidates, and we may never receive them. We may not be profitable even if we or any of our future development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Our business depends on the success of resmetirom~~. If we are unable to ~~obtain regulatory~~ **successfully commercialize or maintain** approval for **Rezdiffra** ~~and successfully commercialize resmetirom, or we experience significant delays in doing so~~, our business **, financial condition, results of operations and prospects and the value of our common stock** will be materially ~~harmed~~ **adversely affected**. **In March 2024, the FDA granted accelerated approval** ~~The primary focus of our product development since mid- 2018 has been resmetirom~~ for **Rezdiffra** ~~potential use~~ in **conjunction with diet and exercise** ~~non- alcoholic steatohepatitis, or NASH. Successful regulatory approval of resmetirom~~ for **the treatment of adults with noncirrhotic** ~~NASH~~ **MASH** ~~is critical~~ **with moderate** to ~~the future success of our business~~ **advanced liver fibrosis (consistent with stages F2 to F3 fibrosis)**. We have invested, and ~~will~~ continue to invest, ~~a~~ significant **efforts** ~~portion of our time~~ and financial resources in the **launch** ~~clinical and commercial development~~ of **Rezdiffra** ~~resmetirom. The future success of resmetirom is subject to a number of risks, including the following: • a delay, or inability to reach agreement with the FDA, concerning approval of resmetirom; • regulators, IRBs or ethics committees may not authorize us or our investigators to continue to conduct ongoing trials or complete a clinical trial; • we may not be able to demonstrate or obtain adequate evidence from clinical trials of efficacy and safety for resmetirom; • we do not know the degree to which resmetirom will be accepted as a therapy by physicians, patients and payors, even if approved; • commercial execution risks; • patients in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to resmetirom, which could delay or prevent clinical development; • we cannot be certain if we will be able to gain full approval of our product candidate following any Subpart H approval based on surrogate endpoints; and • even if we obtain Subpart H approval of resmetirom based on a surrogate endpoint, we are required to conduct complete the clinical outcomes trial under conditions set by FDA to confirm the clinical benefit of the product candidate and if the post- approval trial is not successful we may not be able to continue marketing the product. We could also encounter delays if a clinical trial is placed on clinical hold, suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA, the competent authorities and / or ethics committees of the EU Member States or other regulatory authorities, if a clinical trial is recommended for suspension or termination by the Data Safety Monitoring Board, or DSMB, for such trial, or on account of changes to federal, state, or local laws. A suspension or termination may be imposed due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, competent authorities and / or ethics committees of the EU Member States or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the completion of clinical trials may also ultimately lead to the~~

~~adverse regulatory action. Further, the FDA, EMA or other regulatory authorities may disagree with our clinical trial design for ingoing trials and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials. Any delays in our clinical development programs may harm our business, financial condition and results of operations significantly. Furthermore, even if we do receive regulatory approval to market resmetirom, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the products. If we are unable to obtain regulatory approval for, or, if approved, successfully commercialize resmetirom, we may not be able to generate sufficient revenue to continue our business. If approved, we will be highly dependent on the commercial success of resmetirom. We may not be able to meet expectations with respect to sales of our products if approved by the FDA, or attain profitability and positive cash- flow from operations. We have received breakthrough therapy designation and priority review from the FDA for resmetirom for the treatment of patients with NASH with liver fibrosis, and FDA has assigned a Prescription Drug User Fee Act date for resmetirom of March 14, 2024, the target date by which the FDA intends to complete its review and take action on the NDA. If resmetirom receives FDA approval, the success of our business will depend on the commercial success of resmetirom. Successful commercialization of resmetirom, if approved, is subject to many risks~~ . We have never, as an organization, launched or commercialized any other product, and there is no guarantee that we will be able to successfully commercialize **Rezdiffra** ~~resmetirom if approved~~ . There are numerous examples of failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us. We ~~expect~~ **believe** that ~~future~~ **the** commercial success of **Rezdiffra** ~~resmetirom for the treatment of patients with NASH will depend~~ **depends** on many factors, including the following: **• our ability to effectively educate healthcare providers and patients on the risks of MASH and the potential clinical benefits of Rezdiffra, the first FDA- approved treatment in MASH;** • the efficacy, cost, approved use, and side- effect profile of ~~resmetirom~~ **Rezdiffra** relative to competitive treatment regimens ~~, if approved,~~ for the treatment of ~~NASH~~ **MASH** ; • **Rezdiffra** ~~if approved for NASH, resmetirom~~ may compete with the off- label use of currently marketed products and other therapies in development that may in the future obtain approval for ~~NASH~~ **MASH** ; • the effectiveness of our commercial strategy for the marketing of ~~resmetirom~~ **Rezdiffra** , including our pricing strategy and the effectiveness of our efforts to obtain adequate third- party reimbursements; • developing, maintaining and successfully monitoring commercial manufacturing arrangements for ~~resmetirom~~ **Rezdiffra** with third- party manufacturers to ensure they meet our standards and those of regulatory authorities, including the FDA, which extensively regulate and monitor pharmaceutical manufacturing facilities; • our ability to negotiate and enter into any additional commercial, supply and distribution contracts to support commercialization efforts, and to hire and manage additional qualified personnel; • our ability to meet the demand for commercial supplies of ~~resmetirom~~ **Rezdiffra** at acceptable costs; • the acceptance of ~~resmetirom~~ **Rezdiffra** by physicians, patients and third- party payors; • our ability to remain compliant with laws and regulations that apply to us and our commercial activities; • the actual market- size, ability to identify targeted patients and the demographics of patients eligible for ~~resmetirom~~ **Rezdiffra** , which may be different than what we currently expect; • the occurrence of any side effects, adverse reactions or misuse, or any unfavorable publicity in these areas; • our ability to obtain, maintain or enforce our patents and other intellectual property rights; and • the effect of recent or potential health care legislation in the United States. While we believe that **Rezdiffra has** ~~resmetirom for the treatment of NASH, if approved, should have~~ a commercially competitive profile, we cannot accurately predict the amount of time needed to attain a commercially successful profile or the amount of revenue that would be generated from the sale of ~~resmetirom~~ **Rezdiffra** . If we do not effectively commercialize ~~resmetirom~~ **Rezdiffra** , we will not be able to execute our business plan and may not be able to achieve profitability. If our revenues, market share ~~and /~~ or other indicators of market acceptance of ~~resmetirom~~ **Rezdiffra** do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline. **We obtained** ~~Clinical trials are very expensive, time- consuming and difficult to design and implement and involve uncertain outcomes. Furthermore, the results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate that we advance into clinical trials, including resmetirom, may not have favorable results in later clinical trials or receive~~ regulatory approval **of Rezdiffra** ~~. Drug development has inherent risk. We will be required to demonstrate~~ through ~~adequate and well- controlled clinical trials that our product candidates are safe and effective, with a favorable benefit- risk profile, for use in our target indications before we can seek regulatory approvals for commercial sale. Clinical studies are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. Delay or failure can occur at any stage of development, including after commencement of any of our clinical trials. In addition, success in early clinical trials does not mean that later clinical trials will be successful, because later- stage clinical trials may be conducted in broader patient populations and involve different study designs. Furthermore, our ongoing and future trials will need to demonstrate sufficient safety and efficacy in large patient populations for approval by regulatory authorities. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their~~ -- **the** product candidates performed satisfactorily in preclinical studies..... for commercialization. Resmetirom has neither received Subpart H ~~or~~ **accelerated approval pathway, and** full ~~regulatory~~ approval ~~for the treatment of NASH or any other indication, and unexpected problems may arise that could cause us to delay, suspend or terminate our development efforts in any or all indications. Even if resmetirom receives Subpart H approval for the treatment of NASH or any other indication, we~~ will be ~~required to conduct~~ **contingent on successful completion of a confirmatory** post- **marketing trial. Failure to obtain full** approval **or otherwise meet our** ~~confirmatory trials under conditions specified by FDA. Failure to complete the~~ post- ~~approval trial may jeopardize our ability to market~~ **marketing requirements** ~~resmetirom. Further, the long- term safety consequences of a liver- directed thyroid hormone receptor beta agonist are not known. Regulatory approval of new product candidates such as resmetirom can be more expensive~~ and **commitments** ~~take longer than approval for candidates for the treatment of more well- understood diseases with~~

previously approved products. If clinical trials or regulatory approval processes for our product candidates are prolonged, delayed or suspended, we may be unable to commercialize our product candidates on a timely basis, which would require us to incur additional costs and..... markets for our drug candidates and may have a material adverse effect on our **business** results of operations and financial condition . **The FDA approved Rezdiffra under the accelerated approval pathway** We depend on enrollment of patients in our clinical trials for **new drugs** our product candidates. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or **for serious** otherwise adversely affected. Identifying and qualifying patients to participate in clinical trials of our **or life- threatening illnesses and was supported** product candidates is critical to our success. We may not be able to initiate, continue, or complete clinical trials required by **52- week data from** the FDA or foreign regulatory agencies for resmetirom if we are unable to locate, enroll and maintain a sufficient number of eligible patients to participate. Our Phase 3 clinical trials have significantly more patients than were enrolled in our Phase 2 trials. Although we have satisfied Subpart H patient enrollment for MAESTRO- NASH **trial** , clinical enrollment for **which achieved both primary endpoints — MASH resolution with no worsening of fibrosis and an improvement in fibrosis by at least one stage with no worsening of the NAFLD activity score. In connection with the FDA' s accelerated approval, we have agreed to certain post- marketing commitments, including completing** our MAESTRO- NASH Outcomes **trial to demonstrate a clinical benefit of Rezdiffra on composite endpoints. Our MAESTRO- NASH** trial is **ongoing** not complete as of December 31 **a 54- month outcomes trial designed to generate confirmatory outcomes data that** , 2023 **if positive, is expected to verify a clinical benefit** and significant **support the full approval of Rezdiffra.** additional **Additionally** enrollment **, full approval could also be based on results from our MAESTRO- NASH OUTCOMES trial that** will be necessary **noninvasively measure progression to liver decompensation events in patients with compensated MASH cirrhosis. Positive data from our MAESTRO- NASH OUTCOMES trial is expected to support the full approval of Rezdiffra in noncirrhotic MASH** and **support approval** will be ongoing for **patients with compensated cirrhosis** some time. The timing to conduct and complete clinical trials , **expanding** is affected by many factors, including the **eligible** size and nature of the patient population , the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages and disadvantages of the product candidate being studied in relation to other available therapies. Any product candidate in our current or future clinical trials may cause unacceptable adverse events or side effects or have other properties that may delay or prevent its regulatory approval or commercialization or limit its commercial potential. Unacceptable adverse events or undesirable side effects caused by any of our product candidates in current or future clinical trials could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications and markets. This in turn could prevent us from completing development of or commercializing the affected product candidate and generating revenue from its sale. If any of our product candidates cause unacceptable adverse events in clinical trials, we may not be able to obtain regulatory approval or commercialize such product candidate. Occurrence of serious treatment- related side effects could impede subject recruitment and clinical trial enrollment or the ability of enrolled patients to complete the trial, require us to halt the clinical trial, and prevent receipt of regulatory approval from the FDA. They could also adversely affect physician or patient acceptance of our product candidates or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly. We have received Fast Track Designation from the FDA for resmetirom for NASH; however, such designation may not actually lead to a faster development or regulatory review or approval process, and the designation may be rescinded if the product candidate no longer meets the qualifying criteria for Fast Track. In October 2019, FDA granted Fast Track designation to resmetirom for NASH. Products that have been designated as Fast Track may be eligible for certain action to expedite development and review of the application, including rolling review. The receipt of Fast Track designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Breakthrough therapy or priority review by the FDA for any product candidate may not lead to faster development, regulatory review or approval processes, and it does not increase the likelihood that our product candidates will receive marketing approval. We have received breakthrough therapy designation and priority review from the FDA for resmetirom for the treatment of patients with NASH with liver fibrosis, and we may seek breakthrough therapy designation or priority review for future product candidates if supported by the results of clinical trials. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Priority review is intended to speed the FDA marketing application review timeframe for drugs that treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. For drugs and biologics 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. Sponsors of drugs that are breakthrough therapies may also be able to submit marketing applications on a rolling basis, meaning that the FDA may review portions of a marketing application before the sponsor submits the complete application to the FDA, if the sponsor pays the user fee upon submission of the first portion of the marketing application. For applications that receive priority review, the FDA' s marketing application review goal is shortened to six months, as opposed to ten months under standard review. Designation as a breakthrough therapy or priority review product is within the discretion of the regulatory agency. Accordingly, even if we believe one of our future product candidates meets the criteria for designation as a breakthrough therapy or priority review product, the agency may disagree and instead determine not to make such designation. In any event, the receipt of such a designation for a product candidate may not result in

~~a faster development process, review or approval compared to drugs considered for approval under conventional regulatory procedures and does not assure ultimate marketing approval by the agency. In addition, regarding breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification as a breakthrough therapy or, for priority review products, decide that the period for FDA review or approval will not be shortened. Even if resmetirom or any product candidate receives accelerated approval from the FDA, they face future post- approval development and regulatory requirements, which present additional challenges for us to successfully navigate. We are currently pursuing accelerated approval of our lead product candidate, resmetirom. Under the accelerated approval pathway, continued approval may be contingent upon verification of a clinical benefit in confirmatory trials. These post- approval requirements and commitments may not be feasible and / or could impose significant burdens and costs on us; could negatively impact our development, manufacturing and supply of our products; and could negatively impact our financial results. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval~~ . Failure to meet post- ~~approval~~ **marketing** commitments and requirements, including completion of enrollment of — and in particular, any failure to obtain positive data from — any confirmatory studies required by the FDA, could result in negative regulatory action from the FDA and / or withdrawal of such accelerated approval. The recently enacted ~~FDORA~~ **Food and Drug Omnibus Reform Act** has expanded FDA ~~'~~**'** s expedited withdrawal procedures for drugs approved through the accelerated approval pathway if a sponsor fails to conduct any required post- approval study with due diligence. **The commercial success** ~~Unless otherwise informed by the FDA, an applicant must submit to the FDA for consideration during the preapproval review period copies~~ of **Rezdiffra** ~~all promotional materials, including promotional labeling as well~~ **will depend** ~~as advertisements, intended for dissemination or publication within 120 days following marketing approval. After 120 days following marketing approval, unless otherwise informed by the FDA, the applicant must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the labeling or initial publication of the advertisement. If we or the manufacturing facilities for our products fail to comply with applicable regulatory requirements, the FDA may, among other actions: issue warning letters or untitled letters; seek an injunction or impose civil or criminal penalties or monetary fines; suspend or withdraw or alter the conditions of our marketing approval; suspend any ongoing clinical trials; refuse to approve pending applications or supplements to applications submitted by us; suspend or impose restrictions~~ on ~~operations, including costly new manufacturing requirements; and seize or detain products, refuse to permit the import or export of products or require us to initiate a product recall. Our product candidates will remain subject to ongoing regulatory review even if they~~ - **the degree** ~~receive marketing approval, and if we fail to comply with continuing regulations, we could lose these approvals and the sale~~ of any approved commercial products could be suspended..... approval, they may not gain extensive market acceptance ~~among~~ **by** physicians, patients, ~~and~~ third- party ~~payers~~ **payors and others in** ~~. Efforts to educate~~ the ~~medical~~ **health care** community ~~and~~ **. Despite receiving FDA approval of Rezdiffra, our product may not gain, or over time may not retain, market acceptance by physicians, patients,** third- party ~~payers~~ **payors or others in the health care community. Rezdiffra was the first product approved by the FDA for the treatment of MASH. Accordingly, we must educate healthcare providers and patients** on the **risks of MASH and the potential clinical** benefits **and appropriate use** of **Rezdiffra. If Rezdiffra does not achieve and maintain an adequate level of acceptance, it is likely that we will not generate significant revenue** ~~our~~ - **or become profitable. The degree of market acceptance of Rezdiffra, which we launched in the United States early in the second quarter of 2024, is also dependent on a number of additional factors, including the following: • the willingness of physicians to prescribe, and our target patient population to use, Rezdiffra; • the pricing of Rezdiffra; • the efficacy and potential advantages of Rezdiffra compared to other treatment regimens; • the ability of patients to tolerate Rezdiffra; • sufficient third- party insurance coverage and reimbursement; • the ability of the patient to pay out- of- pocket costs for Rezdiffra; • the timing of market introduction of competitive** ~~product~~ **products** ~~candidates may~~ **and treatments; and • any publicity concerning Rezdiffra or any potential competitive products. Our efforts to educate physicians, patients, third- party payors and others in the health care community on the potential benefits of Rezdiffra will** require significant resources and may not be ~~fully~~ successful. If **the sales** ~~any of our product candidates do not achieve an~~ **and** ~~adequate level of acceptance, we may not generate significant product revenue or any profits from operations. Physicians may decide not to recommend our treatments or a patient though prescribed our product may not receive it for a variety of reasons including: • timing of market introduction of competitive products; • demonstration of clinical safety and efficacy compared to other products; • cost- effectiveness; • limited or no coverage by third- party payers; • convenience and ease of administration; • restrictions in the label of the drug; • other potential advantages of alternative treatment methods; • unanticipated post-~~ marketing **capabilities** ~~events; • ineffective marketing and distribution support of its products; • inability of third- party patient services to achieve patient access to therapy; and • inability of specialty pharmacies to communicate effectively with patients, coordinate shipments and effect adherence to therapy. If any of our product candidates are approved, but fail to achieve full market acceptance or such market is smaller than anticipated, we may not be able to generate significant revenue and our business would suffer. As we evolve from a company that is primarily involved in clinical development to a company that is also involved in commercialization, we may encounter difficulties in expanding our operations successfully, including successfully optimizing manufacturing for our product / product candidate in sufficient quality and quantity or within targeted timelines. As~~ we have ~~been advancing resmetirom through clinical trials~~ **established for the commercialization of Rezdiffra are not effective, Rezdiffra may not be successfully commercialized. While many of our officers and employees have experience commercializing drug products with prior companies** , we have **never** ~~been expanding our development, regulatory, manufacturing, and marketing and sales capabilities and commitments and may need to further contract with third parties to provide these capabilities. As our operations expand, we likely will need to manage additional relationships with such third parties,~~ as ~~well as additional collaborators, distributors, marketers and~~ - **an** ~~suppliers. Maintaining third party relationships for~~ **organization engaged in commercial activities prior to** ~~these~~ -- **the approval** ~~purposes will impose significant added~~

~~responsibilities on members~~ of **Rezdiffra** ~~our management and other personnel~~. We ~~must be able to effectively manage our development efforts, and marketing personnel, effectively manage our participation in ongoing clinical trials and improve our managerial, development, operational and finance systems, all of which may impose a strain on our administrative and operational infrastructure. If we enter into arrangements with third parties (such as ex- US arrangements or arrangements described in the succeeding section) to perform sales, marketing or distribution services, any product revenues that we receive, or the profitability of these product revenues to us, are likely to be lower than if we were to market and sell any products that we develop without the involvement of these third parties. In addition, we may not be successful in entering into arrangements with third parties to sell and market our products or in doing so on terms that are favorable to us. We likely will~~ have ~~little control over such third~~ - **hired** ~~parties,~~ and **trained** ~~any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products. If we are unable to successfully further develop and maintain internal commercialization capabilities, future sales of our products, if approved, may be negatively impacted. In anticipation of potential regulatory approval of resmetirom, we have been hiring and training~~ a commercial team and ~~developing~~ **developed** the organizational infrastructure we believe we need to support the commercial success of ~~resmetirom~~ **Rezdiffra, and we continue to invest time and financial resources in optimizing this infrastructure**. Factors that may inhibit our efforts to maintain and further develop commercial capabilities include: • an inability to retain an adequate number of effective commercial personnel; • an inability to adequately train commercial personnel, who may have limited experience with our company or our ~~products~~ - **product**, to deliver a consistent message regarding **Rezdiffra** ~~our products~~ and be effective in educating physicians **regarding its potential benefits** ~~on how to prescribe our products~~; • an inability to equip commercial field personnel with compliant and effective materials, including marketing literature to help them educate physicians and ~~our~~ healthcare providers regarding **Rezdiffra** ~~our products and their proper administration~~ and educate payors on the safety, efficacy and effectiveness profile of **Rezdiffra** ~~our products~~ to support favorable coverage decisions; and • unforeseen costs and expenses associated with maintaining and further developing an independent commercial organization. If we are not successful in maintaining **our** ~~an effective~~ commercial infrastructure **, of if our commercial capabilities are not effective**, we will encounter difficulty in achieving, maintaining or increasing projected sales of **Rezdiffra** ~~resmetirom once approved~~, which would adversely affect our business and financial position. **We** ~~In addition, we~~ may **become subject** ~~in the future choose~~ to **unfavorable pricing regulations** ~~collaborate with third parties that have direct sales forces and established distribution systems, either to augment our~~ - **or** ~~own sales force and distribution systems or as an alternative to our own sales force and distribution systems. To the extent that we enter into co- promotion or other licensing arrangements, our product revenue may be lower than if we directly marketed or sold any approved products. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third parties, which may not be successful and are generally not within our control. If we are unable to enter into these arrangements on acceptable terms or at all, we may not be able to successfully commercialize any approved products. If we are not successful in commercializing any approved products, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses. The insurance coverage and reimbursement status of newly- approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue. Market acceptance and sales of any one or more of our product candidates will depend on reimbursement policies and may be affected by future healthcare reform measures in the United States and in foreign jurisdictions. Government authorities and~~ third- party **coverage and reimbursement policies, which would harm our business. Our ability to successfully commercialize Rezdiffra and any future product candidate will depend in part on the extent to which coverage and reimbursement for these drugs and drug candidates and related treatments will be available from government authorities, private health insurers and other organizations. See the section titled " Business — Government Regulation — Coverage and Reimbursement " in this Annual Report for more information. In the United States and markets in other countries, patients generally rely on third- party** ~~payers~~ **payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize Rezdiffra and any additional products will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third- party payors**, such as private health insurers and health maintenance organizations, decide which ~~drugs~~ **medications** they will ~~cover~~ **pay for** and establish ~~payment~~ **reimbursement** levels. ~~We cannot~~ **In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services (" CMS "), an agency within the U. S. Department of Health and Human Services (" HHS "). CMS decides whether and to what extent a new medicine will** be ~~certain~~ **covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales of these or other products** that ~~reimbursement~~ **we may identify** will ~~be available for any~~ **depend substantially, both domestically and abroad, on the extent to which the costs** of our ~~product~~ **products** ~~candidates. Also, we cannot be certain that reimbursement policies~~ will **be** ~~not reduce the demand for, or the price~~ paid **by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations,** ~~for~~ - **or reimbursed by government health administration authorities**, ~~our products~~ **private health coverage insurers and other third- party payors**. If **coverage and adequate** reimbursement is not available **,** or is available ~~on a~~ **only to** limited ~~basis~~ **levels**, we may not be able to successfully commercialize **Rezdiffra or** any **other future** product ~~candidates~~ - **candidate** ~~that we develop~~ - ~~The future~~ **Even if coverage is provided, the approved reimbursement amount may not be**

high enough to allow us to establish or maintain pricing ~~, coverage and reimbursement of our product candidates must be adequate to support our commercial infrastructure. Our future per- patient prices must be~~ sufficient to **realize a sufficient return** ~~recover our development and manufacturing costs and potentially achieve profitability. However, sales of any pharmaceutical product depend, in part,~~ on **our investment. A primary trend in** the **U. S.** ~~extent to which such product will be covered by third- party payors, such as federal, state, and foreign government~~ healthcare **industry** ~~programs, commercial insurance~~ and **elsewhere is cost containment** ~~managed healthcare organizations, and the level of reimbursement for such product by third- party payors~~ . **Government authorities** ~~Significant uncertainty exists as to the coverage~~ and ~~reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan- by- plan basis. One third- party payor' s decision to cover a product does not ensure that~~ other ~~payors will also provide coverage for the product. As a result, we do not have assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance or in the future. In addition,~~ third- party payors have ~~increasingly~~ **attempted to control costs by limiting coverage and the amount of reimbursement for particular drugs. Net prices for drugs may also be** reduced ~~reimbursements~~ **by mandatory discounts** ~~for~~ - **or rebates required by** ~~pharmaceutical products. The U. S.~~ government **healthcare** ~~and state legislatures have continued implementing cost- containment~~ programs ~~, including price controls, restrictions on coverage and reimbursement, and requirements for~~ - **or private** ~~substitution of generic products. Third- party~~ payors ~~are increasingly challenging~~ **and by any future relaxation of laws that presently restrict imports of drugs from countries where** ~~the~~ **they may be sold at lower** prices **than** ~~charged, examining the medical necessity, and reviewing the cost effectiveness of pharmaceutical products,~~ in ~~addition to questioning their~~ -- **the United States** ~~safety and efficacy~~ . Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for **drugs** ~~medical products~~ . **We cannot be sure that coverage will be available or maintained** ~~Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. Adoption of price controls and cost- containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit or~~ **for Rezdiffra or** ~~delay sales of~~ any **drug candidate that we commercialize and, if** ~~of our future products. A decision by a third- party payor not to cover~~ **coverage** ~~a product could reduce physician ordering and patient~~ **is available, the level of reimbursement. Reimbursement may impact the** demand for **, or the price of, Rezdiffra or** any ~~of our~~ future **drug** ~~products. In international markets, reimbursement and healthcare payment are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost- containment initiatives in the European Union, Canada and other countries will put pressure on the pricing and usage of our product candidates~~ - **candidate** ~~. In many countries, the prices of medicinal products are subject to varying price control mechanisms as part of national health systems. In general, the prices of therapeutics or medicinal products under such systems are substantially lower than in the U. S. For example, the European Union provides options for its member states to restrict the range of medicinal products~~ for which ~~their national health insurance systems provide~~ **we obtain marketing approval. If** reimbursement ~~and~~ **is not available or is available only** to ~~control~~ **limited levels, we may not be able to successfully commercialize Rezdiffra or any future drug candidate for which we obtain marketing approval. Many pharmaceutical manufacturers must also 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,** ~~the~~ **these** prices ~~of medicinal products~~ for ~~human~~ **drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any 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 not be made permanent. Reimbursement rates may vary according to the** use **of** ~~. Furthermore, there~~ -- **the drug and the clinical setting in which it** is ~~no assurance~~ **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 ~~a product will~~ **presently restrict imports of drugs from countries where they may** be **sold at lower prices than in the United States. Private** ~~considered medically reasonable and necessary for a specific indication, will be considered cost- effective by~~ third- party payors **often rely upon Medicare** ~~, that an adequate level of reimbursement will be established even if~~ coverage **policy in setting** ~~is available, or that the third~~ - **their own** ~~- party payors'~~ reimbursement policies ~~will not~~ **. Our inability to promptly obtain coverage and profitable payment rates from both government- funded and private payors for Rezdiffra or any future approved drugs that we develop could have a material** ~~adversely~~ -- **adverse** ~~affect~~ **effect** ~~the~~ **on our operating results, our** ability ~~of manufacturers~~ to **raise capital needed** ~~sell products profitably. Accordingly, in markets outside the U. S., the reimbursement for our products may be reduced compared with the U. S. and may be insufficient~~ to ~~generate commercially~~ **commercialize drugs** ~~reasonable revenue~~ and ~~profits~~ **our overall financial condition** . The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment. Resulting changes in healthcare law and policy, including recently enacted changes to Medicare, may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition. The United States and several foreign jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and / or expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts

and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products that we develop due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative proposals. **See the section titled " Business — Government Regulation — U. S. Healthcare Reform " in this Annual Report for more information.** The ~~Medicare Prescription Drug~~ **continuing efforts of the government** , ~~Improvement~~ **insurance companies** , ~~and~~ **managed care** ~~Modernization~~ ~~---~~ **organizations and** ~~Act of 2003, also called the~~ **other** ~~Medicare Modernization Act,~~ **payers of healthcare services to contain or reduce costs of healthcare may adversely affect: • the demand** ~~or~~ **for** ~~MMA~~ **any of our product candidates** , ~~changed~~ **if approved; •** the ~~way Medicare covers~~ **ability to set a price that we believe is fair for any of our product candidates, if approved; • our ability to generate revenues** and **achieve or maintain profitability; • the level of taxes that we are required to** ~~pays~~ ~~-~~ **pay; and • the availability of capital. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities** for pharmaceutical **and biologic** products. **We cannot** ~~The legislation established Medicare Part D, which expanded Medicare coverage for outpatient prescription drug purchases by the elderly but provided authority for limiting the number of drugs that will~~ be **sure whether** ~~covered in any therapeutic class. The Patient Protection and Affordable Care Act, as amended, (the ACA) aims to reduce the cost of healthcare and substantially change the way healthcare is financed by both government and private insurers. The ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of, and the price we may charge for, any products we develop that receives regulatory approval. Additional~~ **additional** legislative changes ~~to and~~ **will be enacted, or whether FDA** ~~regulatory~~ **regulations , guidance or interpretations will be changed, or what the impact of such** changes ~~under the ACA remain possible, but the nature and extent of such potential additional changes are uncertain at this time. We expect that the ACA, its implementation, efforts to challenge or modify the ACA or its implementing regulations, or portions thereof, and other healthcare reform measures including those that may be adopted in the future, could have a material adverse effect~~ on **the marketing approvals of** ~~our industry generally and on our ability to maintain or~~ **our** ~~increase sales of existing products or to successfully commercialize~~ product candidates, if ~~approved~~ **any, may be** . In addition **, increased scrutiny by Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. In addition** to the ACA, **the** U. S. ~~governments~~ ~~-~~ **government** ~~continue~~ **continues** to seek to adopt healthcare policies and reforms intended to curb healthcare costs, such as federal or state controls on payment for drugs (including under Medicare, Medicaid, and commercial health plans). The ~~Inflation Reduction Act of 2022, or~~ IRA ~~,~~ among other things, establishes Medicare Part B and Part D inflation rebate schemes. Failure to timely pay a Part B or Part D inflation rebate is subject to a civil monetary penalty. The IRA also creates a drug price negotiation program under which the prices for Medicare units of certain high Medicare spend drugs and biologics without generic or biosimilar competition will be capped by reference to, among other things, a specified non- federal average manufacturer price, starting in 2026. Failure to comply with requirements under the drug price negotiation program is subject to an excise tax and / or a civil monetary penalty. The IRA further makes changes to the Medicare Part D benefit, including a limit on annual out- of- pocket costs, and a change in manufacturer liability under a new discount program which could negatively affect the profitability of our product candidates. Failure to pay a discount under this new program will be subject to a civil monetary penalty. Congress continues to examine various policy proposals that may result in pressure on the prices of prescription drugs in the government health benefit programs. The IRA or other legislative changes could impact the market conditions for our product candidate. ~~The U. S.~~ **Moreover, increasing efforts by** ~~government~~ **governmental** and ~~state~~ **third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing** ~~legislatures~~ ~~-~~ **legislative and enforcement** ~~have shown significant~~ interest in ~~implementing cost containment programs to limit~~ the **United States with respect to specialty** ~~growth of government- paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs~~ ~~-~~ **drug pricing practices** . ~~Additionally~~ **Specifically** , there have been several **recent U. S.** Congressional inquiries and proposed and enacted federal and state legislation ~~and regulatory initiatives~~ designed to, among other things, bring more transparency to ~~product~~ **drug** pricing, ~~evaluate~~ **reduce the cost of prescription drugs under Medicare, review** the relationship between pricing and manufacturer patient programs, and reform government ~~healthcare~~ program reimbursement methodologies for ~~drug products. Individual states in the U. S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including by requiring pharmaceutical manufacturers to report to state agencies when they introduce new~~ drugs ~~to market with prices over a certain threshold, or when they increase the price of a drug over a certain threshold~~ . **We expect** ~~If healthcare policies or reforms intended to curb healthcare costs are adopted, the prices~~ that ~~we charge for any approved products may be limited, our commercial opportunity may be limited and / or our revenues from sales of our product and any future products, if approved, may be negatively impacted. It is possible that the above- mentioned measures, as currently enacted or may be amended in the future, as well as other~~ ~~--~~ **the** healthcare reform measures that ~~may be~~ **have been** adopted **and may be adopted** in the future, may result in ~~additional reductions in Medicare and other healthcare funding,~~ more rigorous coverage criteria ~~,~~ and **in** ~~new payment methodologies and~~ additional downward pressure on ~~coverage and payment and~~ 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 payors. The implementation of ~~additional~~ cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products. **Rezdiffra remains subject to ongoing regulatory review, and if we fail to comply with continuing regulations, we could lose our approval and the sale of Rezdiffra could be suspended. Even though we received FDA accelerated approval for Rezdiffra, the manufacturing, labeling, packaging, distribution,**

adverse event reporting, storage, advertising, promotion, sampling, and record keeping related to our product will remain subject to extensive regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP regulations, and GCPs for any clinical trials that we conduct post- approval, all of which may result in significant expense and limit our ability to commercialize Rezdiffra. As such, we and our contract manufacturers will be subject to periodic review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or other marketing application and previous responses to inspection observations. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the United States. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control. The FDA may also require a REMS program as a condition of approval of Rezdiffra or any future product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. If we fail to comply with the regulatory requirements of the FDA and other applicable domestic and foreign regulatory authorities, or previously unknown problems with Rezdiffra, manufacturer, or manufacturing process are discovered, we could be subject to administrative or judicially imposed sanctions, including: • restrictions on marketing or manufacturing of Rezdiffra; • withdrawal of Rezdiffra from the market; • holds on clinical trials; • warning letters or untitled letters; • civil or criminal penalties; • fines; • injunctions; • product seizures or detentions; • pressure to initiate voluntary product recalls; • suspension or withdrawal of regulatory approvals; and • refusal to approve supplements to approved applications. If any of these events occur, our ability to sell Rezdiffra may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could adversely affect our business, financial condition and results of operations. Rezdiffra could develop unexpected safety or efficacy concerns, which would likely have a material adverse effect on us. Rezdiffra was granted accelerated approval from the FDA based on 52- week data from the MAESTRO- NASH trial and additional safety data from the Phase 3 MAESTRO- NAFLD- 1 and MAESTRO- NAFLD- OLE extensions trials. In the United States, Rezdiffra will now be used by more patients, potentially for longer periods of time, and we and others (including regulatory agencies and private payors) will collect extensive information on the efficacy and safety of Rezdiffra by monitoring its use in the marketplace. In addition, we are generating confirmatory data regarding the longer- term use of Rezdiffra in two ongoing trials. New safety or efficacy data from both market surveillance and our clinical trials may result in negative consequences including the following: • Suspension or withdrawal of regulatory approval; • Modification to product labeling or promotional statements, such as additional boxed or other warnings or contraindications, or the issuance of additional " Dear Doctor Letters " or similar communications to healthcare professionals; • Required changes in the dosing of Rezdiffra; • Imposition of additional post- marketing surveillance, post- marketing clinical trial requirements, distribution restrictions or other risk management measures, such as a REMS or a REMS with elements to assure safe use; • Suspension or termination of ongoing clinical trials or refusal by regulators to grant full approval or approve pending marketing applications or supplements to approved applications; • Suspension of, or imposition of restrictions on, our operations, including costly new manufacturing requirements with respect to Rezdiffra; and • Voluntary or mandatory product recalls or withdrawals from the market and costly product liability claims. Any of the foregoing circumstances could negatively impact Rezdiffra' s market acceptance and would likely materially adversely affect our business. We operate in a highly competitive and changing environment, and if we are unable to adapt to our environment, we may be unable to compete successfully. The biopharmaceutical industry has undergone and is likely to continue to experience rapid and significant change. Our future success will depend in large part on our ability to maintain a competitive position with respect to these technologies and to obtain and maintain protection for our intellectual property. Compounds, products or processes that we develop may become obsolete before we recover any expenses incurred in connection with their development. We face substantial competition from pharmaceutical, biotechnology and other companies, universities and research institutions with respect to MASH, and will face substantial competition with respect to future product candidates we may develop in MASH and other disease areas. Relative to us, many of these entities have substantially greater capital resources, research and development staffs, facilities and experience in conducting clinical studies, obtaining regulatory approvals, and manufacturing and marketing pharmaceutical products. While Rezdiffra is currently the only FDA approved drug for the treatment of MASH, there are over 150 drugs in development for the potential treatment of MASH by companies ranging in size from private biotech companies to large pharma organizations. See the section titled " Business — Competition " in this Annual Report for more information. Our ability to compete successfully will depend on, among other things, our ability to: • effectively commercialize Rezdiffra; • discover and / or in- license medicines that are differentiated from other products in the market; • obtain required regulatory approvals; • obtain patent and / or proprietary protection for our products and technologies; and • attract and retain high- quality research, development and commercial personnel. If we are unable to compete successfully, it will materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock. Rezdiffra was approved for treatment in a limited population of patients with MASH with moderate to advanced liver fibrosis, and additional clinical trials and regulatory applications will be required to expand its indication. We may not be successful in these trials or in obtaining such regulatory approval, which may materially adversely affect our prospects and the value of our common stock. The FDA granted accelerated approval of Rezdiffra for the treatment of MASH with moderate to advanced liver fibrosis

(consistent with stages F2 to F3 fibrosis). A key component to our corporate strategy is to expand the target patient population for Rezdiffra. We have fully enrolled our Phase 3 MAESTRO- NASH OUTCOMES trial. In this trial, we are evaluating progression to liver decompensation events in patients with compensated MASH cirrhosis treated with Rezdiffra versus placebo. A positive outcome is expected to support the full approval of Rezdiffra for noncirrhotic MASH and also expand the eligible patient population for Rezdiffra with an additional indication in patients with compensated MASH cirrhosis. We cannot **guarantee positive results in this trial. If we are unable to expand the indication for use of Rezdiffra, our prospects and the value of our common stock may** be ~~sure whether~~ **materially adversely affected. If we do not obtain regulatory approval of Rezdiffra in foreign jurisdictions, we will not be able to market Rezdiffra in other jurisdictions, which will limit our commercial revenues. While Rezdiffra has been approved by the FDA for the treatment of noncirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), it has not been approved in any other jurisdiction for this indication or for any other indication. In order to market Rezdiffra for other indications or in other jurisdictions, we must obtain regulatory approval for each of those indications and in each of the applicable jurisdictions, and we may never be able to obtain such approval. While our MAA for resmetirom for the treatment of MASH with liver fibrosis has been validated and is now under evaluation with the CHMP, no guarantee can be made that we will receive requisite marketing approvals. In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding clinical trial design, safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve** additional ~~legislative changes~~ **product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market** will be **reduced and** ~~enacted in the U. S. or~~ **our ability to realize the full market potential of Rezdiffra will be harmed. Governments** outside ~~of~~ the ~~U. S.~~ **United States tend to impose strict price controls** , **which may adversely affect** ~~or~~ **our** ~~whether~~ **revenues, if any. If our products are approved in foreign jurisdictions, we will be subject to pricing and reimbursement policies in those jurisdictions. In some countries, including countries in the EU, 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. To obtain reimbursement or pricing approval in some countries, governmental authorities adopt a number of different methodologies for assessing drug costs and reimbursement levels. These include comparisons with currently available medicines for the same indication and / or cost effectiveness assessments as the basis for negotiation. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, and in particular our European expansion efforts, could be materially harmed. If the FDA or other applicable** regulatory ~~changes~~ **authorities approve generic products that compete with Rezdiffra** , ~~guidance our partners' product candidates,~~ the sales of **Rezdiffra** ~~our product candidates~~ would be adversely affected.Once an NDA or marketing authorization application outside the United States is approved,the product covered thereby becomes a " listed drug " that can,in turn,be cited by potential competitors in support of approval of an abbreviated new drug application in the United States **or equivalent marketing authorization application outside the United States** .Agency regulations and other applicable regulations and policies provide incentives to manufacturers to create modified,non- infringing versions of a drug to facilitate the approval of an abbreviated new drug application or other application ~~for or~~ **for** ~~interpretations approved,the product covered thereby becomes a " listed drug " that can,in turn,be cited by potential competitors in support of approval of an abbreviated new drug application in the United States.Agency regulations and other applicable regulations and policies provide incentives to manufacturers to create modified,non- infringing versions of a drug to facilitate the approval of an abbreviated new drug application or other application for~~ generic substitutes in the United States and in nearly every pharmaceutical market around the world.These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient (s),dosage form,strength,route of administration and conditions of use,or labeling,as our product and that the generic product is bioequivalent to our product,meaning it is absorbed in the body at the same rate and to the same extent as our product.These generic equivalents,which must meet the same quality standards as branded pharmaceuticals,would be significantly less costly than our product to bring to market,and companies that produce generic equivalents are generally able to offer their products at lower prices.Thus,after the introduction of a generic competitor,a significant percentage of the sales of any branded product are typically lost to the generic product.Accordingly,competition from generic equivalents to **Rezdiffra** ~~our product or any of our partners' future products,if any,~~ would materially adversely affect our future revenue,profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made ~~and expect to make in our~~ **.We currently rely on a limited number of specialty pharmacies** ~~or~~ **for** ~~any~~ **distribution** of **Rezdiffra in the United States,and the loss of one** ~~our~~ **or more of these specialty pharmacies** ~~partners' product candidates,including resmetirom.Competition that our~~ **or their failure to effectively distribute Rezdiffra** ~~or any of our partners' products may face from generic versions of our products~~ could materially **harm** ~~and adversely impact~~ our **business** ~~future revenue,profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates~~ . ~~Resmetirom has~~ **Rezdiffra is currently** only ~~been studied in~~ **available for distribution through** a limited number of **specialty**

pharmacies in the United States.These specialty pharmacies account for all of our revenue.A specialty pharmacy is a pharmacy that specializes in the dispensing of medications for complex or chronic conditions that often require a high level of patient education and ongoing management.The use of specialty pharmacies involves certain risks,including,but not limited to,risks that these specialty pharmacies:• may not serve a significant portion of our expected patient population;• may not provide us accurate or timely information regarding their inventories,the number of patients ~~.Following commercial launch~~ **using Rezdiffra or complaints about Rezdiffra;• reduce their efforts or discontinue to sell or support Rezdiffra** , **particularly** if **competing therapies enter the marketplace;•** ~~approved,resmetirom will be available to a much larger number of patients,and we~~ do not **devote** ~~know whether~~ the **resources necessary to sell Rezdiffra or support** ~~results of resmetirom' s use in such larger number of~~ patients ~~will~~ **;• are** be ~~consistent with the~~ **unable to satisfy financial obligations to us or others;or •** will ~~be changed,~~ **cease operations. If one or more of** ~~or~~ **our** ~~what~~ **specialty pharmacies do not fulfill** ~~the~~ **their contractual obligations to us, or refuse or fail to adequately serve patients, or their agreements are terminated without adequate notice, shipments of Rezdiffra, and associated revenues, could be adversely affected. We expect that it would take a significant amount of time if we were required to replace one or more of our specialty pharmacies. In addition, if we determine to modify our distribution strategy, we may experience disruptions in the distribution of Rezdiffra, which could adversely** impact **our business. If estimates** of **the size of the potential market for Rezdiffra is overstated or data we have used to identify physicians is inaccurate, our ability to earn revenue to support our business could be materially adversely affected. We have relied on external sources, including market research funded by us and third parties, and internal analyses and calculations to estimate the potential market opportunities for Rezdiffra. The externally sourced information used to develop these estimates has been obtained from sources we believe to be reliable, but we have not verified the data from** such ~~changes~~ **sources, and their accuracy and completeness cannot be assured. With respect to Rezdiffra, our internal analyses and calculations are based upon management' s understanding and assessment of numerous inputs and market conditions. These understandings and assessments necessarily require assumptions subject to significant judgment and may prove to be inaccurate. As a result, our estimates of the size of these potential market for Rezdiffra could prove to be overstated, perhaps materially. In addition, we are relying** on **third- party data to identify the physicians who treat the majority of MASH patients in the United States and to determine how to deploy** our **resources to market to those physicians; however, we may not be marketing to the appropriate physicians and may therefore be limiting our market opportunity. In addition, our market opportunity could be reduced if a regulator limits the proposed treatment population for any future product candidate, similar to the limited population for which Rezdiffra was approved. In either circumstance, even if we obtain regulatory approval, we may be unable to commercialize the product on a scale sufficient to generate significant revenue from such** product candidates, **which could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock. Product liability lawsuits brought against us could cause us to incur substantial liabilities and could limit commercialization of Rezdiffra or any future product candidates that we may develop. We face an inherent risk of product liability lawsuits related to the testing of any product candidates in human clinical trials and an even greater risk in connection with the commercialization of Rezdiffra. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling any approved product. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for Rezdiffra or any of our future approved products; • injury to our reputation; • withdrawal of clinical trial participants; • termination of clinical trial sites or entire trial programs; • significant litigation costs; • substantial monetary awards to or costly settlements with patients or other claimants; • product recalls or a change in the indications for which products may be used; • loss of revenue; • diversion of management and scientific resources from our business operations; and • the inability to commercialize our product candidates. We are highly dependent upon consumer perceptions of us and the safety and quality of Rezdiffra and any future product we commercialize. We could be adversely affected if we are subject to negative publicity. We could also be adversely affected** if any **of our products or any similar products distributed by other companies prove to be** , **or are asserted to be, harmful to patients. Also, because of our dependence upon consumer perceptions, any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our results of operations. Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we may need to further increase our insurance coverage as we begin additional clinical trials or if we successfully commercialize additional drug candidates. Insurance coverage is increasingly expensive. 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. Risks Related to Product Development and Regulatory Approval Pharmaceutical research and development is very expensive, time- consuming and difficult to design and implement and involves uncertain outcomes. Furthermore, the results of preclinical studies and earlier clinical trials are not always predictive of future results. Any product candidate that we advance into clinical trials may not have favorable results in later clinical trials or receive regulatory approval. Drug development is an expensive, high- risk, lengthy, complicated, resource intensive process. In order to successfully develop products, we must, among other things: • identify potential product candidates; • submit for and receive regulatory approval to perform clinical trials; • conduct appropriate preclinical and clinical trials, including confirmatory clinical trials, according to good laboratory practices and good clinical practices and disease- specific expectations of the FDA and other regulatory bodies; • select and recruit clinical investigators and subjects for our clinical trials; • obtain and correctly interpret data establishing adequate safety of our product candidates and demonstrating with statistical**

significance that our product candidates are effective for their proposed indications, as indicated by the achievement of specified endpoints; • receive regulatory approvals for marketing; • manufacture the product candidates according to cGMP and other applicable standards and regulations. We will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are safe and effective, with a favorable benefit- risk profile, for use in our target indications before we can seek regulatory approvals for commercial sale. Clinical trials are expensive, difficult to design and implement, can take ~~may~~ **many years to complete and are uncertain as to outcome. Delay or failure can occur at any stage of development, including after commencement of any of our clinical trials. In addition, success in early clinical trials does not mean that later clinical trials will** be ,corporate changes,and deposit accounts.Additionally,the Loan Agreement contains affirmative and restrictive financial covenants **commencing on January 1,2023** ,including maintenance of a minimum cash,cash equivalents and liquid funds covenant of $ 35.0 million,which may decrease in certain circumstances if the Company achieves both a certain FDA approval for resmetirom and a revenue milestone (the " Minimum Cash Covenant ").The Loan Agreement also includes a revenue- based covenant (the " Revenue Covenant ") that could apply commencing at or after the time that financial reporting ~~became~~ **is** due for the quarter ~~end~~ **ending** September 30,2024;however,the Revenue Covenant will be ~~automatically~~ waived ~~pursuant to the terms of the Loan Agreement~~ at any time in which ~~we~~ **the Company** ~~maintain~~ **maintains** ,as measured monthly ~~,~~(i) a certain level of cash,cash equivalents and liquid funds relative to ~~the~~ **outstanding Hercules** debt ~~outstanding under the Loan Agreement~~ or (ii) a market capitalization of at least $ 1.2 billion. ~~Unless waived~~ **The Revenue Covenant,** as ~~a result~~ **and when effective on or after November** of **2024** ~~the foregoing~~ , **would** ~~the Revenue Covenant requires~~ **require** the Company to ~~achieve~~ **maintain** a minimum amount of trailing three- month net product revenue.Our business may be adversely affected by these restrictions **on our ability** . If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs ~~after we begin participating in these programs~~ , we could be subject to additional rebate requirements, penalties, or other sanctions, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects **. A number of government pricing programs create certain price reporting obligations** . Under the Medicaid Drug Rebate program, a participating manufacturer is required to pay a rebate to each state Medicaid program for its covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by the state Medicaid program as a condition of having federal funds being made available for drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by the manufacturer on a monthly and quarterly basis to CMS. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the ~~U~~ **United States in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions** . ~~S~~ **See the section titled " Business — Government Regulation — Pharmaceutical Price Reporting " in this Annual Report for more information** . **Under the Medicaid Drug Rebate program, a participating manufacturer is required to pay a rebate to each state Medicaid program for its covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by the state Medicaid program as a condition of having federal funds being made available for drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by the manufacturer on a monthly and quarterly basis to CMS. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the United States** in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions. If we fail to pay the required rebate amount or report pricing data on a timely basis, we may be subject to civil monetary penalties and / or termination from the Medicaid Drug Rebate program. Additionally, civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we fail to submit the required price data on a timely basis, or if we misclassify or misreport product information. CMS could also decide to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. The ACA (addressed further above in the section ~~on~~ **titled** " ~~--~~ **Business — Government Regulation —** U. S. Healthcare Reform ") made significant changes to the Medicaid Drug Rebate Program, and CMS issued a final regulation to implement the changes to the Medicaid Drug Rebate Program under the ACA. CMS also issued a final regulation that modified prior Medicaid Drug Rebate Program regulations to permit reporting multiple best price figures with regard to value based purchasing arrangements; and provide definitions for " line extension, " " new formulation, " and related terms, with the practical effect of expanding the scope of drugs considered to be line extensions that are subject to an alternative rebate formula. Our failure to comply with these price reporting and rebate payment options, as well as pharmaceutical benefit manager " accumulator " programs, could negatively impact our financial results. Federal law requires that a manufacturer also participate in the 340B Drug Pricing program in order for federal funds to be available for the manufacturer' s drugs under Medicaid and Medicare Part B ~~. The 340B program requires participating manufacturers to agree to charge no more than the 340B " ceiling price " for the manufacturer' s covered outpatient drugs to a specified " covered entities, " including community health centers and other entities that receive certain federal grants, as well as hospitals that serve a disproportionate share of low- income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program~~ . If we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price, we could be subject to significant civil monetary penalties and / or such failure also could be grounds for HRSA to terminate our agreement to participate in the 340B program, in which case our covered outpatient drugs would no longer be eligible for federal payment under the Medicaid or Medicare Part B program. Further, the IRA established a Medicare Part D inflation rebate scheme and a drug price negotiation program, with the first negotiated prices to take effect in 2026. It

also makes several changes to the Medicare Part D benefit, including the creation of a new manufacturer discount program in place of the current coverage gap discount program (beginning in 2025). Manufacturers may be subject to civil monetary penalties for certain violations of the negotiation and inflation rebate provisions and an excise tax during a noncompliance period under the negotiation program. Drug manufacturers may also be subject to civil monetary penalties with respect to their compliance with the new Part D manufacturer drug discount program. Pricing and rebate calculations are complex, vary across products and programs, and are often subject to interpretation by the manufacturer, governmental agencies, and courts. A manufacturer that becomes aware that its Medicaid reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, is obligated to resubmit corrected data up to three years after those data originally were due. Restatements and recalculations increase the costs for complying with the laws and policies governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. They also may affect the 340B ceiling price and therefore liability under the 340B program. Finally, in order to be eligible to have its products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs (" VA "), Department of Defense (" DoD "), Public Health Service, and Coast Guard (the " Big Four agencies ") and certain federal grantees, a manufacturer is required to participate in the VA Federal Supply Schedule (" FSS ") pricing program, established under Section 603 of the Veterans Health Care Act of 1992. Under this program, the manufacturer is obligated to make its covered drugs available for procurement on an FSS contract and charge a price to the Big Four agencies that is no higher than the Federal Ceiling Price (" FCP "), which is a price calculated pursuant to a statutory formula. The FCP is derived from a calculated price point called the " non- federal average manufacturer price " (" Non FAMP "), which the manufacturer calculates and reports to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non FAMP filing can subject a manufacturer to significant penalties for each item of false information. The FSS contract also contains extensive disclosure and certification requirements. If we overcharge the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, we will be required to refund the difference to the government. Failure to make necessary disclosures and / or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and any response to government investigation or enforcement action, would be expensive and time- consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Under Section 703 of the National Defense Authorization Act, a manufacturer is required to pay quarterly rebates to DoD on utilization of its innovator products that are dispensed through DoD' s Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non FAMP and FCP for the calendar year that the product was dispensed. A manufacturer that overcharges the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, is required to refund the difference to the government. Failure to make necessary disclosures and / or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. If **we** ~~any product liability lawsuits~~ are **found in violation** ~~successfully brought against us or any~~ of **federal** ~~our~~ **or** ~~collaborative partners~~ **state " fraud and abuse " laws**, we may ~~incur substantial liabilities and may~~ be required to ~~limit commercialization of~~ **pay a penalty** ~~our~~ **or** ~~product candidates. We face an inherent risk of product liability lawsuits related to the testing of our product candidates in seriously ill patients and will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims~~ may be **suspended from** ~~brought against us or our partners by participants~~ **participation** ~~enrolled~~ in **federal** ~~our~~ **or state** ~~clinical trials, patients,~~ healthcare ~~providers or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any of our future approved products; • injury to our reputation; • withdrawal of clinical trial participants; • termination of clinical trial sites or entire trial~~ programs **,** ~~; • significant litigation costs; • substantial monetary awards to or costly settlements with patients or other claimants; • product recalls or a change in the indications for~~ which ~~products~~ may **adversely affect** ~~be used; • loss of revenue; • diversion of management and scientific resources from~~ our business **, financial condition, results of** operations ~~;~~ and **prospects** ~~• the inability to commercialize our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us~~ and the **value** ~~safety and quality~~ of our ~~products~~ **common stock** . **In the United States,** ~~We could be adversely affected if~~ we are subject to **various federal and state healthcare " fraud and abuse " laws, including anti- kickback laws, false claims laws and other laws intended to reduce fraud and abuse in federal and state healthcare programs. Although we seek to structure our business arrangements in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, it is possible that our practices may be challenged under these laws. Violations of fraud and abuse laws may be punishable by criminal and / or civil sanctions, including fines or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U. S. government, and our business, financial condition, results of operations and prospects and the value of our common stock may be adversely affected. Our reputation could also suffer. In addition, private individuals have the ability to bring actions on behalf of the government under the federal False Claims Act as well as under the false claims laws of several states. See the section titled " Business — Government Regulation — Other Healthcare Laws " in this Annual Report for more information. Under the ACA and certain state laws, we are required to report information on payments or transfers of value to any U. S. physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, or certified nurse- midwives (in each case who are not bona fide employees of the applicable manufacturer that is reporting the payment) and teaching hospitals, which is posted in searchable form on a public website. Failure to submit required information may result in civil monetary penalties.**

Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. In addition to the federal government, some states, as well as other countries, including France, require the disclosure of certain payments to healthcare professionals. The Health Insurance Portability and Accountability Act of 1996 (“ HIPAA ”), state, and foreign privacy laws may limit access to information identifying those individuals who may be prospective users or limit the ability to market to them. Some of these laws are new or ambiguous as to what is required to comply with their requirements, and we could be subject to penalties if it is determined that we have failed to comply with an applicable legal requirement. We are subject to anti- corruption laws and trade control laws, as well as other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures, legal expenses, and negative publicity **which could adversely affect our business, financial condition, results of operations and prospects and the value of our common stock. Our operations are currently subject to anti- corruption laws, including the U. S. Foreign Corrupt Practices Act (“ FCPA ”). In addition, if we expand sales of Rezdiffra to other jurisdictions, we' ll be subject to anti- corruption or similar laws that apply in countries where we do business. The FCPA and these other laws generally prohibit us, our employees and our intermediaries from making prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted** . We ~~could~~ **are** also **subject to other laws and regulations governing** ~~be adversely affected if any of our products or~~ **our** ~~any similar products distributed~~ **international operations, including regulations administered** by **the U. S. Department of Commerce’ s Bureau of Industry and Security, the U. S. Department of Treasury’ s Office of Foreign Assets Control, and various non- U. S. government entities, including applicable export control regulations, economic sanctions on countries and persons, customs requirements, currency exchange regulations and transfer pricing regulations (collectively, Trade Control laws). We may not be effective in ensuring our compliance with all applicable anti- corruption laws, including the FCPA or** other **legal requirements** ~~companies prove to be~~ , ~~or~~ **including Trade Control laws. If we** are **not in compliance** ~~asserted to be, harmful to patients. Also, because of our dependence upon consumer perceptions, any adverse publicity associated~~ with ~~illness or~~ **the FCPA and** other **anti- corruption laws** ~~adverse effects resulting from patients’ use or misuse of our~~ **or** ~~products or any similar products distributed by~~ **Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and** other ~~companies~~ **sanctions and remedial measures, and legal expenses, which** could have **an** ~~a material~~ adverse impact on our **business, financial condition,** results of operations **and prospects and the value of our common stock** . ~~We do not~~ **Likewise, even an investigation by US or foreign authorities of potential violations of the FCPA other anti- corruption laws or Trade Control laws could have an adverse impact on our reputation, business, financial condition, results of operations and prospects and the value of our common stock. Disruptions at the FDA and other government agencies caused by the change in presidential administration, funding shortages or potential funding shortages could hinder their ability to hire and retain key leadership and other personnel, delay or prevent new products and services from being developed or commercialized in a timely manner, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to operate, including to review and approve new products, provide feedback on clinical trials and development programs, meet with sponsors and otherwise review regulatory submissions can be affected by a variety of factors, including government budget and funding levels; ability to hire and retain key personnel and accept the payment of user fees; and statutory, regulatory, and policy changes, including as a result of shifting policy priorities of the current presidential administration and political appointees tasked to oversee the agency, among other factors. Average review times at the agency may fluctuate as a result. In addition, government funding of other government agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and / or approved by necessary government agencies or to otherwise respond to regulatory submissions, which would adversely affect our business. Over the last several years, the U. S. government has shut down multiple times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities.** ~~currently~~ **Currently** ~~hold~~ **, federal agencies in the United States are operating under a continuing resolution that is set to expire on March 14, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our** product **development activities for the U. S. market could be impacted. If a prolonged government shutdown occurs, it could significantly impact the** ~~liability~~ -- **ability** ~~insurance coverage. Prior to commercialization~~ of **the FDA** ~~our product candidates, we will need~~ to **timely review and process** ~~purchase insurance coverage. As a result, we may be unable to maintain or~~ **our regulatory submissions, which** ~~obtain sufficient insurance at a reasonable cost to protect us against losses that~~ could have a material adverse effect on our business. ~~These liabilities~~ **Failure to comply with health and data protection laws and regulations** could **lead** ~~prevent or interfere with our product development and commercialization efforts. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash resources and adversely affect our business, financial condition and results of operations. Our employees, contractors, vendors and partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading. We are exposed~~ to **government enforcement actions (which** ~~the risk of fraud or other misconduct by our employees, contractors, vendors or partners. Misconduct by these parties~~ could include **civil or criminal penalties), private litigation and / or adverse publicity, and could negatively affect our operating results and business. We may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA imposes privacy and security obligations on covered entity health care providers, health**

plans, and health care clearinghouses, as well as their " business associates " – certain persons or covered entities that create, receive, maintain, or transmit protected health information in connection with providing a specified service or performing a function on behalf of a covered entity. We could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly receive individually identifiable health information maintained by a HIPAA- covered entity in a manner that is not authorized or permitted by HIPAA. Failing to take appropriate steps to keep consumers' personal information secure may also constitute unfair acts or practices in or affecting commerce in violation of Section 5 (a) of the Federal Trade Commission Act (the " FTCA "), 15 U. S. C § 45 (a). The FTC expects a company' s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities. Further, certain state laws govern the privacy and security of personal information. For example, to the extent we collect California resident personal information, we may also be subject to the CCPA. The CCPA, created a comprehensive privacy framework which granted California residents several new rights with regard to their personal information. The CCPA was amended by the California Privacy Rights Act (" CPRA ") ballot initiative which as of January 1, 2023 has introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency (" CPPA "). ~~failures -~~ Failure to comply with **~~FDA~~ the CCPA may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California residents have the right to bring a private right of action in connection with data breaches. These claims may result in significant liability and damages. Similar laws have been passed in numerous other states. Other states have proposed new privacy laws which, 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. These laws and** regulations **~~,~~ are evolving and may impose limitations on our business activities. The existence of comprehensive privacy laws in different states in the country may make our compliance obligations more complex and costly and may increase the likelihood that we may be subject** to **~~provide accurate~~ enforcement actions or otherwise incur liability for noncompliance. There are also states that are specifically regulating health** information **~~to~~. For example, Washington' s My Health My Data Act, which became effective on March 31, 2024, regulates the collection and sharing of health information and 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, ~~the~~ other ~~FDA~~ 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 are discussions in the U. S. Congress of new comprehensive federal data privacy laws to which we could become subject to, if enacted. All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. The obligations** to comply with **new privacy ~~federal and state healthcare fraud and abuse~~** laws **may require ~~and regulations, to report financial information or data timely, completely or accurately, or to disclose unauthorized activities to~~** us **~~. In particular~~ , among ~~sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and~~** other **things, to update ~~abusive practices. These laws and regulations may restrict or~~ our notices ~~prohibit a wide range of pricing, discounting, marketing~~** and **develop new processes internally ~~promotion, sales commission, customer incentive programs~~** and **with our ~~other business arrangements. Third~~ third** - party **~~misconduct could also involve the improper use~~ collaborators, service providers, contractors or consultants to facilitate consumer rights requests, and such laws may impose restrictions on our processing** of **personal** information **~~obtained in~~ that may impact** the **~~course of clinical trials~~ way we operate our business. Any failure or perceived failure by us to comply with any applicable federal , ~~which~~ state or foreign laws and regulations relating to data privacy and security** could result in **damage ~~regulatory sanctions and serious harm~~** to our reputation **~~. We have adopted a Code of Business Conduct and Ethics~~ , as well as proceedings or litigation by governmental agencies or ~~but it is not always possible to identify and deter misconduct, and the~~ other third parties, including class action privacy litigation ~~precautions we take to detect and prevent this activity may not be effective~~** in **certain jurisdictions, which would subject ~~controlling unknown or unmanaged risks or losses or in protecting~~** us **~~from governmental investigations or other actions or lawsuits stemming from a failure~~** to **~~comply with these laws or regulations. If any such actions are instituted against us resulting from this misconduct and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of~~** significant fines **, sanctions, awards, injunctions, penalties or judgments. We may be subject to fines, penalties, or private actions in the event of non- compliance with such laws. The CCPA, the CPRA** or other **~~sanctions~~ domestic privacy and data protection laws and regulations may increase our compliance costs and potential liability . ~~We enter into various contracts in the normal course of~~ In addition, such requirements may require us to modify our data processing practices and policies, utilize management' s time and / ~~our -~~ or divert resources from ~~business in which we indemnify the~~** other **initiatives and projects ~~party to the contract~~ . Any of ~~In the event we have to perform under these -~~ the foregoing ~~indemnification provisions, it~~** could have a material adverse effect on our business, financial condition **~~and ,~~** results of operations **~~liability~~ and prospects** .European data collection is governed by restrictive regulations governing the use,processing and cross- border transfer of personal information.Outside the United States,our clinical trial programs and operations implicate international data protection laws,including the EU General Data Protection

Regulation including as implemented in the UK (collectively,“ GDPR ”).The GDPR increases our responsibility and liability in relation to the processing of personal data of individuals located in the EU.The GDPR,together with the national legislation of the EU member states governing the processing of personal data,places certain obligations on the processing of such personal data including ensuring the lawfulness of processing personal data,health data and samples from clinical trials and adverse event reporting ~~.~~. In **particular,** ~~the~~ **these obligations** ~~normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting~~ and **restrictions concern** ~~other~~ ~~--~~ **the consent of** ~~agreements that contain indemnification provisions. With respect to our academic and other~~ ~~--~~ **the individuals to whom** ~~research agreements, we typically indemnify~~ the ~~institution and~~ **personal data** ~~related~~ **relates where applicable, the processing details disclosed to the individuals, the sharing of personal data with third** parties ~~from losses arising from claims relating to the products~~, ~~processes or services made, used, sold or performed pursuant to~~ the **transfer** ~~agreements for which we have secured licenses, and from claims arising from our or our potential sublicensees' exercise~~ of **personal data out** ~~rights under the agreements. With respect to our commercial agreements, we indemnify our vendors from any third- party product liability claims that could result from the production, use or consumption~~ of the ~~product~~ **EU, security breach notifications** , as well as **substantial potential fines** for **violations** ~~alleged infringements~~ of ~~any patent or other~~ ~~--~~ **the data protection** ~~intellectual property right by a third party. Should our obligation~~ **obligations** ~~to the United States,there are certain unsettled legal issues regarding such data transfers,the resolution of which may adversely affect our ability to transfer personal data or otherwise may cause us to incur significant costs to come into compliance with applicable data transfer impact assessments and implementation of legal data transfer mechanisms.On July 16,2020,the European Court of Justice ruled the EU- U.S.Privacy Shield to be an~~ invalid data transfer mechanism and confirmed that the Model Clauses remain valid,and in June 2021,the ~~EC~~ **European Commission** published updated versions of the Model Clauses,which must be incorporated into new and existing agreements within prescribed timeframes in order to continue to lawfully transfer personal data outside of the EU.Data protection authorities from the different European member states,as well as in the ~~UK~~ **United Kingdom** and Switzerland,have promulgated national privacy laws that impose additional requirements,which add to the complexity of processing and transferring EU personal data,with the ~~UK~~ **United Kingdom** and Switzerland following the EU with the publication of new Model Clauses to be incorporated in all applicable contracts within a specified timeframe in order to legitimize data transfers from those jurisdictions.The UK adopted versions of their Model Clauses during 2022.Our ability to continue to transfer personal data outside of the EU, ~~the UK~~ **United Kingdom** ,or Switzerland may become significantly more expensive and may subject us to increased scrutiny and **liability under the GDPR or similar local laws,and we may experience operating disruptions if we are unable to conduct these transfers in the future.On December,13 2022,the European Commission adopted a draft adequacy decision for the EU- U.S.Data Privacy Framework,which reflects the assessment by the European Commission of the US legal framework.The draft decision concludes that the United States ensures an** under **the GDPR or similar local laws,** ~~an~~ **and we may experience operating disruptions** ~~indemnification provision exceed applicable insurance coverage or~~ if we are ~~denied insurance coverage~~ **unable to conduct these transfers in the future. On December** , **13 2022, the EC adopted a draft adequacy decision for the EU- U. S. Data Privacy Framework, which reflects the assessment by the EC of the U. S. legal framework. The draft decision concludes that the United States ensures an adequate level of protection for personal data transferred from the EU to U. S. companies. After an approval process, the EC is expected to adopt the final adequacy decision, which will allow data to flow freely from the EU to the United States between companies certified under the new framework. Risks associated with operations outside of the United States could adversely affect** our business **. A key component of our strategy is to expand our commercialization of Rezdiffra to Europe** , **pending the receipt of requisite regulatory approvals. International operations and business expansion plans are subject to numerous additional risks, including: • multiple, conflicting and changing laws and regulations such as tax laws, privacy regulations, tariffs, export and import restrictions, employment, immigration and labor laws, regulatory requirements, and other governmental approvals, permits and licenses, compliance with which can increase in complexity as we enter into additional jurisdictions; • difficulties in staffing and managing operations in diverse countries and difficulties in connection with assimilating and integrating any operations and personnel we might acquire into our company; • risks associated with obtaining and maintaining, or the failure to obtain or maintain, regulatory approvals for the sale or use of our products in various countries; • complexities associated with managing government payor systems, multiple payor- reimbursement regimes or patient self- pay systems; •** financial **risks, such as longer payment cycles, difficulty obtaining financing in foreign markets, difficulty enforcing contracts and intellectual property rights, difficulty collecting accounts receivable and exposure to foreign currency exchange rate fluctuations; • general political and economic** ~~condition~~ **conditions in the countries in which** ~~and results of operations could be adversely affected. Similarly, if~~ we ~~are relying~~ **operate, including inflation, political or economic instability, terrorism and political unrest and geopolitical events; and • public health risks, including epidemics and pandemics, and related effects** on ~~a collaborator to indemnify us~~ **new patient starts, clinical trial activity, regulatory agency response times, supply chain, travel** and ~~the collaborator is denied insurance coverage~~ **employee health and availability. Risks Related to Our Intellectual Property Our success depends on** ~~or~~ **our ability** ~~the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available~~ to **protect** ~~indemnify us,~~ our **intellectual property** ~~business, financial condition~~ and **our proprietary technologies** ~~results of operations could be adversely affected~~ . ~~If we fail~~ **Our success depends on our ability** to ~~develop~~ **protect our intellectual property** and **our proprietary technologies. Our** ~~commercialize~~ ~~---~~ **commercial** ~~other~~ **success depends in part on our ability to obtain and maintain patent and / or trade secret protection for our product,** product candidates, **proprietary technologies** ~~we may be unable to grow our business. Although the development and commercialization of resmetirom is our primary focus~~ , ~~as part of our longer- term growth strategy, we plan to evaluate the development~~ and ~~commercialization of other~~ - **their uses** ~~therapies. We will evaluate internal opportunities from our compound~~

~~libraries~~ , ~~and also may choose to in- license or acquire other product candidates~~ as well as ~~commercial products~~ **our ability** to ~~treat~~ **freely operate without infringing upon the proprietary rights of others. We can provide no assurance that our patent applications or those of our licensors will result in additional** ~~patients~~ **patents** ~~suffering from disorders~~ **being issued or that issued patents will afford sufficient protection against competitors** with ~~high unmet medical needs and~~ **similar technologies, nor can we provide any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only** limited ~~treatment options~~ **protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage** . ~~These~~ **This failure to properly protect** ~~other~~ -- **the intellectual property rights relating to our product or** product candidates may require additional, time- consuming..... lose key senior management personnel, it could have a material adverse effect on our ~~business~~ **financial condition** and ~~stock price~~ **results of operations. While we have licensed rights to issued patents in the United States and other jurisdictions for resmetirom and its use, we cannot be certain that the claims in issued patents will not be found invalid or unenforceable if challenged** . We **cannot be certain that the claims in owned** ~~are highly dependent on principal members of our senior management team, including our President~~ and ~~Chief Executive~~ **licensed patent applications covering our product and product candidates will be considered patentable by the United States Patent and Trademark** ~~Officer~~ **Office** ~~, Bill Sibold,~~ **(" USPTO ")** and **valid by courts in the United States** ~~our~~ **or by** ~~President, Research and Development and Chief Medical Officer, Rebecca Taub, M. D. These executives each have significant pharmaceutical industry experience. The loss of any senior member of our management team or scientific staff, including Mr. Sibold or Dr. Taub, could have a material adverse effect on our business and stock price. Our management and other~~ -- **the patent offices** ~~employees may voluntarily terminate their employment with us at any time. The loss of the services of these or other key personnel, or the inability to attract~~ and **courts** ~~retain additional qualified personnel, could result~~ in **foreign jurisdictions** ~~delays to development or approval, loss of sales and diversion of management resources. In addition, we depend on our ability to attract and retain other highly skilled personnel. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all, which would negatively impact our development and commercialization programs~~ . Even if we ~~obtain FDA approval if we~~ owned and licensed patent applications covering our **product and** product candidates,the patents may not be enforced against competitors.For example,a formulation patent may not be enforced against those making and marketing a product that has the same active pharmaceutical ingredient in a different formulation that is not claimed in the formulation patent.Method- of- use patents protect the use of a product for the specified method or for treatment of a particular indication.This type of patent may not be enforced against competitors making and marketing a product that has the same active pharmaceutical ingredient but is used for a method not claimed in the patent.Moreover,even if competitors do not actively promote their product for our targeted indications,physicians may prescribe these products " ~~of~~ **off - label. " Although off- label prescriptions may infringe, induce, or contribute to the infringement of method- of- use patents, the practice is common and such infringement may be difficult to prevent or prosecute. Our composition- of- matter patent licensed from Roche relating to** resmetirom **is scheduled to expire in** ~~or any other future product candidate, we may never obtain approval or commercialize our products outside of~~ the United States **in 2026. Our co-owned patents and pending patent applications that cover our particular solid form** . ~~expire in the United States in 2026.Our co- owned patents and pending patent applications that cover our particular solid form,~~ dosage,method of manufacturing,and uses of resmetirom to treat various indications are scheduled to expire in 2033.Our exclusively- owned pending patent applications that cover companion diagnostics,various solid forms of resmetirom,combination therapy,method of use,and method of manufacturing,if issued,are expected to expire between 2037 and ~~2042~~ **2044** .Our exclusively- owned pending patent application that covers other THR ~~beta~~ **- β** analogs and uses thereof,if issued,is expected to expire in 2043.While patent term adjustments or patent term extensions could result in later expiration dates for each of these patents,there can be no assurances that we will receive any patent adjustments or patent term extensions.The patent application process and patent maintenance and enforcement are subject to numerous risks and uncertainties,and there can be no assurance that we or any of our future development partners will be successful in protecting our **product and** product candidates by obtaining and defending patents.These risks and uncertainties include the following:• the USPTO and various foreign governmental patent agencies require compliance with a number of procedural,documentary **,fee payment and other provisions during the patent process and after a patent has issued.There are situations in** which **noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than** would ~~limit~~ **otherwise have been the case; • patent applications may not result in any patents being issued; • patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable** ~~our~~ **or** ~~ability~~ **otherwise may not provide any competitive advantage; • we and our licensor (s) may not have been the first** to ~~realize~~ **make the inventions covered by pending patent applications or issued patents; • we and our licensor (s) may not have been the first to file patent applications for our product or product candidates or the compositions developed, or for** their ~~full market potential. In order to market any~~ **uses; • others may independently develop identical, similar or alternative** products **or compositions and uses thereof; • we and our licensor (s)' disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability; • others may design around our owned and licensed patent claims to produce competitive products which fall** outside of **the scope of the patents; • others may identify prior art or other bases which could invalidate our or our licensor (s)' patents; • our competitors might conduct research and development activities in** the United States ~~, we must establish~~ and ~~comply with numerous and varying regulatory requirements of~~ other countries **that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where us and our licensor (s) do not have**

patent rights, and then use the information learned from such activities to develop competitive products for sale in major commercial markets; • there may be significant pressure on the United States government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding **worldwide health concerns;** ~~clinical trial design, safety~~ and **• ~~efficacy. Clinical trials conducted in one country~~ countries other than the United States** may ~~not be accepted~~ **have patent laws less favorable to patentees than those upheld** by **United States courts** ~~regulatory authorities in other countries~~, **allowing** ~~and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking~~ foreign **competitors a better opportunity** ~~regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials, which would be costly and time consuming. Regulatory requirements can vary widely from country~~ to ~~country~~ **create, develop** and **market competing** ~~could delay or prevent the introduction of our~~ products ~~in those countries. Satisfying these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays~~. In addition, **we rely on the protection of** our ~~failure~~ **trade secrets and proprietary know- how. Although we have taken steps to protect our trade secrets and unpatented know- how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that any of these parties would not breach the agreements to disclose any proprietary information, including trade secrets, and we may not be able** to obtain ~~know- how,including entering into confidentiality agreements with third parties,and confidential information and inventions agreements with employees,consultants and advisors,we cannot provide any assurances that any of these parties would not breach the agreements to disclose any proprietary information,including trade secrets,and we may not be able to obtain~~ adequate remedies for such breaches.Further,third parties may still obtain this information by other means,such as breaches of our physical or computer security systems.Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult,expensive and time- consuming,and the outcome is unpredictable.Moreover,third parties may come upon this or similar information lawfully and independently.We would have no right to prevent them,or those to whom they communicate it,from using that technology or information to compete with us.Further,intellectual property rights have limitations and do not necessarily address all potential threats to our competitive position.If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know- how,our business may be harmed. ~~Recent~~ **Our rights to develop and commercialize our product are subject in part to the terms and conditions of a license to resmetirom granted to us by Roche.Pursuant to the terms of the Roche Agreement,we assumed control of all development and commercialization of resmetirom and hold exclusive worldwide rights for all potential indications.Under the Roche Agreement,Roche exclusively licensed certain** patent **rights** ~~reform legislation could increase the uncertainties~~ and **know** ~~costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.On September 16,2011,the Leahy~~ - **how relating to resmetirom in exchange for consideration consisting of an upfront payment,milestone payments tied to the achievement of product development and** regulatory ~~approval in any country may delay~~ **milestones, and royalty payments based on net sales of products containing resmetirom, including Rezdiffra,** or **another licensed product, subject to certain reductions. The Roche Agreement will expire, unless earlier terminated pursuant to other provisions thereof, on the last to occur of (i) the expiration of the last valid claim of a licensed patent covering the manufacture, use or sale of products containing resmetirom, or (ii) ten years after the first sale of a product containing resmetirom. Under the Roche Agreement, Roche controls prosecution of the licensed patent rights, although we** have **a right to comment** ~~negative effects on the process for regulatory approval in other countries~~. We do not have **, nor have we had,** any **material disputes with Roche regarding the Roche Agreement. However, if there is any future dispute between us and Roche regarding the parties' rights under the Roche Agreement, our ability to develop and commercialize resmetirom, or any other product candidate covered by the Roche Agreement, may be materially harmed. Any uncured, material breach under the Roche Agreement could result in our loss of exclusive rights to resmetirom and may lead to a complete termination of the Roche Agreement and force us to cease product development efforts for resmetirom. We may fail to comply with any of our obligations under agreements pursuant to which we license rights or technology, which could result in the loss of rights or technology that are material to our business. We may enter into license agreements from time to time. Licensing of intellectual property is important to our business and involves complex legal, business and scientific issues. Disputes may arise regarding intellectual property subject to a license agreement, including but not limited to: • the scope of rights granted under the license agreement and other interpretation- related issues; • the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights; • our diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by us and our licensors and collaborators; and • the priority of invention of patented technology. If disputes over intellectual property and other rights that we have licensed or acquired from third parties 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 or** product candidates ~~approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we or our partners fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our products will be harmed~~. If we do not obtain protection under the Hatch- Waxman Act and similar foreign legislation by extending the term of patents covering ~~each of~~ **our product** ~~our~~ - **or** product candidates, our business may be materially harmed. Depending upon the timing, duration and conditions of FDA marketing approval of our ~~product~~ **products** ~~candidates~~, one or

more of our United States patents may be eligible for limited patent term extension under Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. **A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended.** However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product may not extend beyond the current patent expiration dates and competitors may obtain approval to market competing products sooner. As a result, our revenue could be potentially materially reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. ~~If we~~ **Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of** ~~or~~ **our patent applications and the enforcement** ~~our~~ **or** ~~partners market products in~~ **defense of our issued patents. On September 16, 2011, the Leahy- Smith America Invents Act (the " Leahy- Smith Act ") was signed into law. The Leahy- Smith Act includes** a ~~manner~~ **number of significant changes to U. S. patent law. These include provisions** that **affect** ~~violates fraud and abuse and other~~ **the way patent applications will** ~~healthcare laws, or if we or our partners violate government price reporting laws, we or our partners may~~ be **prosecuted** ~~subject to administrative civil~~ and ~~/ or criminal penalties~~ **may also affect patent litigation** . **In particular** ~~Although we do not currently have any products on the market~~, **under** ~~if we obtain FDA approval for our product candidates, and begin commercializing those~~ **the** ~~products in~~ **Leahy- Smith Act,** the United States ~~, our operations may~~ **transitioned in March 2013 to a " first inventor to file " system in which the first inventor to file a patent application will** be **entitled to the patent.** ~~directly, or indirectly through our prescribers, customers and third~~ **Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and a patent may become subject to post** ~~party payors, subject to various U. S. federal and state healthcare laws and regulations. These laws include~~ **grant proceedings including opposition** , ~~among~~ **derivation, reexamination, inter partes review or interference proceedings challenging our patent rights or the patent rights of** others ~~, the U~~. **An adverse determination in any** ~~S. federal Anti- Kickback Statute and the U. S. federal civil and criminal false claims laws. At~~ such ~~time~~ **submission proceeding** ~~if ever, as we or any of our~~ **or litigation** ~~partners market any of our future approved products, it is possible that some of our business activities and / or our partners~~ could **reduce** ~~be subject to challenge under one or more of these laws. Federal false claims, false statements and civil monetary penalties laws prohibit, among others, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim to the federal government, or knowingly concealing or knowing and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. The federal healthcare program Anti- Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they~~ **the scope** ~~do not qualify for~~ **or enforceability** ~~an exception or safe harbor. There are other federal and state anti- fraud and abuse laws and regulations, as well as laws that require reporting~~ of ~~payments to certain health care professionals and adoption of certain compliance program requirements~~ , ~~that will govern our~~ **or invalidate** ~~operations if and when we begin commercializing our products. In addition~~ , ~~we and / or~~ **our** ~~our partners may be subject to patient~~ **patent rights** ~~data privacy and security regulation~~ , ~~including the Health Insurance Portability and Accountability Act of 1996, and its implementing regulations (" HIPAA "), which impose specified requirements relating to the privacy, security and transmission of protected health information. Most states also have statutes or regulations similar to these federal laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. We and / or our partners may be subject to administrative, civil and criminal sanctions for violations of any of these federal and state laws. Pharmaceutical and other healthcare companies have been sued or found to have violated these laws for a variety of promotional and marketing and other activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; inaccurately reporting to pricing services average prices that are then used by federal programs to set reimbursement rates, rebates, and discounts; engaging in off- label promotion; and knowingly submitting false pricing information to the federal government, knowingly misrepresenting that information, or failing to timely submit that information. Pharmaceutical companies may further be found liable for civil monetary penalties for knowing and intentionally overcharging covered entities under the 340B Drug Pricing Program. Additionally, in order to be eligible to have its products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs (" VA "), Department of Defense (" DoD "), Public Health Service, and Coast Guard (the " Big Four agencies ") and certain federal grantees, a manufacturer is required to list its innovator products on a VA Federal Supply Schedule (" FSS ") contract and charge a price to the Big Four agencies that is no higher than the Federal Ceiling Price (" FCP "), which is a price calculated pursuant to a statutory formula. In addition, manufactures must submit to the VA quarterly and annual " non federal average manufacturer price " (" Non FAMP ") calculations for each NDC- 11 of their innovator drugs. Under Section 703 of the National Defense Authorization Act for FY 2008, the manufacturer is required to pay quarterly rebates to DoD on utilization of~~

~~its innovator products that are dispensed through DoD' s Tricare network pharmacies to Tricare beneficiaries. Ensuring that our internal operations and future 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 do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including (depending on the applicable law) criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private ' ' qui tam'' actions brought by individual whistleblowers in the name of the government or refusal to allow us to enter into supply contracts, including government contracts, and the curtailment or restructuring of our operations, any of~~ which could adversely affect our **competitive position** ~~ability to operate our business and our results of operations . If the~~ **Claims by** third parties ~~on~~ **that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in** which we ~~rely~~ **have and** ~~the fields in which we~~ are developing **products and** product candidates.As the biotechnology industry expands and more patents are issued,the risk increases that our **product and** product candidates may be subject to claims of infringement of the patent rights of third parties.Because patent applications are maintained in secrecy until the application is published,we may be unaware of third party patents that may be infringed by commercialization of resmetirom or our other product candidates.Moreover,because patent applications can take many years to issue,there may be currently- pending patent applications that may later result in issued patents that our product **and product** candidates may infringe.In addition,identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents,incomplete databases and the difficulty in assessing the meaning of patent claims.Any claims of patent infringement asserted by third parties would be time consuming and could likely:• result in costly litigation;• divert the time and attention of our technical personnel and management;• cause development delays;• prevent us from commercializing resmetirom ~~for NASH or~~ for **MASH or our** ~~the~~ **other** ~~conduct~~ **product candidates until the asserted patent expires or is held finally invalid or not infringed in a court** of ~~;• divert the time and attention of our technical personnel and management;• cause development delays;• prevent us from commercializing resmetirom for NASH or our other product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of~~ law;• require us to develop non- infringing technology,which may not be possible on a cost- effective basis;or • require us to enter into royalty or licensing agreements.Although no third party has asserted a claim of patent infringement against us as of the filing date of this report,others may hold proprietary rights that could prevent resmetirom or our other product candidates from being marketed.Any patent- related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product **and product** ~~candidate~~ **candidates** or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market resmetirom or our other product candidates.We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms,if at all.In addition,we cannot be sure that we could redesign our product **or product** ~~candidate~~ **candidates** or processes to avoid infringement,if necessary.Accordingly,an adverse determination in a judicial or administrative proceeding,or the failure to obtain necessary licenses,could prevent us from developing and commercializing resmetirom or our other product candidates,which could harm our business,financial condition and operating results.Moreover,we may be subject to a third party preissuance submission of prior art to the USPTO or in addition to interference proceedings,may become involved in opposition,derivation,reexamination,inter partes review,post- grant review or other post- grant proceedings challenging our patent rights or the patent rights of others.An adverse determination in any such submission,proceeding or litigation could reduce the scope of,or invalidate,our patent rights,allow third parties to commercialize our technology or products and compete directly with us,without payment to us,or result in our inability to manufacture or commercialize products without infringing third party patent rights.In addition,if the breadth or strength of protection provided by our patents and patent applications is threatened,it could dissuade companies from collaborating with us to license,develop or commercialize current or future **products and** product candidates **.** We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors,which could be expensive,time consuming,and unsuccessful.Further,our issued patents could be found invalid or unenforceable if challenged in court.If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent directed at **our product or** one of our product candidates,or one of our future product candidates,the defendant could counterclaim that our patent is invalid and / or unenforceable.In patent litigation in the United States,defendant counterclaims alleging invalidity and / or unenforceability are commonplace.Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements,including lack of novelty,obviousness,non- enablement or insufficient written description.Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution.Third parties may also raise similar claims before the USPTO,even outside the context of litigation.The outcome following legal assertions of invalidity and unenforceability is unpredictable.With respect to the validity question,for example,we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution.If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability,we would lose at least part,and perhaps all,of the patent protection on such product **or product** candidate.Such a loss of patent protection would have a material adverse impact on our business Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of

our licensors.An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party.Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms.Our defense of litigation or interference proceedings may fail and,even if successful, **may result in substantial costs and distract our management and other employees.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 ~~and results do not perform our clinical trial activities in accordance with good clinical practices and related regulatory requirements~~ , **continue** ~~we may be unable to obtain regulatory approval for or~~ **our** ~~commercialize~~ **research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring** our product candidates **to market. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock** . We **may not be successful in obtaining** ~~use third- party service providers to conduct and / or oversee the clinical trials of our~~ **or maintaining necessary rights to our product and** product candidates ~~or maintaining necessary rights to our product candidates~~ through acquisitions and in- licenses.We currently have rights to the intellectual property,through licenses from third parties and under patents that we own or co- own,to develop **and market** our **product and** product candidates.Because our programs may require the use of proprietary rights held by third parties,the growth of our business may depend in part on our ability to acquire,in- license,or use these proprietary rights.For example,our **product or** product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others.We may be unable to acquire or in- license any compositions,methods of use,processes,or other third party intellectual property rights from third parties that we identify as necessary for our **product or** product candidates.The licensing and acquisition of third party intellectual property rights is a competitive area,and a number of more established companies are also pursuing strategies to license or acquire third party intellectual property rights that we may consider attractive.These established companies may have a competitive advantage over us due to their size,cash 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 ~~and~~ **an** ~~expect~~ **appropriate return on our investment. We may collaborate with U. S. and foreign academic institutions and industry collaborators** to ~~continue~~ **accelerate our preclinical or clinical research. Typically, these institutions provide us with an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable** to do so **,** ~~for the foreseeable future. We rely heavily on these~~ **the institution may offer the intellectual property rights to other** parties ~~for successful execution of our clinical trials. Nonetheless~~ , **potentially blocking our ability to pursue our program. If** we are ~~responsible~~ **unable to successfully obtain rights to required third party intellectual property rights** ~~for~~ **or** ~~confirming~~ **maintain the existing intellectual property rights we have, we may have to abandon development of** that **program** ~~each of our clinical trials is conducted in accordance with FDA requirements~~ and our **business** ~~general investigational plan~~ and **financial condition could suffer** ~~protocol. The FDA requires us and our third- party service providers to comply with GCP for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate, and that the trial participants are adequately protected~~ . Our reliance on third parties **requires** us to share our trade secrets,which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.Because we rely on third parties to research and develop and to manufacture our **product and** product candidates,we must,at times,share trade secrets with them.We seek to protect our proprietary technology in part by entering into confidentiality agreements and,if applicable,material transfer agreements,consulting agreements or other similar agreements with our advisors,employees,third party contractors and consultants prior to beginning research or disclosing proprietary information.These agreements typically limit the rights of the third parties to use or disclose our confidential information,including our trade secrets.Despite the contractual provisions employed when working with third parties,the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors,are inadvertently incorporated into the technology of others,or are disclosed or used in violation of these agreements.Any of these could impair our competitive position.In addition,these agreements typically restrict the ability of our advisors,employees,third party contractors and consultants to publish data potentially relating to our trade secrets,although our agreements may contain certain limited publication rights.For example,any academic institution ~~that we may~~ that we ~~to publish data potentially relating to our trade secrets,although our agreements may contain certain limited publication rights.For example,any academic institution that we~~ may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration,provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration,in addition to the opportunity to remove confidential or trade secret information from any such publication.In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements.Despite our efforts to protect our trade secrets,our competitors may discover our trade secrets,either through breach of our agreements with third parties,independent development or publication of information by any of our third party collaborators.A competitor' s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.If our trademarks and trade names are not adequately protected,then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.Our registered or unregistered trademarks or trade names may be challenged,infringed,circumvented or declared generic or determined to be infringing on other marks.We

may not be able to protect our rights to these trademarks and trade names,which we need to build name recognition among potential partners or customers in our markets of interest.At times,competitors may adopt trade names or trademarks similar to ours,thereby impeding our ability to build brand identity and possibly leading to market confusion.In addition,there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names.Over the long term,if we are unable to establish name recognition based on our trademarks and trade names,then we may not be able to compete effectively and our business may be adversely affected.Our efforts to enforce or protect our proprietary rights related to trademarks,trade secrets,domain names,copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.We may not be able to protect our intellectual property rights throughout the world.While we have licensed from Roche issued patents directed at resmetirom in the United States and other countries,filing,prosecuting and defending patents on resmetirom in all countries throughout the world would be prohibitively expensive,and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States.In addition,the laws of some foreign countries may not protect intellectual property rights to the same extent as federal and state laws in the United States.Consequently,we may not be able to prevent third parties from practicing their inventions in all countries outside the United States,or from selling or importing products made using our inventions in and into the United States or other jurisdictions.Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and,further,may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States.These products may compete with resmetirom,and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.Many **companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions.The legal systems of certain countries,particularly certain developing countries,** do not **favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Risks Related to Ownership of Our Common Stock The price of our common stock has been, and may continue to be, volatile. Historically, the market price of our common stock has fluctuated over a wide range, and it is likely that the price of our common stock will continue to be volatile in the future. The closing price of our common stock has ranged from $ 171. 37 to $ 354. 85 per share during the year ended December 31, 2024. The market price of our common stock could be impacted due to a variety of factors, including global market or financial developments; prevailing macroeconomic conditions, including potential recession or economic downturns; U. S. market events (including the potential for unusual market trading activity following external short interest developments or social media activity); the outbreak of war or hostilities; MASH therapeutic company developments or FDA developments, regardless of whether occurring generally or specifically as to our clinical trials and development programs; industry- wide events and the following events or developments: • the losses we may incur, including increased losses resulting from costs associated with increases in our clinical trial activity; • our cash position and rate of expenditures; • our ability to meet the estimates and projections of the investment community or that we may otherwise provide to the public; • product revenue; • regulatory decisions, including our ability to receive full regulatory approval for Rezdiffra and our ability to receive regulatory approval for any future product candidates; • changes in laws or regulations applicable to Rezdiffra and any other future product candidates, including but not limited to clinical trial requirements for approvals; • our ability to successfully commercialize Rezdiffra and any other future product candidates, if approved; • developments in patent or other proprietary rights owned or licensed by us, our collaborative partners or our competitors; • disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; • the progress and results of our clinical trials; • public or regulatory concern as to the safety and efficacy of MASH products developed by us or others or public safety generally; • publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts; • introduction of new products or services offered by us or our competitors, or the release or publication of clinical trial results from competing product candidates; • changes in the market valuations of similar companies; • our ability to obtain coverage and adequate reimbursement of Rezdiffra and any future product candidates, if approved; • our ability to effectively manage our growth; • actual or anticipated variations in quarterly operating results; • announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us or our competitors; • any changes to our relationship with any manufacturers, suppliers, licensors, future collaborators or other strategic partners; • our ability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices; • changes to the structure of healthcare payment systems; • our ability to establish collaborations, if needed; • additions or departures of key scientific or management personnel; • litigation; • issuances of debt or equity securities; • sales of our common stock by us or our stockholders in the future or the perception that such sales may occur; • trading volume of our common stock; • changes in accounting practices; • effectiveness of our internal controls; and • other events or factors, many of which are beyond our** control ~~stock and may be deemed to have substantial control over us~~ ;therefore,your

ability to influence corporate matters may be limited. ~~Our officers and directors and certain~~ **Certain** stockholders affiliated and associated with our officers and directors collectively beneficially own approximately ~~34~~ **24** . ~~6~~ **24** % of our outstanding common stock as of December 31, ~~2024~~ **2023** and ~~,~~acting together,may have the ability to substantially affect matters submitted to our stockholders for approval ~~,as well as our management and affairs~~ .This concentration of ownership may have the effect of delaying,deferring or preventing a strategic transaction,even if such a transaction would benefit other stockholders.Anti-takeover provisions in our ~~restated certificate of incorporation (our " Charter~~ **charter documents** ~~"),our Restated Bylaws (our " Bylaws ")~~ and under Delaware law could make an acquisition of our company,which may be beneficial to our stockholders,more difficult and may prevent attempts by our stockholders to replace or remove our current management ~~,which may depress the trading price of our common stock~~ .Provisions in our ~~Charter~~ **charter** and ~~Bylaws~~ **bylaws** may delay or prevent a merger,acquisition or other change of control that stockholders may consider favorable,including transactions in which you might otherwise receive a premium for your shares. ~~Therefore~~ **These provisions include a classified board of directors.In addition , we are governed by the provisions of Section 203 of the Delaware General Corporation Law,which prohibits,with some exceptions,stockholders owning in excess of 15 % of our outstanding voting stock from merging or combining with us.Although we believe** these provisions ~~could adversely affect the price of our common stock.Among other~~ **together** ~~things,our Charter and Bylaws:•~~ provide for ~~a classified~~ **an opportunity to receive higher bids by requiring potential acquirers to negotiate with our** board of directors ~~with~~ **,they would apply even if** ~~three -~~ **the** ~~classes;• permit~~ **offer may be considered beneficial by some stockholders.Future sales and issuances of our common stock** ~~our -~~ **or** ~~board of directors to issue certain shares of preferred stock,with any~~ rights ~~,preferences and~~ **to purchase common stock** does not ~~relieve~~ **have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) is the sole and exclusive forum for the any stockholder to bring: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to** us **or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our Charter or our Bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court' s having personal jurisdiction over any indispensable parties. The amendment of any** of these **provisions,** ~~responsibilities and requirements. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance~~ with ~~regulatory~~ **the exception of the ability of** ~~or~~ **our** ~~GCP requirements~~ **board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require approval by the holders of at least 80 % of** ~~or~~ **our** ~~the~~ **then - outstanding common stock** ~~respective trial plans and protocols~~ . In addition, ~~third parties~~ **as a Delaware corporation, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits, with some exceptions, stockholders owning 15 % or more of our outstanding voting stock from merging or combining with us for a certain period of time. A Delaware corporation** may **opt out of this provision by express provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have** not **opted out** ~~be able to repeat their past successes in clinical trials. The failure~~ of **this provision. Although we believe** these ~~third parties~~ **provisions together provide for an opportunity** to ~~carry out~~ **receive higher bids by requiring potential acquirers to negotiate with our board of directors, such provisions would apply even if the offer may be considered beneficial by some stockholders. These and** ~~their -~~ **other** ~~obligations~~ **provisions in our Charter and Bylaws and under Delaware law could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then- current board of directors, and** could delay or ~~prevent the development~~ **impede a merger , tender offer** ~~approval and commercialization of our -~~ **or** ~~product candidates~~ **proxy contest involving** ~~or~~ **our** ~~result~~ **company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for you to realize value** in ~~enforcement~~ **a corporate transaction. Our bylaws provide that the Court of Chancery of the State of Delaware and the federal district court of the United States for the District of Delaware will be the exclusive forums for substantially all disputes between us and 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 bylaws provide that, to the fullest extent permitted by law and subject to the court' s having personal jurisdiction over any indispensable parties, the Court of Chancery of the State of Delaware is the exclusive forum for (i) any derivative** action **or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim** against us **or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our Charter or our Bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine. This exclusive forum provision may limit a stockholder' s ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees . If a court were to find such exclusive forum provision to be inapplicable** ~~our -~~ **or** ~~relationship~~ **unenforceable in an action, we may incur further significant additional costs associated** with **resolving** ~~these -~~ **the** ~~third~~ **dispute in other jurisdictions,which could seriously harm our business.Future sales and issuances of our common stock or rights to purchase common stock could result in** additional dilution of the percentage ownership of our stockholders and could cause our share price to fall. ~~We expect that significant~~ **Significant** additional capital ~~will~~ **may** be needed in the future to continue our planned operations.We may sell common stock,convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time.We have in the past ~~utilized~~ **used,and currently have the ability to use,** an " at ~~- the- market " (" ATM ") sales program to raise capital by selling our securities through a sales agent up~~

~~to established limits,and have also issued shares of our~~ ~~party providers terminates~~ **the- market ” (“ ATM ”) sales program to raise capital by selling our securities through a sales agent up to established limits , and have also issued shares of our common stock in registered offerings and shares of convertible preferred equity to institutional investors in registered and private direct offerings. We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent** we **raise additional capital or convertible securities, through any ATM program, public equity offering, direct offering, private offering or otherwise, our stockholders** may **dilution.If** we sell common stock,convertible securities or other equity securities in more than one transaction,investors may be materially diluted by subsequent sales.Such sales may also result in material dilution to our existing stockholders,and new investors could gain rights superior to our existing stockholders.Funds affiliated with Baker Bros.Advisors LP hold a significant portion of our total outstanding shares of common stock (including shares of our common stock issuable upon conversion of shares of our Series A Convertible Preferred Stock and Series B Convertible Preferred Stock and pre- funded warrants),and any sale of such shares into the market,or ~~a~~ perception that ~~such~~ sales could occur,in the future could cause the market price of our common stock to drop significantly.Based on a Schedule 13D / A filed with the SEC on ~~March 25~~ **November 17** , ~~2024~~ **2023** ,667,L.P.and Baker Brothers Life Sciences,L.P.,funds affiliated with Baker Bros.Advisors LP (~~“~~ **"** Baker Bros. ~~”~~ **"**),reported an ~~ownership~~ not **exist, Baker Bros. would** be ~~able~~ **deemed** to ~~enter~~ **beneficially own 7, 050, 177 shares of our common stock (which includes 1, 969, 797 shares of common stock issuable upon the conversion of our Series A Convertible Preferred Stock and 400, 000 shares of common stock issuable upon the conversion of our Series B Convertible Preferred Stock, each of which are common stock equivalents with no voting rights, that are convertible** into ~~arrangements~~ **shares of common stock on a 1- for- 1 basis only to the extent that after giving effect to such conversion the holders thereof and their affiliates and any persons who are members of a Section 13 (d) group** with ~~alternative providers~~ **such holders** or ~~do so on commercially reasonable terms. Switching or adding additional third~~ ~~-~~ **their affiliates would beneficially own (in the aggregate, for purposes of Rule 13d - 3 under** ~~party providers involves substantial cost and requires management time and focus, and could delay development and commercialization of our product candidates. Though we intend to carefully manage our relationships with our third- party providers, there~~ ~~--~~ **the** ~~can be~~ **Exchange Act)** no ~~assurance~~ **more than 4. 99 % of the outstanding common stock. The Series B Convertible Preferred Stock beneficial ownership limitation may be increased or decreased up to 19. 99 % at the holder’ s election, provided** that ~~we~~ **any such increase** will not ~~encounter challenges~~ **be effective until the 61st day after such notice is provided to us. The Series A Convertible Preferred Stock beneficial ownership limitation may be increased or decreased to any other percentage provided that any such increase or decrease will not be effective until the 61st day after such notice is provided to us (the “ Beneficial Ownership Limitations ”). The 7, 050, 177 total shares also includes 2, 705, 790 pre- funded warrants. Without such limitations on conversion or exercise, Baker Bros. total ownership would represent 26 % of** ~~or~~ **our** ~~delays in~~ **total outstanding shares of common stock as of December 31, 2024 on a fully exercised or as- converted to common stock basis. The pre- funded warrants are only exercisable to the extent that, after giving effect to such exercise, the holders thereof, together with** ~~the~~ **their** ~~future~~ **affiliates and any members of a Section 13 (d) group with such holders, would beneficially own,** ~~or~~ **for purposes of Rule 13d- 3 under the Exchange Act, no more than 9. 99 % of the outstanding shares of our common stock (the “ Maximum Percentage ”). By written notice to us, holders of the pre- funded warrants may from time to time increase or decrease the Maximum Percentage to any other percentage not in excess of 19. 99 %. Any such increase in the Maximum Percentage will not be effective until the 61st day after such notice is provided to us. Sales of a substantial number of shares of our common stock in the public market by Baker Bros., or the perception** that these ~~delays~~ **sales might occur, could depress the market price of** ~~or~~ **our** ~~challenges will not~~ **common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales by Baker Bros., or any perception that such sales may occur, may** have ~~a negative impact~~ on **the prevailing market price of our common stock. Sales of a significant number of shares of our common stock in the public markets** ~~our~~ ~~-~~ **or** ~~business~~ **significant short sales of our common stock, or the perception that such sales could occur, could depress the market price of our common stock** and ~~financial condition~~ **impair our ability to raise capital** . ~~We have relied~~ **As of December 31, 2024, there were a number of investors or investor groups that held a significant beneficial ownership interest in our common stock. Dr. Paul Friedman, a member of our board of directors, and Dr. Rebecca Taub, a member of our board of directors and our Chief Medical Officer and President of Research and Development, collectively beneficially own 2, 107, 078 shares (9. 2 %) of our common stock (the “ Friedman / Taub Holdings ”). Based** on **a Schedule 13D / A filed with the SEC on March 25 , 2024, funds affiliated with Baker Bros. Advisors LP beneficially owned (for SEC reporting purposes) 9. 99 % of our common stock and maintained** ~~and~~ ~~-~~ **an** ~~expect~~ **ownership interest in up** to **7, 050, 177 shares of our common stock subject to exercise or conversion limits such as the Beneficial Ownership Limitation and the Maximum Percentage (the “ Baker Bros. Holdings ”), as described in the preceding paragraph. Based on a Schedule 13G / A filed with the SEC on February 14, 2024, funds affiliated with Avoro Capital Advisors LLC reported beneficial ownership of 2, 288, 888 shares of our common stock, including pre- funded warrants to purchase 400, 000 shares of common stock that are subject to the Maximum Percentage (the “ Avoro Holdings ”). In addition, as of December 31, 2024, there are: 2, 263, 222 shares of our common stock issuable upon the exercise of outstanding stock options or the vesting of restricted stock units and performance stock units (assuming the maximum outcome of the performance conditions) under our 2015 Stock Plan, as amended, and 2023 Inducement Plan; pre- funded warrants to purchase shares of common stock pursuant to outstanding pre- funded warrants as described above and 19, 454 shares of our common stock issuable upon the exercise of outstanding vested warrants held by our creditors consisting of Hercules and affiliates. In addition, there are other institutional investors (including funds affiliated with Janus Henderson Group plc, which reported beneficial ownership of 2, 208, 394 shares of our common stock (10. 1 %) in a Schedule 13G / A filed with the SEC on February 14, 2025) who**

from time to time file Schedule 13Gs (or amendments thereto) or Form 13Fs reflecting substantial beneficial ownership of our outstanding common stock. Sales of a substantial number of shares of our common stock by one or more of the investors or groups listed above or other equity- related securities in the public markets could depress the market price of our common stock and impair our ability to raise capital. If there are significant sales or short sales of our stock, the price decline that could result from this activity may cause the share price to decline further, which, in turn, may cause long holders of our common stock to sell their shares, thereby contributing to sales of common stock in the market. See the risk factor titled " The price of our common stock has been, and may continue to **be** ~~rely on~~ , ~~third- party manufacturers to produce~~ **volatile. " for additional information. Such sales** ~~our~~ **or** ~~product candidates~~ **short sales also may impair our ability to raise capital through the sale of additional shares in the future at a time and price that our management deems acceptable, if at all** . We do not **anticipate paying cash dividends** ~~own~~ **on** ~~or~~ **our common stock** ~~operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates~~ , and **accordingly** ~~we lack the resources and the capabilities to do so. As a result~~ , **stockholders must** ~~we currently rely, and expect to~~ rely on **stock appreciation, if any, for any return on** ~~third~~ **their investment. We have never declared or paid any cash dividend on our common stock and do not anticipate paying cash dividends on our common stock in the future. As a result, the only return to stockholders will be appreciation in the price of our common stock, which may never occur. Investors seeking cash dividends should not invest in our common stock. If securities analysts publish negative evaluations of our stock, the price of our stock could decline. The trading market for our common stock depends in part on the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who may cover us issues an adverse opinion about our company, our stock price would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. General Risk Factors We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives. As a public company, we incur significant and ongoing legal, accounting and other expenses. We are subject to the reporting requirements of the Securities Exchange Act of 1934, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes** - ~~party manufacturers~~ **Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq Stock Market (" Nasdaq ")** to ~~supply our product candidates. Reliance~~ **implement provisions of the Sarbanes- Oxley Act, impose significant requirements** on ~~third~~ **public companies, including requiring maintenance of effective disclosure and financial controls and changes in corporate governance practices. 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 required the SEC to adopt additional rules and regulations in areas such as " say on** ~~party~~ -- **pay** ~~manufacturers entails risks~~ **" and proxy access. Stockholder activism, the current political environment and regulatory reform may lead** to **changes in regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in** which we ~~would not be subject if~~ **operate our business in ways** we **cannot currently anticipate** ~~manufactured our product candidates or products ourselves~~ . **We expect** ~~For example, if we do not maintain our key manufacturing relationships, we may fail~~ to **continue** ~~find replacement manufacturers or develop our own manufacturing capabilities, which could delay or impair our ability~~ to **incur** ~~obtain regulatory approval for our products and substantially~~ -- **substantial** ~~increase our~~ costs or deplete profit margins, if any..... the applicable cGMP requirements. Any failure to comply with ~~cGMP~~ **the rules and regulations applicable to public companies. If these** requirements **divert the attention of** ~~or~~ **our management and personnel from** other ~~FDA~~ **business concerns** , ~~European Medicines Agency,~~ **they could have a material adverse effect on** ~~or~~ **our** ~~EMA~~ **business** , **financial condition** and ~~comparable foreign regulatory~~ **results of operations. Any 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. 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** ~~adversely affect our clinical research activities and our ability to develop our product candidates and market~~ -- **make it more difficult** ~~our products following approval. Our current and anticipated future dependence upon others~~ for **us** ~~the manufacture of our product candidates may adversely affect our future profit margins and our ability~~ to **attract** ~~develop our product candidates~~ and **retain qualified persons to serve** ~~commercialize any products that receive regulatory approval~~ on ~~a timely basis~~ **our board of directors, our board committees or as executive officers** . A failure of our information technology infrastructure and cybersecurity threats may adversely affect our business and operations. Our information technology infrastructure is subject to threats from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. In addition, the information technology systems of our current or future third- party collaborators, service providers, contractors and consultants are subject to similar threats, and we depend in part on third- party security measures over which we do not have full control to protect against data security incidents. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and ~~they~~ **such attacks** are being conducted by increasingly sophisticated and organized groups and individuals with a wide range of motives and expertise. **Like other companies in our industry, we have experienced and will likely continue to experience, threats and cybersecurity incidents relating to our data, information technology systems and infrastructure, and the systems of our third- party vendors.** In addition to ~~potentially~~ extracting **information (which could be** sensitive ~~information~~ **)** , such as trade secrets or other intellectual property, such attacks could include the deployment of harmful malware, ransomware, denial- of- service attacks, social engineering and other means, including ransom demands, to affect service reliability and / or threaten the confidentiality, integrity and availability of information. Such an event could result in a material disruption of our operations or development programs and / or produce significant reputational, financial, legal,

regulatory, business or operational harm. For example, any loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any **incident,** disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology **, product** or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of **and regulatory approval efforts for** our product candidates **or commercialization of our product** could be delayed. We have been subject to ~~a~~ cybersecurity ~~attack~~ **attacks** in the past **that have impacted our systems and data** . Although we have taken steps to enhance our cybersecurity protections and minimize the impact of any future event, we cannot provide any assurances that future cyber events will not occur, that these security safeguards will be successful, and that future cyber events, to the extent they occur, will not impact our operations or have any material adverse impact on our business. As a result, we may not in the future successfully prevent service interruptions, exfiltrations or data security incidents that could materially adversely affect our business. In addition, insurance may not cover or be sufficient in type or amount to cover us against claims related **to** cyber incidents. Any failure or perceived failure by us or any third- party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations to third parties, or any data security incidents or other security breaches that result in the unauthorized access, release or transfer of sensitive information, including personally identifiable information, may result in: governmental investigations, litigation, regulatory enforcement actions, fines, sanctions or other penalties, injunctive relief requiring costly compliance measures, required notification and credit monitoring, public statements against us, third parties to lose trust in us, or claims by third parties asserting that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. Moreover, data security incidents and other cybersecurity attacks can be difficult to detect, and any delay in identifying ~~them~~ **such threats or attacks** may lead to increased harm. ~~Failure~~ **Our use of new and evolving technologies, such as artificial intelligence, may present risks and challenges that can impact our business, including by posing cybersecurity and other risks to our confidential and / or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability. We may use and integrate artificial intelligence into our business processes both in our own development and implementation of models and through the adoption of commercially available tools. Use of this technology presents risks and challenges that could affect our business. The development of artificial intelligence models requires resources for design, development, testing and maintenance. We must also endeavor to implement artificial intelligence in accordance with applicable law and regulation, in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. If we enable or use models that contain actual or perceived biases, we may experience brand or reputational harm, competitive harm or legal liability. In addition, the use of artificial intelligence technologies can give rise to intellectual property risks, including by disclosing or otherwise compromising our confidential or proprietary intellectual property, or by undermining our ability to assert or defend ownership rights in intellectual property created with the assistance of artificial intelligence tools. Our vendors may in turn incorporate artificial intelligence tools into their offerings, and the providers of these artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. 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 effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business. If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock. Pursuant to Section 404 of the Sarbanes- Oxley Act (" Section 404 "), our management is required to assess and report annually on the effectiveness of our internal control over financial reporting and to identify any material weaknesses in our internal control over financial reporting. We are also required** to comply with ~~health~~ **the auditor attestation requirements of Section 404 (b). The rules governing the standards that must be met for management** and ~~data protection laws~~ **our independent registered public accounting firm to assess our internal control over financial reporting are complex** and ~~regulations~~ **require significant documentation, testing and possible remediation. In connection with our and our independent registered public accounting firm' s evaluations of our internal control over financial reporting, we may need to upgrade systems, including information technology, implement additional financial and management controls, reporting systems and procedures and hire additional accounting and finance staff. Any failure to implement required new or improved controls, or difficulties encountered in their implementation,** could ~~lead~~ **cause us** to ~~government enforcement actions (~~ **fail to meet our reporting obligations. In addition, any testing by us or our independent registered public accounting firm conducted in connection with Section 404 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 ~~include civil~~ **have a negative effect on the trading price of** ~~or~~ **our** ~~criminal penalties), private~~ **common stock. Internal control deficiencies could also result in a restatement of our financial results in the future. We could become subject to stockholder or other third- party** litigation ~~and / or adverse publicity, and could negatively affect our operating results and business. We may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA imposes privacy and security obligations on covered entity health care providers, health plans, and health care clearinghouses~~ , as well as **investigations by the SEC, Nasdaq or** ~~their~~ **other regulatory authorities** ~~" business associates " – certain persons or covered entities that create~~ , **which** ~~receive, maintain, or transmit protected health~~

~~information in connection with providing a specified service or performing a function on behalf of a covered entity. We~~ could **require** ~~potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly receive individually identifiable health information maintained by a HIPAA- covered entity in a manner that is not authorized or permitted by HIPAA. To the extent we collect California resident personal information, we may also be subject to the CCPA. The CCPA, created new transparency requirements and granted California residents several new rights with regard to their personal information. In addition, California voters approved the California Privacy Rights Act (" CPRA ") ballot initiative which introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency (" CPPA "). The amendments introduced by the CPRA went into effect on January 1, 2023, and implementing regulations continue to be introduced by the CPPA. Failure to comply with the CCPA may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California residents have the right to bring a private right of action in connection with certain types of incidents. These claims may result in significant liability and damages. Virginia and Colorado also have enacted similar laws that impose new privacy obligations for which we may need to take~~ additional **financial** steps to comply. Similarly, there.....- US Privacy Shield to be an **and management resources** invalid data transfer mechanism and confirmed that..... concludes that the United States ensures an **and** ~~adequate level of protection for personal data transferred from the EU to U. S. companies. After an approval process, the European Commission is expected to adopt the final adequacy decision, which will allow data to flow freely from the EU to the U. S between companies certified under the new framework. Risks Relating to Our Intellectual Property Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of a license to resmetirom granted to us by Roche. We entered into a Research, Development and Commercialization Agreement, or the Roche Agreement, with Hoffmann- La Roche, or Roche, on December 18, 2008. Pursuant to the terms of the Roche Agreement, we assumed control of all development and commercialization of resmetirom and hold exclusive worldwide rights for all potential indications. Under the Roche Agreement, Roche exclusively licensed certain patent rights and know- how relating to resmetirom in exchange for consideration consisting of an upfront payment, milestone payments tied to the achievement of product development and regulatory milestones, and royalty payments based on net sales of products containing resmetirom or another licensed product, subject to certain reductions. The Roche Agreement will expire, unless earlier terminated pursuant to other provisions thereof, on the last to occur of (i) the expiration of the last valid claim of a licensed patent covering the manufacture, use or sale of products containing resmetirom, or (ii) ten years after the first sale of a product containing resmetirom. Under the Roche Agreement, Roche controls prosecution of the licensed patent rights, although we have a right to comment. We do not have, nor have we had, any material disputes with Roche regarding the Roche Agreement. However, if there is any future dispute between us and Roche regarding the parties' rights under the Roche Agreement, our ability to develop and commercialize resmetirom, or any other product candidate covered by the Roche Agreement, may be materially harmed. Any uncured, material breach under the Roche Agreement~~ could result in **fines** ~~our loss of exclusive rights to resmetirom and may lead to a complete termination of the Roche Agreement and force us to cease product development efforts for resmetirom. We may fail to comply with any of our obligations under agreements pursuant to which we license rights or technology~~ , ~~which could result in the loss of rights or technology that are material to our business. We may enter into license agreements from time to time. Licensing of intellectual property is important to our business and involves complex legal, business and scientific issues. Disputes may arise regarding~~ --- **trading suspensions** ~~intellectual property subject to a license agreement~~ , including but not limited to: •..... number of procedural, documentary, fee payment ~~and other provisions during the patent process and after a patent has issued. There are situations in which noncompliance can result in abandonment or lapse~~ of a patent or patent application, resulting..... lawsuits that we initiate, and the damages or other remedies awarded, if any, may not..... otherwise agree to terms unfavorable to us . Our ability to use net operating loss **(" NOL ")** and tax credit carryforwards and certain built- in losses to reduce future tax payments may be limited by provisions of the Internal Revenue Code. Our **NOLs** ~~net operating losses~~ have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. **Our NOLs could expire unused and be unavailable to offset future income tax liabilities because of their limited duration. NOLs generated in taxable years beginning before January 1, 2018 are permitted to be carried forward for 20 taxable years under applicable U. S. federal income tax law.** Under **current U. S. federal income tax law, NOLs arising in tax years beginning after December 31, 2020 may not be carried back. Moreover, NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such NOLs generally will be limited in taxable years beginning after December 31, 2020 to 80 % of current year taxable income. As of December 31, 2024, the Company had NOLs for U. S. federal and state income tax purposes of approximately $ 850. 2 million and $ 823. 5 million, respectively, a portion of which expire beginning in 2031 if not utilized. Under** ~~Section~~ **Sections** 382 **and 383** of the Internal Revenue Code of 1986, as amended **(the " Code "),** , if a corporation undergoes an " ownership change " (generally defined as a greater than 50 % change (by value) in its equity ownership over a **rolling** three year period), the corporation' s ability to use its pre- change **NOL** ~~net operating loss~~ carryforwards and other pre- change tax attributes to offset its post- change income may be limited. Similar rules may apply under state tax laws. We have not performed a detailed analysis to determine whether an ownership change under Section 382 of the Code, or similar state provisions, has previously occurred. **We may also experience ownership changes in the future as a result of future transactions in our stock (some of which are outside our control). Furthermore, our ability to utilize NOLs of companies that we may acquire in the future may be subject to limitations. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities, including for state tax purposes.** As a result, if we earn net taxable income, our ability to use **the NOLs reflected on** our **balance sheet** ~~pre- change net operating loss carryforwards~~ to offset U. S. federal taxable income may become subject to limitations, which could ~~potentially~~ **adversely affect our operating results and financial condition. Changes in tax law 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 U. S. Internal Revenue Service and the U. S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect the Company 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 tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in **an** ~~increased~~ **increase** ~~future~~ **in our** tax liability ~~to us and may be substantial. Risks Relating to our~~ **or** Indebtedness Our Loan and Security Agreement contains..... substantially all of our assets, other -- **the** ~~than intellectual property. Until we have repaid such indebtedness, the Loan Agreement subjects us to various terms, conditions and covenants. These include financial reporting obligations, and certain limitations on indebtedness, liens (including a negative pledge on intellectual property and other assets), investments, distributions (including dividends), collateral, investments, distributions, transfers, mergers or acquisitions, taxes~~ -- **tax** , corporate changes, and deposit accounts..... affected by these restrictions on our ability **liability** ~~to operate our business. If we raise any additional debt financing, as permitted by the Loan Agreement and if pursued and secured by the Company, the terms~~ of ~~such additional debt could further restrict our operating and financial flexibility. We may not be able to generate sufficient cash flow or sales to meet the financial covenants or pay the principal and interest under the Term Loans. Furthermore, our future working capital, borrowings or equity financing could be unavailable to repay or refinance the amounts outstanding under the Term Loans. In the event of a liquidation, the lender under the facility would be repaid all outstanding principal and interest prior to distribution of assets to unsecured creditors, and the~~ holders of our common stock ~~would receive a portion of~~ **or require changes in the manner in which we operate in order to minimize or mitigate** any **adverse effects** ~~liquidation proceeds only if all~~ of ~~our creditors then existing~~ **changes in tax law. Tax laws related to U. S. federal** , ~~including the lender~~ **state and local and international income taxation are constantly** under **review by persons involved** ~~the Term Loans, were first repaid~~ in ~~full. Our failure to comply with the covenants or other~~ -- **the** ~~terms of~~ **legislative process and by** the ~~Loan Agreement, including as a result of events beyond our control,~~ **Internal Revenue Service and the U. S. Treasury Department. Changes to tax laws (which may have retroactive application)** could ~~result in a default under the Loan Agreement that could materially and~~ adversely affect **us** ~~our~~ -- **or** ~~business~~ **holders of our common stock** . ~~Additionally~~ **In recent years** , ~~we may~~ **many such changes have been made** ~~be required to repay the outstanding indebtedness under the loan if an~~ **and** ~~event of default~~ **changes are likely to continue to occurs** - **occur** ~~under~~ **in** the ~~Loan Agreement or, if applicable, any~~ future ~~debt facility~~ . **Future changes in tax laws** ~~The Loan Agreement includes customary events of default, including payment defaults, breaches of covenants following any applicable cure period, the occurrence of certain events that~~ could ~~reasonably be expected to~~ have a ~~"~~ material adverse effect **on our business** ~~" as set forth in the Loan Agreement~~ , ~~and cross acceleration. We may not have enough available~~ cash **flow** ~~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~~ **or** results of operations ~~could be materially adversely affected as a result~~ **. We urge investors to consult with their legal and tax advisers regarding the implications** of **potential changes in tax laws on** ~~any~~ - **an investment in** ~~of these events. Risks Relating to Ownership of Our Common Stock The price of~~ our common stock **. Business disruptions could seriously harm our operations, future revenues and financial condition and increase our costs and expenses. Our operations, and those of our CROs, suppliers, and other contractors and consultants, could be subject to geopolitical events, natural disasters, power and other infrastructure failures or shortages, public health crises, pandemics or epidemics, and other natural or man- made disasters or business interruptions. In addition, geopolitical and other events, such** ~~has~~ - **as** ~~been~~ **the Russian invasion of Ukraine or the conflicts in the Middle East** , **could lead** ~~and may continue~~ to ~~be~~ **sanctions** , **embargoes** ~~volatile. Historically~~ , **supply shortages, regional instability, geopolitical shifts, cyberattacks,** ~~the~~ **other retaliatory actions, and adverse effects on macroeconomic conditions, currency exchange rates, and financial** ~~market~~ **markets** ~~price of~~ **, which could adversely impact** our ~~common stock~~ **operations and financial results,** ~~has~~ - **as** ~~fluctuated over a wide range~~ **well as those of third parties with whom we conduct business. The occurrence of any of these business disruptions could seriously harm our operations** , **future revenues** and ~~it~~ **financial condition and increase our costs and expenses. We may be subject to securities litigation, which** is **expensive and could divert management attention** ~~likely that the price of our common stock will continue to be volatile in the future. The closing price of our common stock has ranged from $ 58. 39 to $ 312. 00 per share during the period from December 1, 2022 to January 31, 2024~~ . The market price of our common stock ~~could be impacted due to a variety of factors, including: global market or financial developments; prevailing macroeconomic conditions, including potential recession or economic downturns; US market events (including the potential for unusual market trading activity following external short interest developments or social media activity); the outbreak of war or hostilities; NASH therapeutic company developments and / or FDA developments, regardless of whether occurring generally and / or specifically as to our clinical trials and development programs; industry- wide events; and the following events or developments: • the losses we~~ may ~~incur~~ **be volatile and** , ~~including increased losses resulting from costs associated with increases~~ in ~~our clinical trial activity; • developments in patent or other~~ -- **the past** ~~proprietary rights owned or licensed by us~~ , **companies that have experienced volatility** ~~our collaborative partners or our competitors; • the progress and results of our clinical trials; • public or regulatory concern as to the safety and efficacy of NASH products developed by us or others or public safety generally; and • litigation. In addition, due to one or more of the foregoing factors~~ in ~~one or more future quarters, our results of operations may fall below the expectations of securities analysts and investors. In the event any of the foregoing occur,~~ the market price of **their** ~~our common~~ stock ~~could be highly volatile and may materially decline. A small number of our stockholders beneficially own a substantial amount of our outstanding common stock and may be deemed to~~ have ~~substantial control over~~ **been subject to securities class action litigation. We may be the target of this type of litigation in**

the future. Securities litigation against us ; therefore, your ability to influence..... stock or rights to purchase common stock could result in additional dilution of the percentage ownership of..... or otherwise, our stockholders may experience substantial **costs** dilution. If we sell common stock..... Bros."), reported an **and divert management** ~~ownership interest in (i) Madrigal common stock and (ii) other Madrigal securities with limitations on conversion or exercise to common stock. If such limitations did not exist, Baker Bros. would be deemed to beneficially own 5, 851, 323 shares of our common stock (which includes 1, 969, 797 shares of common stock issuable upon the conversion of our Series A Convertible Preferred Stock and 400, 000 shares of common stock issuable upon the conversion of our Series B Convertible Preferred Stock, each of which are common stock equivalents with no voting rights, that are convertible into shares of common stock on a 1- for- 1 basis only to the extent that after giving effect to such conversion the holders thereof and their affiliates and any persons who are members of a Section 13 (d) group with the holders or their affiliates would beneficially own (in the aggregate, for purposes of Rule 13d- 3 under the Exchange Act) no more than 4. 99 % of the outstanding common stock, which may be increased or decreased up to 19. 99 % at the holder~~ ' s **attention** ~~election on 61 days' notice and certain limitations (the " Beneficial Ownership Limitation "). The 5, 851, 323 total share number above includes 1, 648, 098 pre- funded warrants and without such limitations on conversion or exercise would represent approximately 24. 49 % of our total outstanding shares of common stock as of December 31, 2023 on a fully as- converted and as- exercised to common stock basis. The pre- funded warrants are only exercisable to the extent that after giving effect to such exercise the holders thereof, together with their affiliates and any members of a Section 13 (d) group with such holders, would beneficially own, for purposes of Rule 13d- 3 under the Exchange Act, no more than 9. 99 % of the outstanding shares of Common Stock (the " Maximum Percentage "). By written notice to us, holders of the pre- funded warrants may~~ from ~~time to time increase or decrease the Maximum Percentage to any~~ other **business concerns** ~~percentage not in excess of 19. 99 %. Sales of a substantial number of shares of our common stock in the public market by Baker Bros.~~ , **which** ~~or the perception that these sales might occur,~~ could **seriously harm** ~~depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales by Baker Bros., or~~ **our business** ~~any perception that sales may occur, may have on the prevailing market price of our common stock~~ . **64** ~~Sales of a significant number of shares of our common stock in the public markets or significant short sales of our common stock, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital. As of December 31, 2023, there were a number of investors or investor groups that held a significant beneficial ownership interest in our common stock. Drs. Paul Friedman and Becky Taub (the " Friedman / Taub Holdings "), a director and President of R & D and Chief Medical Officer, respectively collectively beneficially own 2, 212, 070 shares (or 10. 62 %) of our common stock. Based on a Schedule 13D / A filed with the SEC on November 17, 2023, funds affiliated with Baker Bros. Advisors LP beneficially owned (for SEC reporting purposes) 9. 99 % of our common stock and maintained an ownership interest in up to 5, 851, 323 shares of our common stock subject to exercise or conversion limits such as the Beneficial Ownership Limitation and Maximum Percentage (the " Baker Bros. Holdings "), as described in the preceding paragraph. Based on a Schedule 13G / A filed with the SEC on February 14, 2024, funds affiliated with Avoro Capital Advisors LLC (the " Avoro Holdings ") reported beneficial ownership of 2, 288, 888 shares of our Common Stock, including pre- funded warrants to purchase 400, 000 shares of Common Stock that are subject to the Maximum Percentage. In addition, as of December 31, 2023, there are: 2, 881, 896 shares of our common stock issuable upon the exercise of outstanding stock options or the vesting of restricted stock units and performance stock units under our 2015 Stock Plan, as amended and 2023 Inducement Plan; pre- funded warrants to purchase shares of Common Stock pursuant to outstanding pre- funded warrants as described above; and 19, 454 shares of our common stock issuable upon the exercise of outstanding vested warrants held by our creditors consisting of Hercules and affiliates. In addition, there are other institutional investors (including funds affiliated with Janus Henderson Group plc, which reported beneficial ownership of 2, 902, 050 shares of our common stock, or 14. 7 %, in a Schedule 13G / A filed with the SEC on February 13, 2024) who from time to time file Schedule 13Gs (or amendments thereto) or Form 13Fs reflecting substantial beneficial ownership of outstanding common stock. Sales of a substantial number of shares of our common stock by one or more of the investors or groups listed above or other equity- related securities in the public markets, could depress the market price of our common stock and impair our ability to raise capital. If there are significant sales or short sales of our stock, the price decline that could result from this activity may cause the share price to decline further, which, in turn, may cause long holders of the common stock to sell their shares, thereby contributing to sales of common stock in the market. See " Risk Factors; Risks Relating to Ownership of Our Common Stock -- The price of our common stock has been, and may continue to be, volatile. " Such sales or short sales also may impair our ability to raise capital through the sale of additional shares in the future at a time and price that our management deems acceptable, if at all. We do not anticipate paying cash dividends on our common stock, and accordingly, stockholders must rely on stock appreciation for any return on their investment. We have never declared or paid any cash dividend on our common stock and do not anticipate paying cash dividends on our common stock in the future. As a result, the only return to stockholders will be appreciation in the price of our common stock, which may never occur. Investors seeking cash dividends should not invest in our common stock.~~