Risk Factors Comparison 2025-02-27 to 2024-02-28 Form: 10-K

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We operate in a dynamic and rapidly changing environment involving numerous risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. You should carefully consider the risks and uncertainties described below, together with all of the other information included in this ~~annual report~~ **Report** ~~on Form 10 - K~~. Our business faces significant risks and uncertainties, and those described below may not be the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we currently believe are immaterial may also significantly impair our business, financial condition or results of operations. If any of these risks or uncertainties occur, our business, financial condition or results of operations could suffer, the market price of our common stock could decline and you could lose all or part of your investment in our common stock. ~~RISKS RELATED TO~~ **Risks Related to** THE ~~DEVELOPMENT OF IMETELSTAT~~ **Commercialization of RYTELO** Our ~~future success~~ **near- term prospects are wholly** ~~depends~~ **dependent** ~~solely~~ on ~~imetelstat~~ **RYTELO. We have limited experience with the commercialization of RYTELO , and if we are unable to successfully commercialize RYTELO in the U. S. for lower- risk MDS, or to expand its indication of use, our ability to generate meaningful revenue or achieve profitability will be materially and adversely affected. In June 2024, we received FDA approval to commercialize RYTELO in the U. S. for certain patients with lower- risk MDS, and we initiated a commercial launch of RYTELO in the U. S. in that indication. RYTELO is** our only product ~~candidate~~ **approved for marketing by the FDA, and our ability to generate revenue from product sales and achieve profitability is wholly dependent on our ability to successfully commercialize RYTELO in the U. S. for lower- risk MDS or to expand its indications of use. We may not be able to successfully commercialize RYTELO for a number of reasons, including: • we may not be able to establish or demonstrate in the medical community the safety and efficacy of RYTELO and its potential advantages over and side effects compared to existing treatments; • physicians may be reluctant to prescribe RYTELO until longer- term efficacy and safety data exists; • our limited historical experience in marketing, selling and distributing RYTELO; • reimbursement and coverage policies of government and private payors such as Medicare, Medicaid, insurance companies, health maintenance organizations and other plan administrators; • the relative price of RYTELO as compared to alternative treatment options; • the relatively low incidence and prevalence of patients in RYTELO' s approved indication, including the reliability of our market and sales estimates; • future competitive or other market factors may adversely affect the commercial potential of RYTELO; • we may not be able to obtain and maintain regulatory approvals for RYTELO in any other jurisdictions or for any other indications, including in the EU for lower- risk MDS or in any other jurisdiction for relapsed / refractory MF; • changed or increased regulatory restrictions; • changes to the label for RYTELO that further restrict how we market and sell RYTELO, including adverse events observed in ongoing and future studies of imetelstat such as our Phase 3 IMpactMF clinical trial; • the capabilities of third party manufacturers may adversely affect the success of our commercialization of RYTELO; • we may need additional financial or other resources to successfully commercialize RYTELO; and • we may not be able to maintain adequate commercial supplies of RYTELO to meet demand or at an acceptable cost or at all. Moreover, successful commercialization of RYTELO may not generate sufficient revenue from product sales, and we may not become profitable in the near term, or at all. In any event, if we are unable to successfully commercialize RYTELO in the U. S. for lower- risk MDS, or to expand its indications of use, our ability to generate meaningful revenue from product sales and achieve profitability will be materially and adversely affected, which in turn would severely and adversely affect our financial results, business and business prospects, and might cause us to cease operations. We have limited experience as a commercial company and our sales, marketing, and distribution of RYTELO may be unsuccessful or less successful than anticipated. As a company, we have limited prior experience in selling and marketing or commercializing an approved drug product in the U. S., and we have no experience marketing or commercializing an approved drug outside of the U. S. The success of our commercialization efforts is subject to, among other things, managing our internal sales, marketing, and distribution capabilities and our ability to navigate the significant expenses and risks involved with the management of such capabilities. For example, our commercial launch of RYTELO in the U. S. may not continue as planned or anticipated, which may require us to, among others, adjust or amend our commercialization plan and incur significant expenses. Further, given our limited historical experience commercializing drug products, we do not have a track record of successfully executing a commercial launch. If we are unsuccessful in accomplishing our objectives or if our commercialization efforts do not continue as planned, we may not be able to successfully commercialize RYTELO in lower- risk MDS, we may require significant additional capital and financial resources, we may not become profitable, and we may not be able to compete against more established companies in our industry, any of which would severely and adversely affect our financial results, business and business prospects, and might cause us to cease operations. If we are unable to continue to execute on our sales, marketing and distribution plans to commercialize RYTELO, we may be unable to generate meaningful product revenue. To successfully commercialize RYTELO in the U. S., we need to continue to execute on our sales, marketing and distribution plans. The ongoing execution of our sales, marketing and distribution plans requires investment of capital and time** , and we cannot be certain that we will be able to continue to **execute on our plans successfully. In addition, we compete with many companies that currently have extensive, experienced and well- funded sales, distribution and marketing operations to recruit, hire, train and retain marketing and sales personnel. If we are unable to recruit as needed, and to retain and effectively train**

marketing and sales personnel and equip them with compliant and effective materials, our efforts to successfully commercialize RYTELO could be adversely affected. We currently have no marketing or sales organization outside of the U. S., and as a company, we have no experience selling and marketing approved drugs outside of the U. S. To successfully commercialize RYTELO outside of the U. S, we will need to develop ~~imetelstat~~ **these capabilities, either on** ~~or~~ **our own or with others, including third party contractors. Doing so will require additional investment of capital and time. We may seek strategic partnerships, collaborations, alliances or licensing arrangements, at an appropriate time, to assist us in the potential development and commercialization of RYTELO in the EU, or we may seek to self-commercialize and need to establish business operations in such regions. If we receive regulatory approval to commercialize RYTELO in any other regions, such as the EU, we may be unsuccessful in our efforts to recruit, hire, train and retain personnel to support such business operations; or we may be unable to enter into and conduct successful strategic partnerships, collaborations, alliances or licensing arrangements with third parties to commercialize RYTELO in such regions, should we seek to do so. Any failure or delay in the execution of our sales, marketing and distribution plans would adversely impact the commercialization of RYTELO outside the U. S. Further, given our limited experience in marketing and selling RYTELO, our initial estimate of the size of the required sales force may be materially more or less than the size of the sales force actually required to effectively commercialize RYTELO. As such, we may be required to hire substantially more sales representatives and medical support liaisons to adequately support the commercialization of RYTELO, or we may incur excess costs as a result of hiring more sales representatives than necessary. With respect to certain geographical markets where RYTELO may be approved for marketing in the future, such as the EU, or any other regions where we might seek drug product approval for RYTELO, we may enter into arrangements with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such arrangements on favorable terms, if at all. If potential future partners do not commit sufficient resources to commercialize RYTELO and any future products, and we are unable to develop the necessary marketing capabilities on our own, we may be unable to generate sufficient product revenue to sustain our business. In any event, if we are unable to establish and maintain adequate sales and marketing capabilities for RYTELO, whether on our own or through collaborations, our results of operations may be negatively impacted. Any of the foregoing would negatively impact our business and business prospects, severely and adversely affect our financial results, and might cause us to cease operations. If we do not obtain acceptable prices or adequate reimbursement for RYTELO, the use of RYTELO could be severely limited. Our ability to successfully commercialize RYTELO will depend significantly on obtaining acceptable prices and the availability of coverage and adequate reimbursement to patients from third- party payors. Government payors, such as the Medicare and Medicaid programs, and other third- party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and the reimbursement levels. Although CMS assigned a permanent and product specific J- Code (J0870) for RYTELO, which became effective on January 1, 2025, until CMS and commercial payor systems are updated, physicians may continue to use the non-specific miscellaneous J- Code to bill third- party payors for RYTELO. Because miscellaneous J- Codes may be used for a wide variety of products, health plans may have more difficulty determining the actual product used and billed for the patient. These claims increase the provider administrative burden and must often be submitted with additional information and manually processed, which can delay claims processing times as well as increase the likelihood for claim denials and claim errors. Further, the resulting reimbursement payment rates may not be adequate or may require significant restrictions on use or increased co- payments from commercially insured patients that patients may find unacceptably high. Patients are unlikely to use RYTELO unless coverage is provided, and reimbursement is adequate to cover all or a significant portion of its cost. Therefore, coverage and adequate reimbursement will be critical to market acceptance of RYTELO. In addition, government authorities and other third- party payors in the U. S. and other jurisdictions are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices as a condition of coverage, are using restrictive formularies and preferred drug lists to leverage greater discounts in competitive classes, and are challenging the prices charged for medical products. The Inflation Reduction Act of 2022 includes several provisions to lower prescription drug costs for people with Medicare and reduce drug spending by the federal government, which may ultimately have a negative effect on the pricing for RYTELO. However, the Medicare Drug Pricing Negotiation Program provisions of the law are currently subject to legal challenges. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third- party payors in the U. S. As a result, the coverage determination process is often a time- consuming and costly process that will require us to provide scientific and clinical support for the use of RYTELO to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. We cannot be sure that coverage and reimbursement will be available for RYTELO, and, if reimbursement is available, what the level of reimbursement will be. Although we have received a permanent and product- specific J- Code (J0870) for RYTELO which became effective on January 1, 2025, there may also be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar international regulatory authorities. Coverage and reimbursement may impact the demand for, or the price of RYTELO, and reimbursement policies in the U. S. and other jurisdictions may evolve which may adversely impact our ability to successfully commercialize RYTELO. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may**

not be able to successfully commercialize RYTELO, which would negatively impact our business and business prospects. To be commercially successful, RYTELO must be accepted by the healthcare community, which can be slow to adopt or unreceptive to new technologies and products. RYTELO may not achieve market acceptance in the U. S. for lower- risk MDS or any other indication that might be approved by the FDA in the future, or achieve the potential international revenue we believe may be possible if RYTELO is approved outside the U. S., since hospitals, physicians, patients or the medical community in general may decide not to accept and utilize RYTELO. RYTELO competes with a number of conventional and widely accepted drugs and therapies manufactured and marketed by major pharmaceutical companies. The degree of market acceptance of RYTELO depends on a number of factors, including: • the clinical indications for which RYTELO is or may in the future be approved; • the establishment and demonstration to the medical community of the clinical efficacy and safety of RYTELO; • the ability to demonstrate that RYTELO is superior to alternatives on the market at the time, including with respect to efficacy, safety, cost or route of administration; • the willingness of medical professionals to prescribe, and patients to use, RYTELO, or to continue to use RYTELO; • the publication of unfavorable safety or efficacy data concerning RYTELO by third parties or us; • restrictions on use of RYTELO alone or in combination with other products; • the label and promotional claims allowed by the FDA for RYTELO, as well as any such claims allowed by similar international regulatory authorities for RYTELO, if any, including usage for only certain indications and any limitations or warnings about the prevalence or severity of any side effects; • the timing of market introduction of RYTELO as well as competitive products, including sequencing of available products; • the effectiveness of sales, marketing and distribution support for RYTELO; • the ability of the third party distributors and specialty pharmacies we contract with to process prescriptions and dispense RYTELO and the processes required to place orders with such distributors and specialty pharmacies; • the extent to which RYTELO is approved for inclusion on formularies in hospitals and managed care organizations; • the pricing of RYTELO, both in absolute terms and relative to alternative treatments; • the availability of coverage and adequate reimbursement by government and third- party payors; and • the willingness of patients to pay out- of- pocket in the absence of coverage by third- party payors, including governmental authorities. We may be unable to demonstrate any therapeutic or economic ~~advance~~ **advantage** ~~imetelstat~~ **for RYTELO compared** to ~~subsequent patients to pay out- of- pocket in the absence of coverage by third- party payors,including governmental authorities.We may be unable to demonstrate any therapeutic or economic advantage for imetelstat compared to~~ established or standard- of- care therapies,or newly developed therapies,for myeloid hematologic malignancies. **National health insurance and / or** ~~Third~~ **third** - party payors may decide that any potential benefit that ~~imetelstat~~ **RYTELO** may provide to clinical outcomes in myeloid hematologic malignancies is not adequate to justify the **potential adverse effects or the** costs of treatment with ~~imetelstat~~ **RYTELO** .If the healthcare community does not accept ~~imetelstat~~ **RYTELO** for any of the foregoing reasons,or for any other reasons,our ability to ~~further develop or potentially~~ commercialize ~~imetelstat~~ **RYTELO in the U.S.for lower- risk MDS or for any other indications for which RYTELO may be approved,** may be negatively impacted or precluded altogether,which would seriously and adversely affect our business and business prospects.If the market opportunities for ~~imetelstat~~ **RYTELO** are smaller than we believe,our ~~potential~~ revenue may be adversely affected,and our business may suffer. **We are commercializing RYTELO in** ~~Our initial focus for imetelstat development has been on the lead indications of~~ lower- risk MDS **,** and **the** ~~relapsed / refractory MF.The~~ addressable patient ~~populations~~ - **population** ~~,if imetelstat~~ **in lower- risk MDS** is ~~approved in those indications,are~~ based on our estimates.These estimates,which have been derived from a variety of sources,including scientific literature,surveys of clinics,patient foundations and market research,may prove to be incorrect.Further,new information from us or others may change the estimated incidence or prevalence of **patients with lower- risk MDS in** ~~those~~ -- **the** ~~indications~~ **U** . **S.** ~~Any regulatory approval of imetelstat would be limited to the therapeutic indications examined in our~~ - **or** ~~clinical trials and as determined by the FDA and similar international regulatory authorities,which would not permit us to market imetelstat for any other~~ -- **the EU** ~~indications not expressly approved by those regulatory authorities~~ .Additionally,the potentially addressable patient population for ~~imetelstat~~ **RYTELO** may not ultimately be amenable to treatment with **RYTELO,or** ~~imetelstat.Even if~~ we **may** ~~receive regulatory approval for imetelstat,such approval could~~ be **unable to successfully identify** ~~conditioned upon label restrictions that materially limit the addressable patient~~ **patients** ~~population~~ **and achieve a significant market share in RYTELO' s approved indication,or initial sales of RYTELO may deplete the prevalence pool of patients in the RYTELO' s approved indication more quickly than expected,which would have a negative impact on sales of RYTELO in the future** .Our ~~market opportunity may also be~~ **commercialization of RYTELO in the U.S.is** limited ~~by~~ **to certain patients with lower- risk MDS,and any future potential commercialization will be limited to** the ~~pricing~~ **therapeutic indications examined in our** clinical trials **and as determined by the FDA and similar international regulatory authorities** , **which would not permit us to market RYTELO** ~~or~~ **for any other indications not expressly approved by those regulatory authorities. Future regulatory approvals for RYTELO, if any, could be conditioned upon label restrictions that materially limit the addressable patient population. Our market opportunity may also be limited by the pricing, reimbursement and access we are able to achieve for RYTELO, the quality and expiration of our intellectual property rights and regulatory exclusivity, duration of RYTELO treatment in lower- risk MDS and future competitor treatments that enter the market. If any of our estimates prove to be inaccurate, the market opportunities for RYTELO that we or any potential future collaborative partners develop could be significantly diminished, which would have a material adverse impact on our business and business prospects, and would adversely affect our ability to achieve profitability. If competitors develop products, product candidates or technologies that are superior to or more cost- effective than RYTELO, it would significantly impact the development and commercial viability of RYTELO, which would severely and adversely affect our financial results, business and business prospects, and the future of RYTELO, and might cause us to cease operations. The pharmaceutical and biotechnology industries are characterized by intense and dynamic competition with rapidly**

advancing technologies and a strong emphasis on proprietary products. While we believe our proprietary oligonucleotide chemistry; experience with the biological mechanisms related to RYTELO, telomeres and telomerase; clinical data to date indicating potential disease- modifying activity with RYTELO treatment; and knowledge and expertise around the development of potential treatments for myeloid hematologic malignancies provide us with competitive advantages, we face competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions. RYTELO competes with other products and therapies that currently exist, are being developed or will in the future be developed, some of which we may not currently be aware of. A discussion of current and potential future competitors of RYTELO can be found in the sub - section entitled " Competition " in Part I, Item 1, entitled " Business " and elsewhere in this Report. Many of our competitors, either alone or with their strategic partners, could have substantially greater financial, technical and human resources than we do and significantly greater experience in obtaining FDA and other regulatory approvals of treatments and commercializing those treatments. We believe that the commercial success of RYTELO is subject to a number of factors, including: product efficacy and safety; method of product administration; cost of manufacturing; the timing and scope of regulatory consents; status of coverage and reimbursement; price; the level of generic competition; and our patent and regulatory exclusivity position. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. We anticipate increased competition in the future as new companies explore treatments for myeloid hematologic malignancies, which may significantly impact the commercial viability of RYTELO. Academic institutions, government agencies and other public and private research organizations may also conduct research, seek patent protection and establish collaborative arrangements for research, clinical development and marketing of products similar to RYTELO. These companies and institutions compete with us in recruiting and retaining qualified development and management personnel as well as in acquiring technologies complementary to the RYTELO program. As a result of the foregoing, competitors may develop more commercially desirable or affordable products than RYTELO or achieve earlier patent protection or product commercialization than we may be able to achieve with RYTELO. Competitors have developed, or are in the process of developing, technologies that are, or in the future may be, competitive to RYTELO. Some of these products may have an entirely different approach or means of accomplishing therapeutic effects similar or superior to those that may be demonstrated by RYTELO. Competitors may develop products that are safer, more effective, or less costly than RYTELO, or more convenient to administer to patients and, therefore, present a serious competitive threat to RYTELO. In addition, competitors may price their products below what we may determine to be an acceptable price for RYTELO, may receive better third- party payor coverage and / or reimbursement, or may be more cost- effective than RYTELO. Such competitive products or activities by competitors may render RYTELO obsolete, which may cause us to cease any further development or future commercialization of RYTELO, which would severely and adversely affect our financial results, business and business prospects, and the future of RYTELO, and might cause us to cease operations. We rely on a select network of third party distributors, specialty pharmacies and other vendors to distribute RYTELO in the U. S., and any failure by such distributors, specialty pharmacies and vendors could adversely affect our revenues, financial condition, or results of operations. We rely on a select network of third party distributors, specialty pharmacies and other vendors to distribute RYTELO in the U. S., and the financial failure of any of these parties could adversely affect our revenues, financial condition or results of operations. We rely on such distributors and specialty pharmacies to effectively distribute RYTELO in a timely manner, provide certain patient support services, manage prescription intake, collect accurate patient and inventory data and collect payments from payors. While we have entered into agreements with each of these parties, they may not perform as agreed, our strategic priorities may change or they may terminate their agreements with us. Further, an inability by our distributors or specialty pharmacies to meet our patients' needs may lead to reputational harm or patient loss. In the event that such network fails to properly meet our or our patients' needs, we may need to partner with other distributors, specialty pharmacies or vendors to replace or supplement our current network and there is no guarantee that we will be able to do so on commercially reasonable terms or at all. We are seeking regulatory approval to commercialize RYTELO in the EU, and any such approval, if received, will be subject to pricing, drug marketing, post- market and reimbursement regulations in the EU, which may materially affect our ability to commercialize and receive reimbursement coverage for RYTELO in the EU. We are seeking approval to market RYTELO in the EU for lower- risk MDS. Even if we obtain approval for RYTELO in the EU, the competent regulatory authorities may still impose significant restrictions on the indicated uses or marketing of our product or impose ongoing requirements for potentially costly post- approval studies, post- market surveillance or patient or drug restrictions. We will also be subject to rules and regulations in the EU applicable to the manufacturing, marketing, promotion and sale of medicinal products. If we or a regulatory authority discovers previously unknown problems with RYTELO, such as adverse events of unanticipated severity or frequency, or problems with a facility where RYTELO is manufactured, a regulatory authority may impose restrictions relative to RYTELO or the manufacturing facility, including requiring recall or withdrawal of RYTELO from the market or suspension of manufacturing. Moreover, product labeling, advertising and promotion for RYTELO will be subject to regulatory requirements and continuing regulatory review. Failure to comply with EU and EU Member State laws that apply to the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of the marketing authorization, or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the

marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties. In addition, the pricing of RYTELO will be subject to governmental control and other market regulations which could put pressure on the pricing and usage of RYTELO. In the EU, pricing negotiations with governmental authorities can take considerable time after obtaining marketing approval of a product candidate. In addition, if approved, market acceptance and sales of RYTELO will depend significantly on the availability of adequate coverage and reimbursement from third- party payors for RYTELO and may be affected by existing and future healthcare reform measures. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low- priced and high- priced EU Member States, can further reduce prices. An EU Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. If RYTELO is approved for commercialization in the EU, in some countries we may be required to conduct a clinical study or other studies that compare the cost- effectiveness of RYTELO to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for biopharmaceutical products will allow favorable reimbursement and pricing arrangements for RYTELO, if it is approved for marketing in the EU. Historically, products launched in the EU do not follow price structures of the U. S. and generally prices tend to be significantly lower. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of RYTELO is unavailable or limited in scope or amount, our revenues from sales and the potential profitability of RYTELO in those countries would be negatively affected. Much like the federal Anti- Kickback Statute prohibition in the U. S., the provision of benefits or advantages to physicians and other healthcare professionals to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. Interactions between pharmaceutical companies and health care professionals are governed by strict laws, such as national anti- bribery laws of European countries, national sunshine rules, regulations, industry self- regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. Infringement of related laws could result in substantial fines and imprisonment. Payments made to physicians and other healthcare professionals in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians may require prior notification or approval by the physician' s or healthcare professional' s employer, his or her competent professional organization and / or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. RISKS RELATED TO REGULATORY APPROVAL OF RYTELO We may be unable to maintain regulatory approval for RYTELO in the U. S. for lower- risk MDS, which would severely and adversely affect our business and business prospects, and might cause us to cease operations. In June 2024, we received regulatory approval from the FDA to commercialize RYTELO in the U. S. in certain patients with lower- risk MDS. Federal, state and local governments in the U. S. have significant regulations in place that may limit or prevent us from successfully commercializing RYTELO for lower- risk MDS. We do not currently have regulatory approval for RYTELO in any other jurisdiction or for any other indication, and governments in other jurisdictions have significant regulations that may limit or prevent us from successfully commercializing RYTELO in other jurisdictions. Failure to maintain regulatory approval for RYTELO for lower- risk MDS, or delays in obtaining, failure to obtain, or limitations in the scope of such approvals in any other jurisdictions or for any other indications, could: • result in a withdrawal of RYTELO from the market or could otherwise delay, limit or preclude any revenue we may receive from the commercialization of RYTELO for lower- risk MDS; • significantly harm the commercial potential of RYTELO; • impede, halt or increase the costs of our activities and plans for clinical development; • diminish any competitive advantages that may have been available to us; or • delay or preclude any revenue we may receive from the future commercialization of RYTELO in any other jurisdictions or for any other indications, if any. In addition, approved products and their manufacturers, together with other vendors involved in the commercialization process, are subject to continual review, and discovery of previously unknown problems with a product or its manufacturer may result in restrictions on the product or manufacturer, including import restrictions, seizure and withdrawal of the product from the market. Commercialization and sales of RYTELO are subject to government regulations related to numerous matters, including the processes of: • manufacturing; • advertising and promoting; • selling and marketing; • medical information; • labeling; and • distribution. If, and to the extent that, we are unable to comply with these regulations, our ability to earn revenue from the commercialization of RYTELO will be materially and adversely impacted. Further, if RYTELO causes serious or unexpected side effects, or if other safety risks are observed as a result of our commercialization efforts for RYTELO in lower- risk MDS or in current or potential future clinical trials, a number of potential significant negative consequences could result, including: • regulatory authorities may withdraw approval of RYTELO; • we may be required to recall RYTELO, seek to change the way it is administered, conduct additional clinical trials or change the labeling of the product; • regulatory authorities may require revisions to the labeling of RYTELO, including limitations on approved uses or the addition of further warnings, contraindications or other safety information, or may impose restrictions on distribution in the form

of additional requirements in a risk evaluation and management plan or risk management plan; • we may experience manufacturing delays and supply disruptions if regulatory inspectors identify regulatory noncompliance by third- party manufacturers requiring remediation; • RYTELO may be rendered less competitive and sales, if any, may decrease; • our reputation may suffer generally both among clinicians and patients; • we may be exposed to potential lawsuits and associated legal expenses, including costs of resolving claims; • regulatory authorities may refuse to approve pending applications or supplements to approved applications filed by us, or may suspend or revoke license approvals; or • we may be required to change or stop ongoing clinical trials of RYTELO (imetelstat), which would negatively impact the development of RYTELO (imetelstat) for other potential indications. Any of these events could prevent us from achieving or maintaining market acceptance for RYTELO, could substantially increase the costs and expenses of commercializing RYTELO, or could limit its commercial potential, which in turn could delay or prevent us from generating any meaningful revenues from the sale of the RYTELO. If RYTELO is approved outside the U. S., we will be subject to similar requirements, considerations and risks in other regions. Our regulatory approval for RYTELO in the U. S. for lower- risk MDS is subject to post- marketing requirements and commitments, and we may be subject to penalties or product withdrawal if we fail to comply with these regulatory requirements and commitments or if we experience unanticipated problems with RYTELO. Our regulatory approval for RYTELO in lower- risk MDS is subject to non- clinical, clinical and manufacturing post- marketing requirements and commitments, including the requirement of continuing to assess long- term safety of RYTELO (imetelstat) in the IMerge trial and a clinical trial to evaluate alternative dosing regimens in lower- risk MDS, with timelines for completion and reporting established by the FDA. In addition, RYTELO and the manufacturing processes and facilities, post- approval clinical data, labeling, advertising and promotional activities related to RYTELO will be subject to continual requirements of, and review by, the FDA and comparable regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, compliance with good pharmacovigilance practices, registration requirements, current Good Manufacturing Practice, or cGMP, requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding promotional interactions with healthcare professionals. Failure to comply with these post- marketing requirements and commitments or any other regulatory requirements, or later discovery of previously unknown problems with RYTELO, or our manufacturers, or manufacturing processes for RYTELO, may result in actions such as: • restrictions on RYTELO manufacturing, distribution or use; • restrictions on labeling or marketing; • additional post- marketing requirements or commitments; warning letters, withdrawal of RYTELO from the market; • product recalls; • suspension or termination of ongoing clinical trials of imetelstat in other indications; • significant civil, criminal and administrative penalties, including fines, restitutions or disgorgement of profits or revenues; • refusal to permit the import or export of RYTELO; • product seizure or detentions; injunctions or the imposition of civil or criminal penalties; and • adverse publicity. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. In addition, the regulations, policies or guidance of the FDA or any other regulatory authority may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post- approval activities. We also cannot predict the likelihood, nature, or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are unable to fulfill the post-marketing requirements and commitments established by the FDA for RYTELO in lower- risk MDS, or that may be applied to the approval and commercialization of RYTELO by any regulatory authority, or are unable to adapt to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, there may be a negative impact to our business and continued regulatory approval of RYTELO. Under such circumstances, we or our respective service providers may be subject to the actions listed above, including losing marketing approval for RYTELO, which would severely and adversely affect our business and business prospects, and might cause us to cease operations. If RYTELO is approved outside the U. S., we will be subject to similar requirements, considerations and risks in other regions. We may be unable to obtain regulatory approval to commercialize RYTELO in any other jurisdictions or for any new indications, or may experience significant delays in doing so, any of which could severely and adversely affect our business and business prospects, and might cause us to cease operations. We may never receive regulatory approval for **RYTELO in any other jurisdictions or ~~or~~ for any new indications. It can take many years to obtain approval, if approval is obtained at all. Of the large number of drugs in development, only a small percentage complete the development and regulatory approval process and are successfully commercialized. In addition, the lengthy review process and the unpredictability of future or ongoing clinical trials may result in a delay in obtaining, or our failure to obtain, regulatory approval for RYTELO in lower- risk MDS in any jurisdiction other than the U. S., or our inability to obtain regulatory approval for RYTELO for relapsed / refractory MF or for any other indications, which could significantly harm our business and business prospects, and might cause us to cease operations. Securing marketing approval requires the submission of extensive non- clinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish to the satisfaction of such regulatory authorities the product candidate' s safety and efficacy, as well as information about the product manufacturing process and any inspections of manufacturing facilities conducted by regulatory authorities through the filing of an NDA in the U. S. and an MAA in the EU. Although RYTELO is approved in the U. S. in lower- risk MDS and the EMA is reviewing our MAA for RYTELO for lower- risk MDS, there can be no assurance that we will receive regulatory approval from the EC for the commercialization of RYTELO for lower- risk MDS or in any other jurisdiction or for any new indications. Any marketing approval that we may receive for RYTELO in the EU for lower- risk MDS, or in any other jurisdiction or for**

any other indication may also be limited or subject to restrictions or post- approval commitments that increase our costs or render RYTELO not commercially viable, which would harm our business and business prospects. Regulatory authorities may also not approve the labeling claims that are necessary or desirable for the successful commercialization of a drug, such as RYTELO. For example, although we received regulatory approval from the FDA in June 2024 to commercialize **RYTELO in lower- risk MDS, any future regulatory clearances that we might obtain for RYTELO may be limited to fewer or narrower indications than we might request, or may be granted subject to the performance of post- marketing studies, which may impose further requirements or restrictions on the distribution or use of RYTELO, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe- use criteria, and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for RYTELO and affect reimbursement by third- party payors. Future regulatory clearances, if any, may be limited to a smaller patient population, or may require a different drug formulation or a different manufacturing process, than we might in the future decide to seek. Any delay in obtaining or failure to obtain required approvals of RYTELO in any other jurisdictions or for any other indications, or limitations on any regulatory approval that we might receive in the future, if any, could reduce the potential commercial use of RYTELO, and potential market demand for RYTELO and therefore result in decreased revenue for us from any commercialization of RYTELO in any other jurisdictions or for any other indications, any of which could severely and adversely affect our financial results and ability to raise additional capital, if needed, the price of our common stock, our business and business prospects, and might cause us to cease operations. We may experience additional risks related to operating outside of the U. S. that could materially adversely affect our business. We have employees located outside of the U. S., conduct clinical trials outside of the U. S., and are seeking to obtain regulatory approval to market RYTELO in the EU, which may subject us to additional risks related to operating outside of the U. S., such as: • the EC and other foreign regulatory approvals, if any, may take longer and be more costly to obtain than approvals in the U. S., due to differing regulatory requirements in foreign countries; • approval policies or regulations in the EU or of regulatory authorities outside of the U. S. may significantly change in a manner rendering our clinical data insufficient for potential approval; • the EMA and other regulatory authorities outside of the U. S. may disagree with the design, implementation or results of our clinical trials or our interpretation of data from nonclinical studies or clinical trials; • we may experience unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements; • risks of potential noncompliance with legal requirements applicable to privacy, data protection, information security and other matters; • risks of potential noncompliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • increased taxes outside of the U. S., including withholding and payroll taxes; • significant foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; • difficulties staffing and managing operations outside of the U. S.; • complexities associated with managing multiple payor reimbursement regimes and government payors in foreign countries; • workforce uncertainty in countries where labor unrest is more common than in the U. S.; • potential liability under the Foreign Corrupt Practices Act of 1977 or comparable regulations outside of the U. S.; and • business interruptions resulting from geopolitical actions, including war and terrorism. For example, the new Trump administration has called for substantial changes to foreign trade policy and has raised the possibility of imposing significant increases in tariffs on international trade. We cannot predict what effects these and potential additional tariffs will have on our business, including in the context of escalating global trade and political tensions. However, such tariffs and other trade restrictions could increase our cost of doing business, reduce our gross margins or otherwise negatively impact our financial results. These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations. Uncertainty in the regulatory framework and future legislation could lead to disruption in the execution of international multi- center clinical trials, the monitoring of adverse events through pharmacovigilance programs, the evaluation of the benefit- risk profiles of new medicinal products, and determination of marketing authorization across different jurisdictions. Changes to existing regulations may add considerably to the time from clinical development to marketing authorization and commercialization of products in foreign jurisdictions and increase our costs. We cannot predict the impact of such changes and future regulation on our business or the results of our operations. Although orphan drug designation has been granted to RYTELO for the treatment of MDS and MF in the U. S. and in the EU, these designations may not be maintained, which would eliminate the benefits associated with orphan drug designation, including market exclusivity, which could limit the period of exclusivity we are able to maintain for the commercialization of RYTELO, and would likely harm our business and business prospects. The FDA granted orphan drug designation to RYTELO in June 2015 for the treatment of MF and for the treatment of MDS in December 2015, and the EC granted orphan drug designation in December 2015 to RYTELO for the treatment of MF and in July 2020 for the treatment of MDS. Orphan drug exclusivity confers seven and 10 years of exclusivity in the U. S. and EU, respectively, following approval, subject to satisfying regulatory requirements. The FDA has confirmed seven years of orphan drug exclusivity for RYTELO following its approval on June 6, 2024 for its approved indication in lower- risk MDS. As part of its review of our MAA for RYTELO, the EMA reviewed the grant of orphan drug designation for the treatment of certain patients with MDS. Designation as an orphan drug does not guarantee that any regulatory authority will accelerate regulatory review of, or ultimately approve, RYTELO for any indication, or at all, in the U. S., EU or any other country, nor does it limit the ability of any regulatory authority to grant orphan drug designation to product candidates of other companies that treat the same indications as RYTELO prior to RYTELO receiving any exclusive marketing approval. We may lose orphan drug exclusivity for certain reasons, including if the FDA or the EMA determines that the request for orphan drug**

designation was materially defective or if we cannot ensure sufficient quantities of RYTELO to meet the needs of patients with lower- risk MDS or MF. Failure to maintain orphan designation status, or failure to agree to and complete any agreed upon pediatric plan, would lead to the inability to obtain or the loss of such regulatory exclusivity. Even if we maintain orphan drug exclusivity for RYTELO, the exclusivity may not effectively protect RYTELO from all competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug product is approved, the FDA or other regulatory authorities can subsequently approve a different drug with the same active moiety for the same condition, if the FDA or other regulatory authorities conclude that the later drug is safer, more effective, or makes a major contribution to patient care. The occurrence of any of these events could limit the period of exclusivity we are able to maintain for RYTELO, and may harm our business and business prospects. In addition, for any other indication that we are currently or may in the future seek to develop or obtain regulatory approval for RYTELO, orphan drug designation will neither shorten the development time nor regulatory review time for RYTELO, and it does not give RYTELO any advantage in the regulatory review or approval process. Even though we reported positive top- line results from IMerge Phase 3 in January 2023 and received regulatory approval from the FDA in June 2024 to commercialize RYTELO in the U. S. for lower- risk MDS, the top- line results from IMerge Phase 3 are not necessarily predictive of RYTELO' s activity in other indications, such as from IMpactMF. Even though we reported positive top- line results from IMerge Phase 3 in January 2023 and received regulatory approval from the FDA in June 2024 to commercialize RYTELO in lower- risk MDS, the top- line results from IMerge Phase 3 are not necessarily predictive of RYTELO' s activity in other indications and for other pivotal trials that may be needed to support any application to the FDA or similar international regulatory authorities for such other indications, such as from IMpactMF. In addition, with respect to the trial design for IMpactMF, the FDA urged us to consider adding a third dosing arm to the trial to assess a lower dose and / or a more frequent dosing schedule that might improve the trial' s chance of success by identifying a less toxic regimen and / or more effective spleen response, one of the trial' s secondary endpoints. Based on data from IMbark, we believe that testing a lower dose regimen would likely result in a lower median OS, which is the trial' s primary endpoint, in the imetelstat treatment arm. Existing data also suggest that lowering the dose would not result in a clinically meaningful reduction in toxicity, and for these reasons we determined not to add a third dosing arm to the trial design and the FDA did not object to our proposed imetelstat sodium dose and schedule of 9. 4 mg / kg every three weeks. Our belief may ultimately be incorrect. Therefore, our failure to add a third dosing arm could result in a failure to maintain regulatory clearance from the FDA and similar international regulatory authorities for relapsed / refractory MF, could result in the trial' s failure, or could otherwise delay, limit or prevent marketing approval of imetelstat for relapsed / refractory MF by the FDA or similar international regulatory authorities. Regulatory authorities have substantial discretion in the approval process and can delay, limit or deny approval of RYTELO in other jurisdictions or indications, or require us to conduct additional non- clinical or clinical testing or abandon a program for many reasons, including: • disagreement with the design or implementation of our clinical trials, including our statistical analysis of trial results; • failure to demonstrate that RYTELO' s efficacy results provide sufficient evidence of overall clinical benefit; • unfavorable benefit- to- risk assessment, in the case of marginal efficacy and / or clinically relevant safety concerns, for any proposed indication; • serious and unexpected drug- related side effects experienced by participants in our clinical trials or by individuals using RYTELO or drugs similar to RYTELO; • disagreement with our interpretation of data from non- clinical studies or clinical trials; • rejection by the FDA of foreign data included in any future supplemental NDA, or sNDA, submissions for any future indications and the non- applicability of this data to the U. S. population and U. S. medical practice; • identification of critical issues as a result of a pre- approval health authority inspection that could negatively impact the integrity of data in the MAA and any future sNDA and lead to a rejection by the FDA, EMA, or similar international regulatory authorities; • a determination by international regulatory authorities that regulatory approval for RYTELO should be narrowed or made more restrictive than our current approval in the U. S. for lower- risk MDS or any future indication for which approval is sought, if any; • disagreement regarding the formulation, labeling and / or the specifications for RYTELO; • the failure of the quality or stability of RYTELO to meet acceptable regulatory standards; • the EMA or the competent authorities of the individual EU Member States or similar international regulatory authorities may lack resources or be delayed in conducting pre- approval inspections due to lack of resources or other reasons; • we or any third- party service providers may be unable to demonstrate compliance with GMP, GCP, or other applicable regulatory and other requirements to the satisfaction of the FDA, the EMA, the competent authorities of the individual EU Member States or similar international regulatory authorities; or • changes in regulatory policies or approval processes, or potential reduction of unmet medical need with the entry of competitive therapies to the market, could render our clinical efficacy or safety data insufficient for approval. Any of these events may result in a failure to further develop, obtain regulatory approval for or commercialize RYTELO in any jurisdiction or in any indication other than lower- risk MDS in the U. S., which could severely and adversely affect our business and business prospects. Furthermore, in recent years, there has been increased public and political scrutiny on the FDA and similar international regulatory authorities with respect to the approval process for new drugs, and as a result regulatory authorities may apply more stringent regulatory standards, especially regarding drug safety, when reviewing regulatory submissions. RISKS RELATED TO COMPLIANCE WITH HEALTHCARE LAWS The FDA, DOJ and other regulatory authorities actively enforce regulations related to the promotion and advertisement of pharmaceutical products, and if we were found to have violated the Food, Drug and Cosmetic Act, we could be subject to significant civil, criminal and administrative penalties. The FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product' s approved labeling. The FDA,

DOJ and other agencies actively enforce regulations related to the promotion and advertisement of pharmaceutical products. If we were found to have violated the Food, Drug, and Cosmetic Act, we could be subject to significant civil, criminal and administrative penalties, which could inhibit our ability to commercialize RYTELO and generate revenue, require us to expend significant time and resources in response, and generate negative publicity. Enforcement actions include, among others: • adverse regulatory inspection findings; • fines, warning letters, or untitled letters; • voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals; • restrictions on, or prohibitions against, marketing RYTELO; • restrictions on, or prohibitions against, importation or exportation of RYTELO; • suspension of review or refusal to approve pending applications or supplements to approved applications; • exclusion from participation in government- funded healthcare programs; • exclusion from eligibility for the award of government contracts for RYTELO; • suspension or withdrawal of regulatory approval for RYTELO; • product seizures; • injunctions; and • civil and criminal penalties and fines. The imposition of any of these penalties or other commercial limitations, including equivalent penalties or commercial limitations imposed by foreign regulatory authorities, could severely and adversely affect our financial results, business and business prospects, including the commercialization of RYTELO, and might cause us to cease operations. Similar requirements and related consequences apply outside the U. S. Enhanced governmental and private scrutiny over, or investigations or litigation involving, pharmaceutical manufacturer donations to patient assistance programs offered by charitable foundations may require us to modify our programs and could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses. To help patients afford our products, we have a patient assistance program and also occasionally make donations to independent charitable foundations that help financially needy patients. These types of programs designed to assist patients in affording pharmaceuticals have become the subject of scrutiny. In recent years, some pharmaceutical manufacturers were named in class action lawsuits challenging the legality of their patient assistance programs and support of independent charitable patient support foundations under a variety of federal and state laws. At least one insurer also has directed its network pharmacies to no longer accept manufacturer co- payment coupons for certain specialty drugs the insurer identified. Our patient assistance program and support of independent charitable foundations could become the target of similar litigation. In addition, there has been regulatory review and enhanced government scrutiny of donations by pharmaceutical companies to patient assistance programs operated by charitable foundations. For example, the Office of Inspector General of the U. S. Department of Health & Human Services, or OIG, has established specific guidelines permitting pharmaceutical manufacturers to make donations to charitable organizations who provide co- pay assistance to Medicare patients, provided that such organizations are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first- come basis according to consistent financial criteria, and do not link aid to use of a donor' s product. If we or our vendors or donation recipients are deemed to fail to comply with laws or regulations in the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. A government investigation could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses. If our business activities become subject to challenge under supranational, national, federal, state or international healthcare laws, including fraud and abuse, transparency, and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payors and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including federal and state fraud and abuse laws, including anti- kickback and false claims laws; data privacy and security laws, including the Health Insurance Portability and Accountability Act, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH; and transparency laws related to payments and / or other transfers of value made to physicians, other healthcare professionals and teaching hospitals. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we market, sell and distribute RYTELO. For details regarding the restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate, see Item 1 " Business- Government Regulation- Fraud and Abuse, and Transparency Laws and Regulations " of this Report. Federal and state enforcement bodies have increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. If our operations are found to be in violation of any of these or any other healthcare and privacy- related regulatory laws that may apply to us, our ability to operate our business and our results of operations could be adversely affected by: • the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement and imprisonment; • possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs or comparable foreign programs; • reputational harm; • diminished profits and future earnings; • additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws; and • curtailment of our operations. Defending against any such actions can be costly, time- consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. The adoption of health policy changes and healthcare reform both in the U. S. and outside the U. S. may adversely affect our business and financial results. In the U. S. and some jurisdictions outside the U. S., there have been a number of legislative and regulatory changes and

proposed changes regarding the healthcare system that could impact our business. Generally, there has been increasing legislative and enforcement interest in the U. S. with respect to drug pricing, including specialty drug pricing practices, in light of the rising cost of prescription drugs and biologics. Specifically, there have been U. S. Congressional inquiries and federal and state legislative activity designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the price of drugs under Medicare, and reform government program reimbursement methodologies for drugs and biologics. For details regarding these legislative and regulatory changes and proposed changes regarding the healthcare system that may affect our ability to operate, see Item 1 " Business- Healthcare Reform " in this Report. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business and financial results. Managed care organizations, as well as Medicaid and other government authorities, continue to seek price discounts. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biologic product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on future sales of RYTELO in the U. S., and outside the U. S. if approved in other jurisdictions. RISKS RELATED TO THE FURTHER DEVELOPMENT OF RYTELO (IMETELSTAT) We cannot be certain that we will be able to continue to develop RYTELO or advance it in clinical trials, or that we will be able to receive regulatory approval for RYTELO in any other indications in the U. S., the EU or any other region , on a timely basis or at all. **We** ~~Imetelstat is our sole product candidate, upon whose success we~~ are wholly dependent **on the success of RYTELO (imetelstat), which is our only approved product, and our ability to generate revenue from product sales and achieve profitability is wholly dependent on our ability to successfully commercialize RYTELO for lower- risk MDS or to expand its indications of use. In this regard, in addition to lower- risk MDS, which is the only indication for which RYTELO has received marketing approval in the U. S., we are developing imetelstat for the treatment of several myeloid hematologic malignancies** . Our ability to **further** develop imetelstat and ~~launch~~ **to expand** ~~it its~~ ~~commercially~~ **indications of use to other myeloid hematologic malignancies** is subject to significant risks and uncertainties, including, among other things, our ability to: • receive regulatory approval to commercialize ~~imetelstat~~ **RYTELO** in lower- risk MDS from the **EC** ~~FDA and European Commission,~~ without the requirement for the conduct and completion of additional pre- approval clinical trials or further analyses, testing or development commitments, if at all, any of which could result in increased costs to us, and delay, limit or preclude our ability to generate revenue **in the EU** ; • generate sufficient safety and efficacy data from the IMpactMF clinical trial to support any application for regulatory approval in relapsed / refractory MF, without clinically meaningful safety issues, side effects or dose- limiting toxicities related to imetelstat that may negatively impact its benefit- risk profile; • ascertain that the use of imetelstat does not result in significant systemic or organ toxicities, including hepatotoxicity, or other safety issues resulting in an unacceptable benefit- risk profile; • obtain additional capital **if and** when needed in order to enable us to further advance ~~the~~ imetelstat ~~program~~ **clinical trials in other myeloid hematologic malignancies** ; • obtain and maintain required regulatory clearances and approvals to enable continued clinical development ~~, as well as potential commercialization,~~ of imetelstat; • enter into and maintain commercially reasonable arrangements with third parties to provide services needed to further research ~~and~~ **,** develop ~~,~~ and ~~to potentially~~ commercialize **RYTELO** ~~, imetelstat~~ , including maintaining the agreements with our contract research organizations, or CROs, and third- party manufacturers; • recruit and retain sufficient qualified and experienced personnel to support the development and **commercialization of RYTELO in** potential ~~commercialization of imetelstat in~~ **other approved indications and jurisdictions outside** the U. S.; • enter into and maintain arrangements with third parties to provide services needed to support the ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO** for territories outside of the U. S. in compliance with applicable laws; • achieve acceptance of **RYTELO treatment** ~~imetelstat, if approved,~~ by patients and the relevant medical communities; • compete effectively with other approved treatments in lower- risk MDS **,** and relapsed / refractory MF if imetelstat is approved in ~~those indications~~ **relapsed / refractory MF, and potentially other myeloid hematologic malignancies** ; • obtain appropriate coverage and reimbursement levels for the cost of ~~imetelstat~~ **RYTELO** from governmental authorities, private health insurers and other third- party payors; and • obtain, maintain and enforce adequate intellectual property and regulatory exclusivity for **RYTELO** ~~imetelstat both~~ in the U. S. and globally. If we are not able to successfully achieve these goals and overcome other challenges that we may encounter in the research, development, manufacturing and ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO in indications other than lower- risk MDS** , we may be forced to abandon our development and / or ~~planned~~ commercialization of ~~imetelstat~~ **RYTELO in indications other than lower- risk MDS** , which ~~would~~ **could** severely harm our business ~~,~~ **and business** prospects ~~and our ability to raise additional capital, and might cause us to cease operations~~ . Our clinical trials of imetelstat could be interrupted, delayed, terminated or abandoned for a variety of reasons which could severely and adversely affect our financial results, business and business prospects ~~, and the future of imetelstat~~ . The conduct and completion of our clinical trials could be interrupted, delayed or abandoned for a variety of reasons, including as a result of clinical trial failures, suspensions, terminations or delays related to: • patient recruitment, enrollment and retention challenges and operational delays, including in connection with opening new clinical **trial** sites, while also competing with clinical trials for other investigational drugs in the same patient population; • use of trial endpoints such as overall survival, that inherently require prolonged periods of clinical observation or analysis of the resulting data to determine trial outcomes, including the need for a certain number of events, or deaths, to occur in IMpactMF prior to the **interim or** final analysis in that trial of overall survival; • obtaining and / or maintaining regulatory clearances in the U. S. or other ~~countries~~ **jurisdictions** to commence, conduct or modify current or potential future clinical trials of imetelstat, in a

timely manner, or at all; • investigational new drug applications, or INDs, and equivalent submissions in other countries for imetelstat being placed on full or partial clinical hold, suspended or subject to other requirements by the FDA or other similar international regulatory authorities; • contracting with a sufficient number of clinical trial sites to conduct current and potential future clinical trials, and ensuring that such contracts contain all necessary terms and conditions required by applicable laws, including providing for valid mechanisms to engage in cross- border data transfers, as well as identifying, recruiting and training suitable clinical investigators; • obtaining or accessing necessary clinical data in accordance with appropriate clinical or quality practices and regulatory requirements, in a timely and accurate manner to ensure complete data sets; • responding to safety findings, recommendations or conclusions by the data safety review committees, independent data monitoring committees and / or expert committees of current and potential future clinical trials of imetelstat based on emerging data occurring during such clinical trials; • manufacturing sufficient quantities that meet our specifications, cost and quality requirements, and timelines for imetelstat, or **for** other clinical trial materials, in a manner that meets the quality standards of the FDA and other similar international regulatory authorities, and responding to any disruptions to drug supply, clinical trial materials or quality issues that may arise; • the effects of macroeconomic or other global conditions, such as inflation, rising interest rates, prospects of a recession, government shutdowns **, changes in tariffs or other trade restrictions** , bank failures and other disruptions to financial systems, civil or political unrest, military conflicts, pandemics or other health crises and supply chain and resource issues; • complying with current and future regulatory requirements, policies or guidelines, including domestic and international laws and regulations pertaining to fraud and abuse, transparency, and the privacy and security of health information; • reaching agreement on acceptable terms and on a timely basis, if at all, with collaborators, physician investigators, vendors and other third parties located in the U. S. or other countries, including our CROs, laboratory service providers and clinical trial sites, on all aspects of clinical development and collaborating with them successfully; and • third- party clinical contractors, including investigators or our CROs not performing our clinical trials according to our anticipated schedule or consistent with the clinical trial protocol, good clinical practices, or GCP, or other regulatory requirements, or not performing data collection or analyses in a timely or accurate manner. Failures or delays with respect to any of these events could adversely affect our ability to conduct or complete the clinical trials being conducted by us or our investigators, or to commence, conduct and complete potential future clinical trials of imetelstat, which could increase development costs, or interrupt, further delay or halt our development **,** ~~or potential commercialization~~ of imetelstat, any of which could severely and adversely affect our financial results, business and business prospects ~~, and the future of imetelstat~~ . ~~Imetelstat~~ **RYTELO** may cause, or have attributed to it, undesirable or unintended side effects or other adverse events that could **halt or limit its** further **commercialization** ~~delay or prevent the commencement and / or completion of clinical trials for imetelstat~~ , delay or prevent its regulatory approval **in any other jurisdiction or indication** , **or cause us to delay or terminate our clinical trials. RYTELO (imetelstat) has been administered only to a limited number of patients in clinical trials. While the FDA granted approval of RYTELO based on the data included in our NDA, including data from the Phase 3 IMerge trial, we do not know whether the results when a larger number of patients receive RYTELO from commercial use, including results related to safety, will be consistent with the results from earlier clinical trials that served as the basis for its approval. In addition, because remaining patients in ongoing clinical trials continue to receive imetelstat, additional or more severe toxicities or safety issues may be observed, and the benefit- risk profile of imetelstat will continue to be assessed, including the risk of hepatotoxicity, severe cytopenias, fatal bleeding with or without any associated thrombocytopenia, patient injury or death. New data relating to imetelstat, including from adverse event reports and our post- marketing requirements in the United States, and from ongoing clinical trials of imetelstat, may result in changes to the product label and may adversely affect sales, or result in withdrawal of imetelstat from the market. The FDA and regulatory authorities in other jurisdictions may also consider the new data in reviewing our marketing applications for additional indications and / or in other jurisdictions, or impose post- approval requirements. If any of these actions were to occur, it could result in significant expense and delay** or limit ~~its commercial~~ **our ability to generate sales revenues. Further, as a result of commercialization of RYTELO, or in current or** potential ~~. Imetelstat~~ **future clinical trials, RYTELO** may cause, or have attributed to it, undesirable or unintended side effects or other adverse events affecting its safety or efficacy that could interrupt, further delay or halt **its commercialization or** current or potential future clinical trials ~~of imetelstat, as well as our expanded access program~~ . In this regard, adverse events and dose- limiting toxicities observed in previous and ongoing clinical trials ~~of imetelstat~~ include: • hematologic toxicities, such as profound and / or prolonged thrombocytopenia or neutropenia; • bleeding events, with or without thrombocytopenia, including Grade 3 / 4 bleeding events; • febrile neutropenia; • hepatotoxicity and liver function test abnormalities, as well as hepatic failure; • gastrointestinal events; • infection events, with or without neutropenia, including Grade 3 / 4 infection events; • muscular and joint pain; • fatigue; • headache; and • infusion- related reactions. If patients **who receive RYTELO as a result of commercialization or** in any clinical trials ~~of imetelstat or our expanded access program~~ experience similar or more severe adverse events, or new or unusual adverse events, or if the FDA or other similar international regulatory authorities determine that efficacy and safety data **from our commercialization efforts or** in clinical trials ~~of imetelstat~~ do not support an adequate benefit- risk profile to justify continued treatment of patients, then the FDA or other similar international regulatory authorities may **halt or restrict the commercialization of RYTELO or** place one or more of ~~the~~ **our** INDs ~~for imetelstat~~ on clinical hold, as occurred in March 2014. If this were to occur, there ~~would~~ **could** be a significant delay in, or possible termination of, one or more of **our** ~~the imetelstat~~ clinical trials **,** and **our** ~~any potential~~ commercialization efforts **could be halted** , which might cause us to cease operations. ~~For example, we are aware of a case in our IMpactMF clinical trial of a patient with myelofibrosis associated with underlying progressive bone marrow failure, who died from febrile neutropenia, pulmonary hemorrhage and bilateral pneumonia, which, at the time of reporting, the investigator related to imetelstat.~~ If such toxicities or other safety issues **identified as a result of our commercialization of RYTELO or** in any clinical trial ~~of imetelstat~~ are determined by us, the FDA or similar international regulatory authorities to result in an

unacceptable benefit- risk profile, then: • **the FDA could withdraw or restrict regulatory approval for RYTELO in the U. S. for lower- risk MDS; •** additional information supporting the benefit- risk profile of ~~imetelstat~~ **RYTELO** may be requested by the FDA or similar international regulatory authorities and if any such information is not available or, if available, not deemed acceptable, **regulatory approval could be withdrawn by the FDA in the U. S., and / or** current clinical trials ~~of imetelstat~~ could be suspended, terminated, or placed on clinical hold by the FDA or similar international regulatory authorities; • the ability to retain enrolled patients in our current clinical trials may be negatively affected, resulting in incomplete data sets and the inability to adequately assess the benefit- risk profile of ~~imetelstat~~ **RYTELO** in a specific patient population; • additional, unexpected clinical trials or non- clinical studies may be required to be conducted; or • ~~imetelstat~~ **RYTELO** may not receive or maintain ~~any~~ regulatory **clearances** ~~authorizations, including for commercial use. Further, clinical trials by their nature examine the effect of a potential therapy in a sample of the potential future patient population. As such, clinical trials conducted with imetelstat, to date~~ and **approvals required to enable its** ~~in the future, may not uncover all possible adverse events that patients treated with imetelstat may experience. Because remaining patients in ongoing clinical trials and in our expanded access program continue~~ **continued development** ~~to receive imetelstat treatment, additional or more severe toxicities or safety issues may be observed, and the benefit- risk profile of imetelstat will continue to be assessed, including the risk of hepatotoxicity, severe cytopenias, fatal bleeding with or without any associated thrombocytopenia, patient injury or death~~ . The occurrence of any of these events could interrupt, further delay, or halt, ~~any~~ **our commercialization or RYTELO or its further** development, and as a result, **could** ~~impact or~~ preclude the ~~potential regulatory approval and~~ commercialization of ~~imetelstat~~ **RYTELO in any additional indications** , as well as increase costs ~~to~~ **for continued** ~~develop~~ **development** ~~imetelstat~~ **in additional indications** , which would have a severe adverse effect on our results of operations, financial condition and ability to raise additional capital, business **and business** prospects ~~and the future of imetelstat~~ , any of which might cause us to cease operations. Results and data we disclosed from prior non- clinical studies and clinical trials may not predict success in later clinical trials, and we cannot assure you that any ongoing or future clinical trials of imetelstat **, including IMpactMF,** will lead to similar results and data that could potentially enable us to obtain any **further** regulatory approvals. The design of a clinical trial can determine whether its results will support regulatory approval of a product, and flaws in the trial design may not become apparent until the clinical trial is well advanced or during the approval process after the trial is completed. A clinical trial design that is considered appropriate for regulatory approval includes a sufficiently large sample size with appropriate statistical power, as well as proper control of bias, to allow a meaningful interpretation of the results. The preliminary results of imetelstat clinical trials with smaller sample sizes can be disproportionately influenced by the impact the treatment had on a few individuals, which limits the ability to generalize the results across a broader community, making the trial results of clinical trials with smaller sample sizes less reliable than trials with a larger number of patients. As a result, there may be less certainty that imetelstat will achieve a statistically significant effect in any future clinical trials. Further, success in non- clinical testing and early clinical trials, including Phase 2 clinical trials, such as IMbark, does not ensure that later clinical trials will be successful, nor does it predict final clinical trial results. In addition, even though we reported positive top- line results from IMerge Phase 3 in January 2023, this does not ensure that any other clinical trials of imetelstat will be successful. Later stage clinical trials of imetelstat may fail to show an acceptable benefit- risk profile despite having progressed through non- clinical studies and initial clinical trials. Many companies in the biopharmaceutical industry have frequently suffered significant setbacks in later clinical trials, even after achieving promising results in earlier non- clinical studies or clinical trials. In general, Phase 3 clinical trials with larger numbers of patients or longer durations of therapy may fail to replicate efficacy and safety results observed in earlier clinical trials, such as IMbark, and if this were to occur with IMpactMF, this would adversely affect future development prospects of imetelstat, and as a result, impact the potential commercialization of imetelstat in relapsed / refractory MF, which would have a severe adverse effect on our results of operations, financial condition and ability to raise additional capital, **if needed, business and** business prospects ~~and the future of imetelstat~~ , any of which might cause us to cease operations. Furthermore, non- clinical and clinical data are often susceptible to varying interpretations and analyses. In some instances, there can be significant variability between different clinical trials of imetelstat due to numerous factors, including changes in trial procedures set forth in trial protocols, differences in the size and type of patient populations, and changes in and adherence to the dosing regimens. For example, although the statistical analyses comparing IMbark data to closely matched real world data, or RWD, published in the September 2021 issue of the Annals of Hematology, suggest potentially favorable overall survival in relapsed / refractory MF patients treated with imetelstat, compared to BAT using closely matched patients' RWD, such comparative analyses between RWD and our clinical trial data have several limitations. For instance, the analyses create a balance between treatment groups with respect to commonly available covariates, but do not take into account the unmeasured and unknown covariates that may affect the outcomes of the analyses. Potential biases are introduced by factors which include, for example, the selection of the patients included in the analyses, misclassification in the matching process, the small sample size, and estimates that may not represent the outcomes for the true treated patient population. Failure to achieve results supporting a positive benefit- risk profile in current or potential future imetelstat clinical trials would interrupt, further delay, or halt, any development ~~, and as a result, prevent potential regulatory approval and commercialization~~ of imetelstat, which would have a severe adverse effect on our results of operations, financial condition and ability to raise additional capital, **if needed, business and** business prospects ~~and the future of imetelstat~~ . Further, preliminary data are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. Additional or updated safety and efficacy data from current or potential future clinical trials of imetelstat may result in a benefit- risk profile that does not justify the continued development and / or potential regulatory approval of imetelstat in a particular patient population, or at all. Any data reported from IMpactMF may materially differ from and be less positive than data

previously reported from IMbark. Thus, reported data should be considered carefully and with caution, and not relied upon as indicative of future clinical results. Such additional data could result in a lower benefit- risk profile than initially expected, which could **halt the commercialization of RYTELO,** hinder the potential success of IMpactMF, IMproveMF or IMpress, or cause us to abandon further development of imetelstat entirely. Top- line results and data may differ from future results of the same study, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Moreover, as remaining patients in IMerge Phase 3 continue to be treated and followed under the extension phase of the trial and longer- term outcomes are assessed, these additional and more mature data may alter the benefit- risk profile of imetelstat in an adverse manner, including with respect to overall survival. Material adverse differences in future results, compared to preliminary, interim or top- line data, could severely and adversely affect our financial results, business and business prospects, ~~and the future of imetelstat,~~ including the ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO** , and might cause us to cease operations. We rely on third parties to conduct our current and potential future clinical trials of imetelstat. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to continue the development of ~~, obtain regulatory approval for, or commercialize~~ imetelstat. We do not have the ability to independently conduct clinical trials. Therefore, we rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, service providers, vendors, suppliers and consultants, to conduct clinical trials of imetelstat. The third parties we contract with for execution of our current and potential future clinical or investigator- sponsored trials of imetelstat play a critical role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we have limited ability to control their performance, or the amount or timing of resources that they devote to imetelstat. For example, we have retained CROs to support our ~~imetelstat~~ clinical development activities, and any failure by our CROs to perform their contractual obligations, or disputes with our CROs about the quality of their performance or other matters, could further delay or halt our ~~imetelstat~~ clinical development activities. These third parties may also have relationships with other commercial entities, some of which may compete with us. Under certain circumstances, these third parties may terminate their agreements with us without cause and upon immediate written notice. Although we rely on third parties to conduct our ~~imetelstat~~ clinical trials, we remain responsible for ensuring that each clinical trial is conducted in accordance with its investigational plan and protocol, and applicable laws. Moreover, the FDA and similar international regulatory authorities require us to comply with GCP regulations and standards for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the rights, integrity and confidentiality of patients participating in clinical trials are protected, including being adequately informed of the potential risks. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, or similar international regulatory authorities, may require us to perform additional clinical trials ~~before approving any application for regulatory approval~~ . We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP or other applicable regulations. In addition, our clinical trials must be conducted with imetelstat produced under applicable GMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials ~~, which would further delay the process for any regulatory approval~~ . Our ability to comply with these regulations and standards may be contingent upon activities conducted by third parties, and if they fail to perform in accordance with contractual obligations and legal requirements, our development of imetelstat may be interrupted, further delayed or halted. Any failures by us or third parties noted above would have a severe adverse effect on our results of operations, financial condition and ability to raise additional capital, **if needed, business and** business prospects ~~and the future of imetelstat~~ , including the ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO** , any of which might cause us to cease operations. Furthermore, the execution of clinical trials and the subsequent compilation and analysis of the data produced, including the interim and final analyses for IMpactMF, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. If the quality or accuracy of the clinical data obtained, compiled or analyzed by third parties is compromised due to their failure to adhere to our clinical trial protocols, GCP or GMP requirements, or for any other reason, we may need to enter into new arrangements with alternative third parties, which would cause delay, and could be difficult, costly or impossible. Switching or adding **clinical research organizations, or** CROs, investigators, vendors and other third parties involves additional costs and delays because of the time it takes to finalize a contract with a new CRO and for their commencement of work. Although we carefully manage our relationships with our CROs, investigators, vendors and other third parties, we and any of these third parties may nonetheless encounter challenges or delays in the future, which could have a material and adverse impact on our business ~~,~~ **and** business prospects ~~and the future of imetelstat~~ . In addition, certain principal investigators for our clinical trials serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA **or comparable foreign regulatory authorities** . The FDA **or comparable foreign regulatory authorities** may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected conduct of the trial. The FDA **or comparable foreign regulatory authorities** may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of any **future** applications for **regulatory** approval **of imetelstat, including in any additional indications** by the FDA ~~and may ultimately lead to the denial of approval of imetelstat~~ . We do not control the conduct of current or any potential future investigator- led clinical trials, and data from such trials could show marginal efficacy and / or clinically relevant safety concerns related to imetelstat resulting in an unfavorable benefit- risk assessment that could materially and adversely impact our ongoing clinical trials, ~~our~~ **or** ~~imetelstat~~ **our** development program as a whole ~~, and / or the prospect for approval for imetelstat~~ . We do not

control the design or administration of ~~the~~ investigator- led clinical ~~trial, IMpress, or any potential future investigator- led~~ trials, nor the submission, approval or maintenance of any IND or international equivalent filings required to conduct these clinical trials. In addition, we do not have control over the timing and reporting of the data from any such investigator- led clinical trials. A delay in the timely completion of or reporting of data from any **current or** potential future investigator- led clinical trial could have a material adverse effect on our ability to **maintain regulatory approval for RYTELO in lower- risk MDS, or to** further develop ~~imetelstat~~ or ~~to~~ advance **it in** ~~imetelstat to subsequent~~ clinical trials. Investigator- led clinical trials may be conducted under less rigorous clinical standards than those used in company- sponsored clinical trials. Accordingly, regulatory authorities may closely scrutinize the data collected from these investigator- led clinical trials. In addition, any investigator- led clinical trials could show marginal efficacy and / or clinically relevant safety concerns that could delay, limit or preclude the further clinical development or marketing approval of ~~imetelstat~~ **RYTELO** in any indication ~~, including lower- risk MDS~~. To the extent that the results of any investigator- led clinical trials raise safety or other concerns ~~regarding imetelstat~~, regulatory authorities may **withdraw or restrict approval for RYTELO,** question the results of such investigator- led clinical trials, or question the results of any of our clinical trials. Safety concerns arising from future investigator- led clinical trials could result in **withdrawal of approval of RYTELO,** partial or full clinical holds being placed on **our** ~~the imetelstat~~ INDs by the FDA or other similar international regulatory authorities, as occurred in March 2014, which would further delay or prevent us from **commercializing RYTELO or** advancing ~~imetelstat~~ **it** into further clinical development ~~,~~**. Any of the foregoing** would delay or preclude any **future** marketing approvals for ~~imetelstat~~ **RYTELO** and could cause us to discontinue our development of ~~imetelstat~~ **it** , ~~any of~~ which would severely harm our business and prospects ~~, including the potential commercialization of imetelstat,~~ and could potentially cause us to cease operations. Risks Related to ~~Regulatory APPROVAL and Commercialization of Imetelstat Our inability to obtain and maintain regulatory clearances and approvals to continue the clinical development of, and to potentially commercialize, imetelstat, would severely and adversely affect imetelstat' s future value, and our business and business prospects, and might cause us to cease operations. Federal, state and local governments in the U. S. and governments in other countries have significant regulations in place that govern drug research and development and may prevent us from successfully conducting development efforts or potentially commercializing imetelstat. Delays in obtaining or failure to maintain regulatory clearances and approvals, or limitations in the scope of such clearances or approvals, could: • impede, halt or increase the costs of our plans for clinical development and commercialization; • significantly harm the commercial potential of imetelstat; • diminish any competitive advantages that may have been available to us; or • delay or preclude any revenue we may receive from the future commercialization of imetelstat, if any. The occurrence of any such event would significantly harm our business, business prospects, including any potential commercialization of imetelstat, and the future value of imetelstat and might cause us to cease operations. If we are unable to obtain regulatory approval for and successfully commercialize imetelstat, or experience significant delays in doing so, our business will be severely harmed. The process of obtaining marketing approvals, both in the U. S. and in other countries, is lengthy, expensive and uncertain. It may take many years to obtain approval, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Of the large number of drugs in development, only a small percentage complete the regulatory approval process and are successfully commercialized. In addition, the lengthy review process as well as the unpredictability of future clinical trial results may result in a delay in obtaining, or our failure to obtain, regulatory approval for imetelstat in lower- risk MDS, relapsed / refractory MF, or any other indication, which would significantly harm our business, business prospects, including the potential commercialization of imetelstat, and the future value of imetelstat and might cause us to cease operations. Securing marketing approval requires the submission of extensive non- clinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish to the satisfaction of such regulatory authorities the product candidate' s safety and efficacy, as well as information about the product manufacturing process and any inspections of manufacturing facilities conducted by regulatory authorities through the filing of an NDA in the U. S. and an MAA in Europe. Although the FDA has accepted for standard review our NDA for imetelstat for the treatment of transfusion- dependent anemia in adult patients with lower- risk MDS who have failed to respond or have lost response to or are ineligible for ESAs, and the EMA has validated our MAA for imetelstat for the same proposed indication, there can be no assurance that we will receive regulatory approval by the FDA or the European Commission for the commercialization of imetelstat in a timely manner or at all. Further, because non- clinical and clinical data are often susceptible to varying interpretations and analyses, regulatory authorities, including the FDA and EMA, may disagree with our interpretation of the data and may require additional clinical testing and / or further analyses from completed clinical or non- clinical trials before we can obtain regulatory approval and begin commercialization of imetelstat, if at all, any of which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects. For example, in connection with the anticipated FDA oncology drug advisory committee meeting concerning the NDA for imetelstat in lower- risk MDS, the FDA will release its review of our data, which may differ, perhaps materially, from our interpretation of our data. Additionally, many sponsors experience volatility in the stock price surrounding the advisory committee' s discussion and vote, even though FDA is not obligated to follow the advisory committee' s input. Furthermore, in IMerge Phase 3 we shortened the follow- up period after the last patient has been enrolled from 15 months to 12 months to enable an earlier clinical cut- off date for the primary analysis. Although we reported positive top- line results from IMerge Phase 3 in January 2023, our decision to shorten the follow- up period after the last patient has been enrolled may result in further clinical responses that may have occurred after the 12- month clinical cut- off date being excluded from the primary analysis. The exclusion of this future data from the primary analysis could reduce the overall efficacy results, including durability of transfusion independence, which could otherwise delay, limit or prevent marketing approval of imetelstat in lower- risk MDS by the FDA or similar international regulatory authorities or require additional clinical trials and further testing prior to granting any regulatory approval to market imetelstat in lower- risk MDS. Even though we reported positive top- line results from IMerge Phase 3 in January 2023, those results are not necessarily~~

predictive of imetelstat activity in other indications and for other pivotal trials that may be needed to support any application to the FDA or similar international regulatory authorities for such other indications, such as from IMpactMF. Any of these events may result in a failure to further develop, obtain regulatory approval for or commercialize imetelstat, which would severely and adversely affect our business and business prospects, and might cause us to cease operations. In addition, with respect to the trial design for IMpactMF, the FDA urged us to consider adding a third dosing arm to the trial to assess a lower dose and / or a more frequent dosing schedule that might improve the trial' s chance of success by identifying a less toxic regimen and / or more effective spleen response, one of the trial' s secondary endpoints. Based on data from IMbark, we believe that testing a lower dose regimen would likely result in a lower median OS, which is the trial' s primary endpoint, in the imetelstat treatment arm. Existing data also suggest that lowering the dose would not result in a clinically meaningful reduction in toxicity, and for these reasons we determined not to add a third dosing arm to the trial design and the FDA did not object to our proposed imetelstat dose and schedule of 9. 4 mg / kg every three weeks. Our belief may ultimately be incorrect. Therefore, our failure to add a third dosing arm could result in a failure to maintain regulatory clearance from the FDA and similar international regulatory authorities, could result in the trial' s failure, or could otherwise delay, limit or prevent marketing approval of imetelstat for relapsed / refractory MF by the FDA or similar international regulatory authorities. Imetelstat must receive all relevant regulatory approvals before it may be marketed in the U. S. or other countries. Regulatory authorities have substantial discretion in the approval process and can delay, limit or deny approval of imetelstat or require us to conduct additional non- clinical or clinical testing or abandon a program for many reasons, including: • disagreement with the design or implementation of our clinical trials, including our statistical analysis of trial results; • failure to demonstrate to the FDA or similar international regulatory authorities that imetelstat' s efficacy results provide sufficient evidence of overall clinical benefit; • unfavorable benefit- to- risk assessment, in the case of marginal efficacy and / or clinically relevant safety concerns, for any proposed indication; • serious and unexpected drug- related side effects experienced by participants in our clinical trials or by individuals using drugs similar to imetelstat; • disagreement with our interpretation of data from non- clinical studies or clinical trials, including disagreement from the oncology drug advisory committee that the FDA has scheduled for March 14, 2024 in connection with the review of the NDA for imetelstat in lower- risk MDS; • rejection by the FDA of foreign data included in the NDA and the non- applicability of this data to the U. S. population and U. S. medical practice; • identification of critical issues as a result of a pre- approval health authority inspection that could negatively impact the integrity of data in an NDA or MAA and lead to a rejection by the FDA, European Commission, or similar international health authorities; • a determination by the FDA, EMA, or similar international regulatory authorities that the appropriate indication for commercial use of imetelstat is narrower or more restrictive than anticipated; • failure to satisfy the requirement to develop a risk evaluation and mitigation strategy, or REMS, for the U. S. and a risk management plan for the EU including post- marketing studies, as a potential condition to approval; • disagreement regarding the formulation, labeling and / or the specifications for imetelstat; • the failure of the quality or stability of imetelstat to meet acceptable regulatory standards; • the FDA, EMA, the competent authorities of the individual EU Member States or similar international regulatory authorities may lack resources or be delayed in conducting pre- approval inspections due to lack of resources or other reasons; • we or any third- party service providers may be unable to demonstrate compliance with GMP, GCP, or other applicable regulatory and other requirements to the satisfaction of the FDA, the competent authorities of the individual EU Member States or similar international regulatory authorities; or • changes in regulatory policies or approval processes, or potential reduction of unmet medical need with the entry of competitive therapies to the market, could render our clinical efficacy or safety data insufficient for approval. Furthermore, in recent years, there has been increased public and political scrutiny on the FDA and similar international regulatory authorities with respect to the approval process for new drugs, and as a result regulatory authorities may apply more stringent regulatory standards, especially regarding drug safety, when reviewing regulatory submissions for new drugs. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post- approval commitments that increase our costs or render imetelstat not commercially viable, which would harm imetelstat' s future value and our business and business prospects. Regulatory authorities may also not approve the labeling claims that are necessary or desirable for the successful commercialization of a drug, such as imetelstat. For example, regulatory authorities may not agree with our belief in the disease- modifying properties of imetelstat, and future regulatory clearances, if any, that we might obtain for imetelstat may be limited to fewer or narrower indications than we might request, or may be granted subject to the performance of post- marketing studies, which may impose further requirements or restrictions on the distribution or use of imetelstat, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe- use criteria, and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for imetelstat and affect reimbursement by third- party payors. Future regulatory clearances, if any, may be limited to a smaller patient population, or may require a different drug formulation or a different manufacturing process, than we might in the future decide to seek. In addition, failure by our former collaborator to comply with applicable regulatory guidelines prior to our assumption of sponsorship of the imetelstat program, or to provide information if requested by regulatory authorities, could result in administrative or judicially imposed sanctions on us, including warning letters, civil and criminal penalties, injunctions, product seizures or detention, product recalls, total or partial suspension of manufacturing activities, and the potential refusal to approve any NDAs, including the NDA for imetelstat in lower- risk MDS. Any delay in obtaining or failure to obtain required approvals of imetelstat, or limitations on any regulatory approval that we might receive in the future, if any, could reduce the potential commercial use of imetelstat, and potential market demand for imetelstat and therefore result in decreased revenue for us from any commercialization of imetelstat, any of which would severely and adversely affect our financial results and ability to raise additional capital, the price of our common stock, our business and business prospects, including the potential commercialization of imetelstat, and the future of imetelstat, and might cause us to cease operations. Any regulatory approval that we may potentially receive for imetelstat could be subject to restrictions, and we may be subject to penalties or product

withdrawal if we fail to comply with regulatory requirements or if we experience unanticipated problems with imetelstat. Any regulatory approval that we may potentially receive for imetelstat could be subject to restrictions or conditions of approval that may require potentially costly post- marketing clinical trials or surveillance to monitor safety and efficacy of the drug candidate. In addition, imetelstat and the manufacturing processes and facilities, post- approval clinical data, labeling, advertising and promotional activities related to imetelstat will be subject to continual requirements of, and review by, the FDA and comparable regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration requirements, current Good Manufacturing Practice **RYTELO** (cGMP **IMETELSTAT**) requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding promotional interactions with healthcare professionals. Failure to comply with these regulatory requirements or later discovery of previously unknown problems with imetelstat, or our manufacturers, or manufacturing processes for imetelstat, may result in actions such as restrictions on imetelstat manufacturing, distribution or use; restrictions on labeling or marketing; requirements to conduct post- marketing studies or clinical trials; warning letters, withdrawal of imetelstat from the market; refusal to approve our pending regulatory applications, or any supplements to approved applications that we might submit; recalls; suspension or termination of ongoing clinical trials; fines, restitutions or disgorgement of profits or revenues; refusal to permit the import or export of imetelstat; product seizure or detentions; injunctions or the imposition of civil or criminal penalties; and adverse publicity. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. In addition, the FDA' s regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post- approval activities. We also cannot predict the likelihood, nature, or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are unable to fulfill any potential post approval commitments that may be applied to the approval and commercialization of imetelstat by any regulatory authority, or are unable to adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements or policies, there may be a negative impact to our business and continued regulatory approval of imetelstat. Under such circumstances, we or our respective clinical investigators may be subject to the actions listed above, including losing marketing approval for imetelstat, which would severely and adversely affect our business and business prospects, including the potential commercialization of imetelstat, and the future of imetelstat, and might cause us to cease operations. If imetelstat is approved for commercialization and we are unable to establish and maintain effective sales, marketing and distribution capabilities or enter into agreements with third parties to commercialize imetelstat, we will be unable to successfully commercialize imetelstat if and when it is approved. We need to complete substantial preparations to be ready for any potential future commercialization of imetelstat, and we are in the process of establishing sales, marketing and distribution capabilities. As a company, we have no experience in selling and marketing products. To advance imetelstat to potential marketing approval and commercialization, we will be required to complete our commercialization preparatory activities, including obtaining and maintaining state licenses where required for us to sell imetelstat, and continue to incur related expenses, before we obtain any marketing approval. These activities include, among other things, the development of an in- house marketing and sales force, which will continue to require significant capital expenditures, management resources and time. We will have to compete with other companies to recruit, hire, train and retain qualified marketing and sales personnel. If we are unable to adequately prepare for the potential future commercialization of imetelstat, we may not be able to generate product revenue if marketing authorization is obtained. There are risks involved with both establishing our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of imetelstat for which we recruit a sales and marketing force and establish distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses, which would be costly. Even if imetelstat is approved in lower- risk MDS and we are able to establish our own sales and marketing capabilities, imetelstat will be a newly- marketed drug. If we are unable to effectively train sales personnel and equip them with compliant and effective materials, our efforts to successfully commercialize imetelstat could be adversely affected, which would negatively impact our business, business prospects and the future value of imetelstat. If we enter into arrangements with third parties to perform commercialization services like sales, marketing and distribution, we will be reliant on the efforts of such third parties, and our sales revenue from sales of imetelstat or the profitability from such sales to us are likely to be lower than if we were to market and sell imetelstat ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize imetelstat or may be unable to do so on terms that are favorable to us. In entering into third- party commercialization arrangements, any revenue we receive will depend upon the efforts of the third parties, and we cannot assure you that such third parties will establish adequate commercialization capabilities or devote the necessary resources and attention to commercialize imetelstat effectively. We also face competition in our search for third parties to assist us with the commercialization efforts of imetelstat. Our inability to successfully establish and maintain effective commercialization capabilities for imetelstat, if we receive regulatory approval to do so, would severely and adversely affect our financial results, business and business prospects, including the potential commercialization of imetelstat, and the future of imetelstat. If we do not obtain acceptable prices or adequate reimbursement for imetelstat, the use of imetelstat could be severely limited. The ability to successfully commercialize imetelstat, if approved, will depend significantly on obtaining acceptable prices and the availability of coverage and adequate reimbursement to the patient from third- party payors. Government payors, such as the Medicare and Medicaid programs, and other third- party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and the reimbursement levels. Assuming we obtain coverage for imetelstat by a third- party payor, the resulting reimbursement payment rates may not be adequate or may require co- payments that patients find unacceptably high. If imetelstat is approved for commercial sale, patients are unlikely to use it unless coverage

is provided, and reimbursement is adequate to cover all or a significant portion of its cost. Therefore, coverage and adequate reimbursement will be critical to new product acceptance. Government authorities and other third- party payors are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices as a condition of coverage, are using restrictive formularies and preferred drug lists to leverage greater discounts in competitive classes, and are challenging the prices charged for medical products. The Inflation Reduction Act of 2022, or the Inflation Reduction Act, includes several provisions to lower prescription drug costs for people with Medicare and reduce drug spending by the federal government, which may ultimately have a negative effect on the pricing for imetelstat, should it receive regulatory approval. However, the Medicare drug pricing negotiation program provisions of the law are currently subject to legal challenges. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third- party payors in the U. S. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of imetelstat to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. We cannot be sure that coverage and reimbursement will be available for imetelstat, if approved for commercial sale, and, if reimbursement is available, what the level of reimbursement will be. There may also be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar international regulatory authorities. Coverage and reimbursement may impact the demand for, or the price of imetelstat, if marketing approval is obtained. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize imetelstat, even if marketing approval is obtained, which would negatively impact our business and business prospects. Although orphan drug designation has been granted to imetelstat for the treatment of MF and MDS in the U. S. and in the EU, these designations may not be maintained, which would eliminate the benefits associated with orphan drug designation, including the potential for market exclusivity, which would likely result in decreased sales revenue from commercialization of imetelstat, if any, and would likely harm our business and business prospects. The FDA granted orphan drug designation to imetelstat in June 2015 for the treatment of MF and for the treatment of MDS in December 2015, and the European Commission granted orphan drug designation in December 2015 to imetelstat for the treatment of MF and in July 2020 for the treatment of MDS. The designation of imetelstat as an orphan drug does not guarantee that any regulatory authority will accelerate regulatory review of, or ultimately approve, imetelstat, nor does it limit the ability of any regulatory authority to grant orphan drug designation to product candidates of other companies that treat the same indications as imetelstat prior to imetelstat receiving any exclusive marketing approval. We may lose orphan drug exclusivity for certain reasons, including if the FDA or the European Commission determines that the request for orphan drug designation was materially defective or if we cannot ensure sufficient quantities of imetelstat to meet the needs of patients with MF or MDS. Failure to maintain orphan designation status, or failure to agree to and complete any agreed upon pediatric plan, would lead to the inability to obtain or the loss of such regulatory exclusivity. Even if we maintain orphan drug exclusivity for imetelstat, the exclusivity may not effectively protect imetelstat from all competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug product is approved, the FDA or the European Commission can subsequently approve a different drug with the same active moiety for the same condition, if the FDA or the European Commission concludes that the later drug is safer, more effective, or makes a major contribution to patient care. The occurrence of any of these events could result in decreased sales of imetelstat, should it ever receive marketing approval, and may harm our business and business prospects. In addition, orphan drug designation will neither shorten the development time nor regulatory review time for imetelstat, and it does not give imetelstat any advantage in the regulatory review or approval process. Although imetelstat has received Fast Track designation by the FDA for MDS and MF, this does not guarantee marketing approval and may not lead to a faster development, regulatory review or approval process. In October 2017, the FDA granted Fast Track designation to imetelstat for the treatment of adult patients with transfusion- dependent low red blood cell counts, or anemia, due to non- del (5q) lower- risk MDS and who are refractory or resistant to treatment with an ESA. In September 2019, the FDA granted Fast Track designation to imetelstat for the treatment of adult patients with relapsed / refractory MF. Fast Track designation provides opportunities for frequent interactions with FDA review staff, as well as eligibility for priority review, if relevant criteria are met, and rolling review of the sponsor' s NDA. Fast Track designation is intended to facilitate and expedite development and review of an NDA to address unmet medical needs in the treatment of serious or life- threatening conditions. However, Fast Track designation does not accelerate conduct of clinical trials or mean that the regulatory requirements are less stringent, nor does it ensure that any imetelstat NDA will be approved or that any approval will be granted within any particular timeframe. In addition, the FDA may withdraw Fast Track designation for any indication if it believes that the designation is no longer supported by data emerging from the imetelstat clinical development program. Failure to achieve continued compliance with government regulations could delay or halt potential commercialization of imetelstat. Approved products and their manufacturers are subject to continual review, and discovery of previously unknown problems with a product or its manufacturer may result in restrictions on the product or manufacturer, including import restrictions, seizure and withdrawal of the product from the market. If approved for commercial sale, future sales of imetelstat will be subject to government regulation related to numerous matters, including the processes of: • manufacturing; • advertising and promoting; • selling and marketing; • medical information; • labeling; and • distribution. If, and to the extent that, we are unable to comply with these regulations, our ability to earn potential revenue from the commercialization of imetelstat, if any, would be materially and adversely impacted. In addition, if imetelstat causes serious or unexpected side effects or is associated with other safety risks after receiving marketing approval, a number of potential significant negative consequences could result, including, but not limited to: • regulatory authorities may withdraw their approval of imetelstat; • we may be required to recall imetelstat, seek to change the way it is administered, conduct additional clinical trials or change the labeling of the product; •

regulatory authorities may require revisions to the labeling of imetelstat, including limitations on approved uses or the addition of further warnings, contraindications or other safety information, or may impose restrictions on distribution in the form of REMS in connection with approval, if any; • we may experience manufacturing delays and supply disruptions if regulatory inspectors identify regulatory noncompliance by third- party manufacturers requiring remediation; • imetelstat may be rendered less competitive and sales may decrease; • our reputation may suffer generally both among clinicians and patients; • we may be exposed to potential lawsuits and associated legal expenses, including costs of resolving claims; • the FDA or similar international regulatory authorities may refuse to approve pending applications or supplements to approved applications filed by us, or may suspend or revoke license approvals; or • we may be required to change or stop ongoing clinical trials of imetelstat, which would negatively impact the development of imetelstat for other potential indications. Any of these events could prevent us from achieving or maintaining market acceptance for imetelstat or could substantially increase the costs and expenses of commercializing imetelstat, which in turn could delay or prevent us from generating any revenues from the sale of the imetelstat. Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product' s approved labeling. The FDA and other agencies actively enforce regulations prohibiting the promotion of any drug product for off- label uses. If we were found to have improperly promoted off- label use of imetelstat, we would be subject to significant civil, criminal and administrative penalties, which would inhibit our ability to commercialize imetelstat and generate revenue, require us to expend significant time and resources in response, and generate negative publicity. Enforcement actions include, among others: • adverse regulatory inspection findings; • fines, warning letters, or untitled letters; • voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals; • restrictions on, or prohibitions against, marketing imetelstat; • restrictions on, or prohibitions against, importation or exportation of imetelstat; • suspension of review or refusal to approve pending applications or supplements to approved applications; • exclusion from participation in government- funded healthcare programs; • exclusion from eligibility for the award of government contracts for imetelstat; • suspension or withdrawal of product approvals; • product seizures; • injunctions; and • civil and criminal penalties and fines. The imposition of any of these penalties or other commercial limitations, including equivalent penalties or commercial limitations imposed by foreign regulatory authorities, would severely and adversely affect our financial results, business and business prospects, including the potential commercialization of imetelstat, and the future of imetelstat, and might cause us to cease operations. We are seeking regulatory approval to market imetelstat in Europe, and as a result, we may experience additional risks related to marketing outside of the U. S. that would materially adversely affect our business. We are seeking regulatory approval to market imetelstat in Europe, and may be subject to additional risks, including, if regulatory approval is obtained from the European Commission, risks related to operating outside of the U. S., such as: • European Commission and other foreign regulatory approvals, if any, may take longer and be more costly to obtain than approvals in the U. S., due to differing regulatory requirements in foreign countries; • EMA and other regulatory authorities outside of the U. S. may disagree with the design, implementation or results of our clinical trials or our interpretation of data from nonclinical studies or clinical trials; • approval policies or regulations of EMA or other regulatory authorities outside of the U. S. may significantly change in a manner rendering our clinical data insufficient for potential approval; • we may experience unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements; • risks of potential noncompliance with legal requirements applicable to privacy, data protection, information security and other matters; • risks of potential noncompliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • increased taxes outside of the U. S., including withholding and payroll taxes; • significant foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; • difficulties staffing and managing operations outside of the U. S.; • complexities associated with managing multiple payor reimbursement regimes and government payors in foreign countries; • workforce uncertainty in countries where labor unrest is more common than in the U. S.; • potential liability under the Foreign Corrupt Practices Act of 1977 or comparable regulations outside of the U. S.; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and • business interruptions resulting from geopolitical actions, including war and terrorism. These and other risks associated with international operations may materially adversely affect our ability to attain or maintain profitable operations. Uncertainty in the regulatory framework and future legislation could lead to disruption in the execution of international multi- center clinical trials, the monitoring of adverse events through pharmacovigilance programs, the evaluation of the benefit- risk profiles of new medicinal products, and determination of marketing authorization across different jurisdictions. Changes to existing regulations may add considerably to the time from clinical development to marketing authorization and commercialization of products in the EU and increase our costs. We cannot predict the impact of such changes and future regulation on our business or the results of our operations. If we fail to comply with federal, state and international healthcare laws, including fraud and abuse, transparency, and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payors and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including federal and state fraud and abuse laws, including anti- kickback and false claims laws; data privacy and security laws, including the Health Insurance Portability and Accountability Act, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH; and transparency laws related to payments and / or other transfers of value made to physicians, other healthcare professionals and teaching hospitals. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute imetelstat, if marketing approval is obtained. For details regarding the restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate, see Item 1 " Business — Government Regulation — Fraud and Abuse, and Transparency Laws and

~~Regulations." Federal and state enforcement bodies have increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. If our operations are found to be in violation of any of these or any other healthcare and privacy- related regulatory laws that may apply to us, our ability to operate our business and our results of operations could be adversely affected by: • the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement and imprisonment; • possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs; • reputational harm; • diminished profits and future earnings; • additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws; and • curtailment of our operations. Defending against any such actions can be costly, time- consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Risks Related to Manufacturing Imetelstat~~ Failure by us to ~~establish and / or~~ maintain a manufacturing supply chain to appropriately and adequately supply ~~imetelstat~~ **RYTELO** for **commercial and** future clinical ~~and commercial~~ uses would **adversely affect our ability to commercialize RYTELO and** result in a further delay in or cessation of clinical trials ~~and a delay in our ability to obtain regulatory approvals of imetelstat, and affect our ability to commercialize imetelstat~~ , and our business and business prospects could be severely harmed, and we could cease operations. The manufacture of **RYTELO (** imetelstat **)** must comply with applicable regulatory standards for **commercial uses and** current and potential future clinical trials ~~and potential commercial uses~~ . The process of manufacturing ~~imetelstat~~ **RYTELO** is complex and subject to several risks, including: • the ability to **consistently manufacture** ~~scale- up~~ and attain sufficient production yields with ~~appropriate~~ **acceptable** quality control and quality assurance to meet **market demand for our commercialization of RYTELO, as well as** the needs ~~of our~~ **for continuing** clinical trials **; • our ability** ~~and potential future market demand, and~~ to ~~establish~~ **maintain existing** commercial supply agreements **and to establish additional or alternative supply agreements if necessary, including our ability to successfully transfer manufacturing technology and attain regulatory approval at any such additional or alternative suppliers** ; • reliance on third- party manufacturers and suppliers, whose efforts we do not control; • supply chain issues, including the timely availability **of product** and **management of** shelf ~~-~~ life ~~requirements of~~ **, including** raw materials **, drug substance, and drug product** and other supplies, any of which may be impacted by a number of factors, including the effects of macroeconomic or other global conditions; • shortage of qualified personnel **at any of our third party suppliers** ; and • regulatory acceptance and compliance with regulatory requirements, which are less well- defined for oligonucleotide products than for small molecule drugs and vary in each country ~~where imetelstat might be sold or used~~ . As a result of these and other risks, we may be unable to ~~establish and / or~~ maintain a manufacturing infrastructure and supply chain capable of providing ~~imetelstat~~ **RYTELO** for ~~our~~ clinical ~~trials, our expanded access program,~~ and ~~potential future~~ commercial ~~uses~~ **use** , which would delay or **adversely affect our RYTELO commercialization efforts; result in lost sales; delay or** result in a cessation of ~~such~~ **our** current or potential future clinical trials ~~,~~ **; delay or preclude** potential **future** regulatory approvals ~~and commercialization~~ of ~~imetelstat~~ **RYTELO in other jurisdictions or indications;** and **could** cause financial and reputational harm. If third parties that manufacture ~~imetelstat~~ **RYTELO** fail to perform as needed, the **commercial and** clinical ~~and commercial~~ supply of ~~imetelstat will~~ **RYTELO could** be **interrupted or** limited, and we may be unable to **successfully commercialize RYTELO or** conduct or complete current or potential future clinical trials ~~of imetelstat or to commercialize imetelstat in the future~~ . Our ~~imetelstat~~ **RYTELO** manufacturing supply chain relies, and will continue to rely, solely upon third- party manufacturers to perform certain ~~process development or~~ **manufacturing, quality control, and** other technical and scientific work with respect to ~~imetelstat~~ **RYTELO** , as well as to supply starting materials and manufacture drug substance and drug product **for our commercialization of RYTELO, as well as current and potential future clinical trials** . While we have established arrangements with third parties for the manufacture of ~~imetelstat~~ **RYTELO** , our manufacturing supply chain is highly specialized, and as such we are reliant upon a small group of third- party manufacturers to supply starting materials, drug substance and drug product. Failure by such third- party manufacturers to perform in a timely manner and in compliance with all regulatory requirements, or at all, could further delay, perhaps substantially, or preclude our ability to **commercialize RYTELO and / or** pursue ~~imetelstat~~ **further** development **of RYTELO** on our own, increase our costs **, result in lost sales,** and otherwise negatively affect our financial results, business and business prospects. In this regard, recent FDA inspections of one of our third- party **drug product** manufacturers identified certain deficiencies in the manufacturer' s processes and facilities which, while not directly related to the **FDA approval or ongoing** production of ~~imetelstat~~ **RYTELO** , could impact the manufacturer' s ability to produce and deliver products, including ~~imetelstat~~ **RYTELO** , if not remediated by the manufacturer, and could lead to delays or shortages in drug supply, or the inability to manufacture or ship drug supply necessary for non- clinical and clinical activities and commercialization. We expect to rely on third- party manufacturers to produce and deliver sufficient quantities of ~~imetelstat~~ **RYTELO** and other materials to support **commercialization and** clinical trials ~~and potential commercialization~~ on a timely basis and to comply with applicable regulatory requirements. We do not have direct control over these third- party personnel or operations. Reliance on these third- party manufacturers is subject to numerous risks, including: • the inability to execute timely contracts **or production orders** with **any additional** third- party manufacturers and suppliers **that we may identify** on acceptable terms, or at all; • delays and disruptions experienced by third- party manufacturers that adversely impact the ability of such parties to fulfill their contractual obligations to us **, including to provide the quantities of RYTELO required to meet commercial and clinical needs** ; • capacity limitations and scheduling constraints experienced by third- party manufacturers due to scheduling **, maintenance** and other commitments, and queued manufacturing activities in contracted facilities; • requirements by regulatory authorities to validate and qualify significant activities for any current or ~~replacement~~ **additional** manufacturer, which could involve **technology transfer,** new testing ~~and ,~~ compliance inspections **, and would likely require FDA or comparable foreign regulatory authority approval** ; • the inability of third- party manufacturers to timely formulate and manufacture

~~imetelstat~~ **RYTELO** or to produce or ship ~~imetelstat~~ **RYTELO** in the quantities or of the quality required to meet **commercial and** clinical ~~and commercial~~ needs; • the possible mislabeling by third- party manufacturers of **finished drug product for both commercial and** clinical ~~supplies~~ **use**, potentially resulting in **product recall and harm to** ~~the wrong dose amounts being supplied or~~ **our business** ~~active drug or comparator not being properly identified~~; • decisions by third- party manufacturers to exit the contract manufacturing business during the time required to supply clinical trials or to successfully produce, store and distribute ~~imetelstat~~ **RYTELO** to meet commercial needs; • compliance by third- party manufacturers with GMP standards mandated by the FDA and state agencies and other government regulations, including foreign governing regulations, corresponding to similar international regulatory authorities, including any deficiencies identified during regulatory inspections, such as those identified in a recent FDA inspection of one of our third- party manufacturers; • breach or termination of manufacturing or supply contracts; • inadequate storage or maintenance at contracted facilities resulting in theft or spoilage; and • natural disasters that affect contracted facilities **, including manufacturing, warehousing, and distribution facilities**. Each of these risks could lead to delays or shortages in drug supply, or the inability to manufacture or ship drug supply necessary for **commercialization, and** non- clinical and clinical activities, ~~and commercialization,~~ which could severely and adversely affect our financial results, business and business prospects ~~, and the future of imetelstat and cause reputational harm~~. In addition, third- party manufacturers and / or any other manufacturers may need to make substantial investments to enable sufficient capacity increases and cost reductions, and to implement those regulatory and compliance standards necessary for successful **commercialization** ~~Phase 3 clinical trials and commercial production~~ of ~~imetelstat~~ **RYTELO**. These third- party manufacturers may not be willing or able to achieve such capacity increases, cost reductions, or regulatory and compliance standards, and even if they do, such achievements may not be at commercially reasonable costs. Changing manufacturers may be prolonged and difficult due to inherent technical complexities **, regulatory risks,** and because the number of potential manufacturers **for oligonucleotide products** is limited. It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms, or at all. Risks Related to Our **OPERATING RESULTS AND** Financial Position **We have a history of net losses and may not achieve consistent future profitability for some time, if ever. We are incurring and have incurred net losses every year since our operations began in 1990, except for one. As of December 31, 2024, our accumulated deficit was approximately $ 1. 8 billion. Losses have resulted principally from costs incurred in connection with our research and development activities and from general and administrative costs associated with our operations. Although we have recently begun to commercialize RYTELO, our revenue and profit potential is unproven and our very limited operating history as a commercial company makes our future operating results difficult to predict. If we do not generate sufficient revenue from commercial sales of RYTELO, or if we experience unforeseen events or choose to make other investments in our business, we may continue to experience negative cash flow as we fund our operations and imetelstat clinical development activities and research programs, and continue with the commercialization of RYTELO, including as a result of our obligation to pay royalty payments under the Royalty Pharma Agreement and service our debt obligations. We will need to generate significant revenues to achieve consistent future profitability, and we may never achieve consistent future profitability. Even if we do become profitable in the future, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to achieve consistent future profitability could negatively impact the market price of our common stock and our ability to sustain operations. Our operating results are unpredictable and may fluctuate. If our operating results are below the expectations of securities analysts or investors, the trading price of our common stock could decline. Our operating results are difficult to predict and will likely fluctuate from quarter to quarter and year to year. Due to the limited historical sales data of RYTELO in lower- risk MDS since its approval by the FDA in June 2024, RYTELO sales will be difficult to predict from period to period and as a result, you should not rely on RYTELO sales results in any period as being indicative of future performance. Sales of RYTELO may be below our own guidance or the expectations of securities analysts or investors in the future. To the extent that we do not meet our guidance, our financial projections or estimates, or the expectations of analysts or investors, our stock price may be adversely impacted, perhaps significantly. We believe that our quarterly and annual results of operations may be affected by a variety of factors, including: • the level of demand for RYTELO; • the extent to which coverage and reimbursement for RYTELO is available from government and health administration authorities, private health insurers, managed care programs and other third- party payors; • changes in the amount of deductions from gross sales, including government- mandated rebates, chargebacks and discounts that can vary because of changes to the government discount percentage, including increases in the government discount percentage resulting from price increases we may take in the future, or due to different levels of utilization by entities entitled to government rebates and discounts and changes in patient demographics; • increases in the scope of eligibility for customers to purchase RYTELO at the discounted government price or to obtain government- mandated rebates on purchases of RYTELO; • changes in our cost of sales; • the timing and level of royalty payments under the Royalty Pharma Agreement; • the timing, cost and level of investment in our sales and marketing efforts to support RYTELO sales; • the timing, cost and level of investment in our research and development activities involving imetelstat and potential future product candidates; and • expenditures we may incur to develop and / or commercialize any additional products, product candidates, or technologies that we may develop, in- license, or acquire. Further, changes in our operations, such as increased development, manufacturing and clinical trial expenses, or our undertaking of additional programs, business activities, or entry into strategic transactions, including potential future acquisitions of products, technologies or businesses may also cause significant fluctuations in our expenses. In addition, we measure compensation cost for stock- based awards made to employees at the grant date of the award, based on the fair value of the award, and recognize the cost as ~~and~~ an ~~Need~~ expense over the employee' s requisite service period. As the variables that we use as a basis for valuing these awards change over time, including our underlying stock price, the magnitude of the expense that we must recognize

may vary significantly. For ~~Additional Financing~~ **these and other reasons, it is difficult for us to accurately forecast future sales of RYTELO, operating expenses or future profits or losses. As a result, our operating results in future periods could be below our guidance or the expectations of securities analysts or investors, which could cause the trading price of our common stock to decline, perhaps significantly. Our financial projections and estimates are subject to significant risks, assumptions, and uncertainties, and our actual results may differ materially. Our financial projections and estimates are subject to significant risks, assumptions, and uncertainties, and our actual results may differ materially. These projections and estimates include estimates of the total addressable market for RYTELO, assumptions regarding patient market share and duration of therapy, as well as assumptions regarding our ability to meet demand. These projections and estimates are subject to various factors beyond our control, including, for example, the level of demand for RYTELO, the extent to which coverage and reimbursement for RYTELO is available from government and health administration authorities, private health insurers, managed care programs and other third- party payors, increased costs in the supply chain, increased labor costs, changes in the regulatory environment, the impact of global health crises and changes in our senior management team. Our financial projections and estimates constitute forward- looking statements, are for illustrative purposes only and should not be relied upon as necessarily being indicative of future results. The assumptions and estimates underlying such financial projections and estimates are inherently uncertain and are subject to a wide variety of significant business, economic, competitive and other risks and uncertainties. Actual results may differ materially from the results contemplated by the financial projections. Our independent auditors have not studied, reviewed, compiled or performed any procedures with respect to the projections, and accordingly, they did not express an opinion or provide any other form of assurance with respect thereto. While all financial projections, estimates and targets are necessarily speculative, we believe that the preparation of financial projections involves increasingly higher levels of uncertainty the further out the projection, estimate or target extends from the date of preparation. Accordingly, there can be no assurance that the prospective results are indicative of our future performance or that actual results will not differ materially from those presented in the financial projections or estimates.** Our failure to obtain additional capital **, if and when needed,** would force us to further delay, reduce or eliminate **the further** development ~~and potential future~~ **of RYTELO, or to halt the** commercialization of ~~imetelstat~~ **RYTELO** , any of which would severely and adversely affect our financial results, business and business prospects, and might cause us to cease operations. Successful drug development and commercialization requires significant amounts of capital. As of December 31, ~~2023~~ **2024** , we had approximately $ ~~378~~ **502** . ~~1~~ **9** million in cash, cash equivalents, restricted cash and ~~current and noncurrent~~ marketable securities. **While** ~~Based on our current operating plan and our assumptions regarding the timing of the potential approval and commercial launch of imetelstat in lower- risk MDS in the U. S.,~~ we believe that **, based on our current operating plans and assumptions,** our existing cash, cash equivalents, and ~~current and noncurrent~~ marketable securities, together with ~~projected~~ **anticipated net** revenues from ~~U. S.~~ sales of **RYTELO** ~~imetelstat, if approved, potential proceeds from the exercise of outstanding warrants, and potential future drawdowns under the Loan Agreement~~ , will be sufficient to fund our projected operating requirements ~~into~~ **for** the **foreseeable future, if we do not** ~~third quarter of 2025. Our ability to~~ generate **net** revenues from **commercial** sales of ~~imetelstat in~~ **RYTELO at** the **levels we anticipate** ~~U. S.~~ , if **we experience unforeseen events or choose** ~~regulatory approval is granted, depends on us being able~~ to **make** ~~establish sales and marketing capabilities and gain acceptance in the~~ **other** ~~marketplace~~ **investments in our business, or our assumptions regarding our projected operating expenses are otherwise incorrect, we may require additional funding** , which **could include** ~~we may be unable to do in~~ a **combination of public** ~~timely manner or at all. In addition, we cannot predict with any certainty whether and to what extent the remaining outstanding warrants will be exercised for~~ - **or** ~~cash~~ **private equity offerings** , **debt financings (including** ~~or the timing or availability of~~ additional ~~funds~~ **tranches** under the **Pharmakon** Loan Agreement, if **available), collaborations, strategic alliances, licensing arrangements** ~~at all. Our ability to drawdown any remaining tranches under the Loan Agreement is subject to our~~ - **or marketing** ~~achievement of certain regulatory milestones~~ and **distribution arrangements** ~~satisfaction of certain capitalization requirements~~ , **which may not be possible. For example, changes in our operations, such** as ~~well as approval by~~ **increased development, manufacturing** ~~an~~ **and clinical trial expenses,** ~~investment committee comprised of Hercules and SVB for~~ - **or our undertaking of** ~~the final $ 25. 0 million tranche. In addition~~ **additional programs** , ~~even if imetelstat is approved in lower- risk MDS and commercialized by~~ **business activities, or entry into strategic transactions, including potential future acquisitions of products, technologies or businesses, may cause our operating expenses to increase, perhaps significantly, which could require** us ~~in the U. S. in that indication and we are able~~ to **raise** ~~drawdown the remaining tranches under the Loan Agreement in full, we will still require substantial~~ additional funding ~~to further advance the imetelstat program, including through the completion of our ongoing clinical trials and any potential future clinical trials, as well as conducting the clinical, regulatory and potential commercialization activities necessary to potentially bring imetelstat to market in relapsed / refractory MF and any other indications we are pursuing or may pursue, and our need for additional funds may arise sooner than planned~~ . If adequate funds are not available ~~on a timely basis~~ **to us when we need them** , ~~if at all,~~ **our RYTELO commercialization efforts may be adversely affected and** we may be unable to pursue further development ~~or potential commercialization~~ of imetelstat, which would severely harm our business and we might cease operations. ~~Because~~ **Despite FDA approval of RYTELO in June 2024,** the outcome of any clinical activities and / or regulatory approval process is highly uncertain, **and** we cannot reasonably estimate whether ~~any~~ **our future** development activities ~~we~~ may ~~undertake will~~ succeed ~~;~~ **,** whether we will obtain regulatory approval for ~~imetelstat~~ **RYTELO** in **the EU** ~~any indication we pursue, including~~ in lower- risk MDS ~~; or~~ , ~~if approved~~ **or in any other jurisdictions or indications we are pursuing or may in the future pursue** , **or** whether we will be able to effectively commercialize ~~imetelstat~~ **RYTELO in the U. S. for lower- risk MDS or other potential jurisdictions or indications** , if at all. We may never recoup our investment in any ~~imetelstat~~ **RYTELO** development which would adversely affect our financial condition and our business and business prospects, and might cause us

to cease operations. In addition, our plans and timing expectations could be further delayed or interrupted by the effects of macroeconomic or other global conditions, including those resulting from inflation, rising interest rates, prospects of a recession, **government shutdowns, further changes in tariffs and other trade restrictions,** bank failures and other disruptions to financial systems, civil or political unrest, military conflicts, pandemics or other health crises and supply chain and resource issues. Further, our future capital requirements are difficult to forecast and will depend on many factors, including: • the accuracy of the assumptions underlying our estimates for our capital needs; • the **level of sales and market acceptance of RYTELO; • the** scope, progress, timing, magnitude and costs of non- clinical and clinical development, manufacturing and **commercialization of RYTELO, including** potential commercialization ~~of imetelstat~~ **in the EU for lower- risk MDS** , ~~including~~ **if approved, or in any** ~~the~~ **other** ~~number of~~ **jurisdictions or other** ~~indications~~ - **indication** ~~being~~ **we may** ~~pursued~~ - **pursue** , subject to clearances and approvals by the FDA and similar international regulatory authorities; • delays or disruptions in opening sites, screening and enrolling patients or treating and following patients, in our current or any potential future clinical trials of ~~imetelstat~~ **RYTELO** ; • the costs, timing and outcomes of regulatory reviews or other regulatory actions related to ~~imetelstat~~ **RYTELO** , including with respect to our **MAA** ~~NDA and EMA submissions~~ - **submission** for ~~imetelstat~~ **RYTELO** in **the EU for** lower- risk MDS; • the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property- related claims; • the costs of manufacturing, developing, commercializing and marketing ~~imetelstat~~ **RYTELO** , including with respect to third- party vendors and service providers and our ability to achieve any meaningful reduction in manufacturing costs ~~, if imetelstat receives future regulatory approval or clearance, in the U. S., EU or other countries~~ ; • the sales price for **RYTELO** ~~imetelstat, if any~~ ; • the availability of coverage and adequate third- party reimbursement for **RYTELO** ~~imetelstat, if any~~ ; • the extent to which we acquire or in- license other drugs and technologies, or invest in businesses, products or technologies, although we currently have no commitments or agreements relating to any of these types of transactions, or to which we out- license ~~imetelstat~~ **RYTELO** ; • the extent to which we are able to enter into and conduct successful ~~strategic partnerships, collaborations and alliances or licensing~~ arrangements with third parties, including for the commercialization and marketing of ~~imetelstat~~ **RYTELO** in **any** ~~certain global~~ regions **outside of the U. S.** ; • the extent and scope of our **selling,** general and administrative expenses, including expenses associated with potential future litigation; • our level of indebtedness and associated debt service obligations; • the costs of maintaining and operating facilities in California and New Jersey, as well as higher expenses for travel; • macroeconomic or other global conditions that may reduce our ability to access **equity or** debt capital or **other** financing on preferable terms, which may adversely affect future capital requirements and forecasts; and • the costs of enabling our personnel to work remotely, including providing supplies, equipment and technology necessary for them to perform their responsibilities. ~~Until~~ **In the event** we ~~can generate a sufficient amount of revenue from imetelstat to finance our cash requirements, which we may never achieve, we expect to finance future cash needs~~ - **need to raise** ~~through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements, which may not be possible. Availability of such financing sources may be negatively impacted by any further delays in our clinical trials, regulatory developments, or the other risks described in this section. Additional~~ **additional** ~~financing through public~~ **capital to fund** ~~or~~ **our business** ~~private debt or equity financings~~ , including pursuant to the 2023 Sales Agreement with B. Riley Securities, Inc., ~~or~~ **the Tranche** B **Loan and** ~~. Riley,~~ the ~~remaining tranches~~ - **Tranche C Loan** ~~of up to $ 45. 0 million available~~ under the **Pharmakon** Loan Agreement, which are subject to ~~the achievement of~~ certain **funding conditions** ~~clinical and regulatory milestones and satisfaction of certain capitalization and other requirements, as well as approval by an investment committee comprised of Hercules and SVB for the final $ 25. 0 million tranche~~ ; capital lease transactions or other financing sources, **such additional capital** may not be available on acceptable terms, or at all. We may be unable to raise equity capital, or may be forced to do so at a stock price or on other terms that could result in substantial dilution of ownership for our stockholders. The receptivity of the public and private debt and equity markets to proposed financings has been substantially affected by uncertainty in the general economic, market and political climate due to the effects of macroeconomic or other global conditions, such as inflation, rising interest rates, prospects of a recession, government shutdowns **, further changes in tariffs and other trade restrictions** , bank failures and other disruptions to financial systems, civil or political unrest, military conflicts, pandemics or other health crises and supply chain and resource issues, and may in the future be affected by other factors which are unpredictable and over which we have no control. These effects have increased market volatility and could result in a significant long- term disruption of global financial markets, which could reduce or eliminate our ability to raise additional funds through financings, and could negatively impact the terms upon which we may raise those funds. Similarly, these macroeconomic conditions have created extreme volatility and disruption in the capital markets and is expected to have further global economic consequences. If the equity and credit markets deteriorate, including as a result of macroeconomic or other global conditions, such as inflation, rising interest rates, prospects of a recession, government shutdowns, **further changes in tariffs and other trade restrictions,** bank failures and other disruptions to financial systems, civil or political unrest, military conflicts, pandemics or other health crises and supply chain and resource issues, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. If we are unable to **effectively commercialize RYTELO, or** raise additional capital **, if needed,** or establish alternative collaborative arrangements with third- party collaborative partners for ~~imetelstat~~ **RYTELO when needed** , the development and ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO** may be further delayed, altered or abandoned, which might cause us to cease operations. In addition, we may seek additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Due to uncertainty in the general economic, market and political climate, we may determine that it is necessary or appropriate to raise additional funds proactively to meet longer- term anticipated operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, including pursuant to the 2023 Sales Agreement, your ownership interest as a stockholder may be diluted, and the terms may include liquidation or other preferences that materially and

adversely affect your rights as a stockholder. In addition, we have borrowed, and in the future may borrow, additional capital from institutional and commercial banking sources to fund ~~imetelstat~~ development and our future growth, including pursuant to our **Pharmakon** Loan Agreement or potentially pursuant to new arrangements with different lenders. We may borrow funds on terms under agreements, such as ~~the~~ **our Pharmakon** Loan Agreement, that include restrictive covenants, including covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Moreover, if we raise additional funds through alliance, collaborative or licensing arrangements with third parties, we may have to relinquish valuable rights to ~~imetelstat~~ **RYTELO** or our technologies or grant licenses on terms that are not favorable to us. ~~We cannot assure you that our existing capital resources, future interest income, future revenues from sales of imetelstat, if approved, potential future sales of our common stock, including under the 2023 Sales Agreement, and potential future drawdowns, if available, of the remaining tranches under the Loan Agreement, will be sufficient to fund our operating plans. Moreover, while we did not hold cash deposits or securities at SVB, if other banks and financial institutions enter receivership, become insolvent or otherwise fail in the future in response to financial conditions affecting the banking system and financial markets or otherwise, our ability to access our cash, cash equivalents and marketable securities may be delayed or precluded, which could have a material adverse effect on our business, business prospects and financial position. We currently have no source of product revenue and may never become profitable. Although in the past we have received license and other payments under former license and collaboration agreements, we do not currently have any material revenue- generating license or collaboration agreements, have no products approved for commercialization and have never generated any revenue from product sales. In addition, we are incurring and have incurred operating losses every year since our operations began in 1990, except for one. As of December 31, 2023, our accumulated deficit was approximately $ 1. 6 billion. Losses have resulted principally from costs incurred in connection with our research and development activities and from general and administrative costs associated with our operations. Substantially all of our revenues to date have been payments under collaboration agreements and milestones, royalties and other revenues from our licensing arrangements. Our license agreements related to our human telomerase reverse transcriptase, or hTERT, technology have expired or been terminated due to expiration of the underlying hTERT patents, and will not generate any further revenues. We have no ongoing collaborations related to imetelstat and have no current plans to enter into any corporate collaboration, partnership or license agreements that result in revenues, although we may seek a collaborative partner or partners, at an appropriate time, to assist us in the potential development and commercialization of imetelstat, especially outside the U. S., and to provide funding for such activities. We also expect to experience increased negative cash flow for the foreseeable future as we fund our operations and imetelstat clinical development activities and research programs continue, and we prepare for potential commercialization of imetelstat. This will result in decreases in our working capital, total assets and stockholders' equity. We will need to generate significant revenues to achieve consistent future profitability. We may never achieve consistent future profitability. Even if we do become profitable in the future, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to achieve consistent future profitability could negatively impact the market price of our common stock and our ability to sustain operations.~~ Risks Related to our Indebtedness **and ROYALTY PAYMENT OBLIGATIONS** Our level of indebtedness and debt service obligations could adversely affect our financial condition and may make it more difficult for us to fund our operations. **On November 1** ~~As of December 31~~, ~~2023~~ **2024 , we entered into the Pharmakon Loan Agreement. We drew the Tranche A Loan of $ 125. 0 million on November 1, 2024 and as of November 1, 2024** , the total outstanding principal amount under the **Pharmakon** Loan Agreement was $ ~~80~~ **125** . 0 million. The tranches for the remaining $ ~~45~~ **125** . 0 million available to us under the **Pharmakon** Loan Agreement are as follows: (a) **a** ~~the first remaining tranche~~ **Tranche B Loan** of $ ~~20~~ **75** . 0 million **, which** is available until December ~~15~~ **31** , ~~2024~~ **2025 and is available at our option** , subject to ~~the achievement of a~~ certain **customary** ~~regulatory milestone,~~ and **limited conditions** ~~satisfaction of certain capitalization requirements~~ ; and (b) **a** ~~the second remaining tranche~~ **Tranche C Loan** of $ ~~25~~ **50** . 0 million **, which** is available ~~through~~ **until** December 31, ~~2024~~ **2025** , subject to ~~approval by an investment committee comprised of Hercules and SVB~~ **certain conditions including achieving a certain revenue milestone on or prior to November 30, 2025** . ~~Without the~~ **If we do not** ~~achievement~~ ---- **achieve** ~~of~~ **such revenue milestone within** the required **timeline** ~~regulatory milestone and satisfaction of certain capitalization and other requirements~~ , we will not be eligible to draw **down** ~~funds under~~ the ~~first remaining tranche~~ **Tranche C** ~~. If we do not receive investment committee approval, we will not be eligible to draw funds under the second remaining tranche under the~~ Loan ~~Agreement~~ . In addition, before we would consider drawing down any of the remaining tranches under the **Pharmakon** Loan Agreement, if available, we must first satisfy ourselves that we will have access to future alternate sources of capital, such as from commercial revenues or the equity capital markets or debt capital markets, in order to repay any additional principal borrowed, which we may be unable to do, in which case, our liquidity and ability to fund our operations may be substantially impaired. All obligations under the **Pharmakon** Loan Agreement are secured by substantially all of our assets, ~~excluding~~ **including our** intellectual property ~~, which is subject to a negative pledge~~ . Further, the terms of the **Pharmakon** Loan Agreement place restrictions on our operating and financial flexibility, and limit or prohibit our ability to dispose of certain assets, change our line of business, and engage in other significant transactions. This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing the outstanding debt obligations at maturity. If we ~~are able to~~ draw down any of the remaining tranches under the **Pharmakon** Loan Agreement, our indebtedness will increase, which would further increase our risk of being unable to pay off or refinance our outstanding debt obligations at maturity. Our indebtedness could also have important negative consequences, including: • we will need to repay the indebtedness by making payments of interest and principal, which will reduce the amount of cash available to finance our operations, our research and development efforts and other general corporate activities; and • our failure to comply with the obligations of our affirmative and restrictive covenants in the **Pharmakon** Loan Agreement could result in an event of default that, if not cured or waived, would **permit the Lenders to** accelerate our obligation to repay this

indebtedness, and **the Lenders** ~~Hercules and SVB~~ could seek to enforce their security interest in the assets securing such indebtedness. In addition, we may borrow additional capital in the future to fund ~~imetelstat~~ **clinical** development and our future growth, including pursuant to the **Pharmakon** Loan Agreement or potentially pursuant to new arrangements with different lenders. To the extent additional debt is added to our current debt levels, the risks described above could increase. The terms of the **Pharmakon** Loan Agreement place restrictions on our operating and financial flexibility. The **Pharmakon** Loan Agreement imposes operating and other restrictions on us. Such restrictions will affect, and in many respects limit or prohibit, our ability and the ability of **our** ~~any future~~ subsidiaries to, among other things: • dispose of certain assets; • change our line of business; • engage in mergers, acquisitions or consolidations; • incur additional indebtedness; • create liens on assets; • pay dividends and make contributions or repurchase our capital stock; and • engage in certain transactions with affiliates. ~~The Loan Agreement also contains financial covenants, including that we must maintain a minimum cash balance. The breach of any of these restrictive covenants or any other terms of the Loan Agreement would accelerate our obligation to repay our indebtedness under the Loan Agreement, which could have a material adverse effect on our business, business prospects and financial position.~~ We may not have cash available in an amount sufficient to enable us to make interest or principal payments on our indebtedness when due. Our ability to make scheduled **interest** payments on or to refinance our indebtedness depends on our future performance and ability to raise additional sources of cash, which is subject to economic, financial, competitive and other factors beyond our control. If we are unable to generate sufficient cash to service our debt, we may be required to adopt one or more alternatives, such as selling assets, restructuring our debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. If we desire to refinance our indebtedness, our ability to do so will depend on the state of the capital and lending markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Failure to satisfy our current and future debt obligations under the **Pharmakon** Loan Agreement or to comply with certain covenants in the **Pharmakon** Loan Agreement could result in an event of default, the occurrence and continuance of which ~~provide~~ **provides the lenders** ~~Hercules and SVB~~ with the right to demand immediate repayment of all outstanding obligations under the **Pharmakon** Loan Agreement **(and in the case of certain insolvency, liquidation, bankruptcy or similar events, automatically requires immediate repayment of all outstanding obligations under the Pharmakon Loan Agreement)** , and to exercise remedies against us and the collateral securing the **Pharmakon** Loan Agreement. These events of default include, among other things: • insolvency, liquidation, bankruptcy or similar events; • failure to observe ~~any covenant~~ **covenants** ~~or secured obligation~~ under the **Pharmakon** Loan Agreement **and ancillary collateral documents** , which failure, in ~~most~~ **certain limited** cases, is not cured within ~~15~~ **10 or 20** days; • **the** occurrence of ~~an~~ **a withdrawal** event **in respect** ~~that could reasonably be expected~~ to ~~have~~ **RYTELO; • the occurrence of** a material adverse **change** ~~effect on our business, operations, properties, assets or financial condition~~ ; • material misrepresentations; • ~~occurrence of any~~ **certain cross-** default **of third- party** ~~under any other agreement involving~~ indebtedness ~~in excess of specified amounts,~~ or **certain** ~~the occurrence of a~~ default **or termination events of hedging assessments** ~~under any agreement that could reasonably be expected to have a material adverse effect on us~~ ; ~~and~~ • certain money judgments being entered against us **which are not timely paid, discharged** or ~~any portion of~~ **stayed; and •** our assets are attached or seized. In the event of default, **the lenders** ~~Hercules and SVB~~ could accelerate all of the amounts due under the **Pharmakon** Loan Agreement. Under such circumstances, we may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time of such acceleration. In that case, we may be required to delay, limit, reduce or terminate ~~imetelstat~~ **our RYTELO** development or ~~potential~~ commercialization efforts or grant to others rights to develop and market ~~imetelstat~~ **RYTELO** . **The lenders** ~~Hercules and SVB~~ could also exercise their rights to take possession and dispose of the collateral securing the **Pharmakon** Loan Agreement, which collateral includes substantially all of our property ~~other than~~ **including, without limitation, our** intellectual property **, subject to certain exceptions** . Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events. **The Royalty Pharma Agreement places certain restrictions on our operational flexibility. The Royalty Pharma Agreement contains covenants that impose on us certain obligations with respect to royalty payments, diligence, reporting, indemnification and includes restriction on intellectual property transfers and out- licenses, and certain other actions. The Royalty Pharma Agreement also limits our ability to create or incur liens or dispose of certain assets related to imetelstat. We have no rights to repurchase the revenue interests in RYTELO sold to Royalty Pharma (other than in connection with a change of control event), thereby limiting our ability to eliminate future applicability of the covenants contained in the Royalty Pharma Agreement. Compliance with these covenants may limit our flexibility in operating our business and our ability to take actions that might otherwise be advantageous to us and our stockholders.** Risks Related to Protecting Our Intellectual Property If we are unable to obtain and maintain sufficient intellectual property protection **and relevant regulatory exclusivities** for ~~imetelstat~~ **RYTELO** , both in the U. S. and in other countries, our competitors could develop and commercialize products similar or identical to ~~imetelstat~~ **RYTELO** , and our ability to successfully commercialize ~~imetelstat~~ **RYTELO** may be adversely affected. Protection of our proprietary technology is critically important to our business. Our success and the success of our **commercialization and** planned future development ~~and commercialization~~ of ~~imetelstat~~ **RYTELO** will depend on our ability to protect our technologies and ~~imetelstat~~ **RYTELO** through patents **, regulatory exclusivity,** and other intellectual property rights. Our success will depend in part on our ability to obtain, maintain, enforce, and extend our patents and maintain trade secrets, both in the U. S. and in other countries. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the U. S. and in other countries. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing ~~imetelstat~~ **RYTELO** or our technology and / or limit the duration of the patent protection for ~~imetelstat~~ **RYTELO** and our technology. In the event that we are unsuccessful in obtaining, maintaining, enforcing and extending our patents and other intellectual property rights or having

our licensors maintain the intellectual property rights we have licensed, the value of ~~imetelstat~~ **RYTELO** and / or our technologies will be adversely affected, and we may not be able to further develop or ~~potentially~~ commercialize ~~imetelstat~~ **RYTELO** . While we have method- of- use patents that protect the use of ~~imetelstat~~ **RYTELO** for the treatment of certain diseases, this type of patent does not prevent a generic competitor from making and marketing a product that is identical to ~~imetelstat~~ **RYTELO** for an indication that is outside the scope of our approved use after our composition- of- matter patents or their patent term extensions **, and any regulatory exclusivities** have expired. Moreover, even if competitors do not actively promote their product for our approved indications, physicians may prescribe or use these generic products " off- label, " which would result in decreased sales for us. **In addition to our patents covering RYTELO, we also expect to rely on regulatory exclusivity, including orphan drug exclusivity of up to 7 years in the U. S. and 10 years in the EU following approval, to protect our rights to commercialize RYTELO for its approved uses, but such regulatory exclusivity may be limited or withdrawn. See " Risks Related to Regulatory Approval of RYTELO-- Although orphan drug designation has been granted to RYTELO for the treatment of MDS and MF in the U. S. and in the EU, these designations may not be maintained, which would eliminate the benefits associated with orphan drug designation, including market exclusivity, which could limit the period of exclusivity we are able to maintain for the commercialization of RYTELO, and would likely harm our business and business prospects. " In addition to orphan drug exclusivity, we expect to rely on other forms of regulatory exclusivity to protect our ability to commercialize RYTELO. In the U. S., New Chemical Entity, or NCE, exclusivity would entitle us to four years of data exclusivity and one year of market exclusivity, for a total of five years of NCE exclusivity from the date of approval of the first- approved indication. Our request for NCE exclusivity is still pending with FDA, and might not be awarded or could be awarded and then later withdrawn. In Europe, New Active Substance, or NAS, exclusivity is expected to entitle us to eight years of data exclusivity and two years of market exclusivity, for a total of ten years of NAS exclusivity for the first- approved indication, but as with other forms of regulatory exclusivity, NAS exclusivity could be limited or withdrawn.** Loss or impairment of our intellectual property rights related to ~~imetelstat~~ **RYTELO** might further delay or halt ongoing or potential future clinical trials of ~~imetelstat~~ **RYTELO** and any applications for regulatory approval, and might further delay or preclude any future development or commercialization of ~~imetelstat~~ **RYTELO** by us. Furthermore ~~, if imetelstat is approved for commercial sale~~ , such loss of intellectual property rights could impair our ability to exclude others from commercializing products similar or identical to ~~imetelstat~~ **RYTELO** and therefore result in decreased sales for us. Occurrence of any of these events would materially and adversely affect our financial results, business and business prospects ~~and the future of imetelstat~~ , and might cause us to cease operations. Obtaining and maintaining our patent rights depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements. The **USPTO** ~~U. S. Patent and Trademark Office, or the Patent Office,~~ and various governmental patent agencies in other countries require compliance with a number of procedural, documentary, fee payment, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and / or patent applications. Failure to respond to official actions within prescribed time limits, and nonpayment of fees, for example, maintenance fees, renewal fees, and annuity fees could result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the jurisdiction. In such an event, potential competitors might be able to enter the market with ~~imetelstat~~ **the same** or similar products **to RYTELO** , and this circumstance could harm our financial condition, business and business prospects ~~and the future of imetelstat~~ . In addition, if we are responsible for patent prosecution and maintenance of patent rights in- licensed to us or jointly owned with us, any of the foregoing could expose us to liability to the applicable patent owner or patent co- owner. Patent terms may be inadequate to protect our competitive position on ~~imetelstat~~ **RYTELO** for an adequate amount of time. Patents have a limited lifespan. In the U. S., the natural expiration of a patent is generally 20 years after its first effective nonprovisional filing date. ~~Given the amount of time required for the development, testing and regulatory review of imetelstat, patents protecting imetelstat might expire before imetelstat is commercialized.~~ As a result, our intellectual property may not provide us with sufficient **patent** rights to exclude others from commercializing products similar or identical to ~~imetelstat~~ **RYTELO** . In the U. S., the Hatch- Waxman Act permits one patent per approved product to receive a patent term extension of up to five years beyond its normal expiration. The length of the patent term extension is typically calculated as one half of the clinical trial period plus the entire period of time during the review of the NDA by the FDA, minus any time of delay by us during these periods. There is also a limit on the patent term extension to a term that is no greater than fourteen years from drug approval. Only one U. S. patent may ~~be eligible~~ **receive patent term extension under the Hatch- Waxman Act. We have applied to the USPTO** for patent term extension **of some of our** ~~under the Hatch- Waxman Act. We plan to apply to the Patent Office for patent~~ **patents** ~~term extension of one or more patent (s)~~ . Once the **USPTO** ~~Patent Office~~ and the FDA determine the extension period for each proposed eligible patent, we will select the one patent to be extended. **We expect to apply any patent term extension that is granted in the U. S. to our method of treatment patent for MDS and MF that expires on March 15, 2033. If such patent term extension is granted, we expect the term of the patent to extend through August 2037, although such timing is subject to approval by the USPTO as part of its review of our application for patent term extension and could differ from our calculation.** Currently, communication of patent term extension approval and the length of the granted extension period by the **USPTO** ~~Patent Office~~ may occur up to ~~five~~ **several** years from filing of an application for patent term extension. Accordingly, we will decide on the specific patent to be extended only after such communication from the **USPTO** ~~Patent Office~~ . Similar extensions are also available in certain countries and territories outside the U. S., such as in Japan, and in Europe as Supplementary Protection Certificates, or SPCs **. However, we might not be granted a patent term extension at all because of failure to satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the USPTO in the U. S., and any equivalent regulatory authorities and patent offices in other countries, may not agree with our assessment of whether such extensions are**

available, may refuse to grant extensions to our patents, or may grant more limited extensions than we request and could be less than five years . If we select and are granted a patent term extension on a recently filed and issued patent, we may not receive the full benefit of a possible patent term extension, if at all. ~~We might also not be granted a patent term extension at all, because of, for example, failure to apply within the applicable period, failure to apply prior to the expiration of relevant patents or otherwise failure to satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the Patent Office in the U. S., and any equivalent regulatory authorities in other countries, may not agree with our assessment of whether such extensions are available, may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If we fail to apply for applicable patent term extensions or adjustments, we will have a more limited time during which we can enforce our granted patent rights. Should we seek a patent term extension, we may not be granted any such patent term extension and / or the applicable time period of such patent term extension could be less than five years.~~ Moreover, in some countries ~~, including the U. S.~~ , the scope of protection for claims under ~~such~~ patent term ~~extensions~~ **extension** , if any, ~~does not extend to the full scope of the claims but~~ is limited to the product composition as approved and, for a method of treatment patent, ~~is limited~~ to the approved ~~indication~~ **indications** . ~~Thus, for example, if we do not receive a patent term extension for our U. S. composition- of- matter patent for imetelstat, as approved by the regulatory authorities, our U. S. composition- of- matter patent will expire in December 2025~~ . If we do not have sufficient patent life **and regulatory exclusivity** to protect ~~imetelstat~~ **RYTELO** , our financial results, business and business prospects ~~, and the future of imetelstat~~ would be materially and adversely affected, which might cause us to cease operations. In Europe and other countries, our composition of matter patent coverage ~~expires~~ **expired** in September 2024, and our method of treatment patent rights for MDS and MF expire in November 2033. Our method of treatment patents may be eligible for patent term extension **of up to five years** under **an** ~~a Supplementary Protection Certificate, or~~ SPC, permitted under European Council (EC) Regulation No. 469 / 2009, or the European SPC Regulation, upon receipt of drug product approval, such as, for example, our method of treatment patent for MDS. ~~Since~~ **In Europe,** we ~~do not expect to receive marketing approval~~ **have separate method of treatment patents covering MDS** and ~~submit~~ **MF, and** a ~~request for an~~ SPC **may only be applied to one** ~~before September 2024, our European composition of matter~~ patent ~~will expire~~ **. Accordingly,** in countries of the ~~European Economic Area, or~~ EEA, ~~and~~ we must rely on regulatory exclusivity and our method of treatment patents. If regulatory approval of ~~imetelstat~~ **RYTELO** occurs after a patent has expired in a country that does not allow interim patent term extensions, as is the case in many countries and territories including Europe, we will be unable to obtain any patent term extension of that expired patent, and the duration of our patent rights may be limited. **Accordingly, in Europe and such other similar countries and territories, we will not be able to seek patent term extension of our composition of matter patent, as it expired in September 2024.** If we do not have sufficient patent life **and regulatory exclusivity** to protect ~~imetelstat~~ **RYTELO** , our financial results, business and business prospects ~~, and the future of imetelstat~~ would be materially and adversely affected, which might cause us to cease operations. Also, there are regulations for the listing of patents in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. **Some of our** ~~If we submit a patent~~ **patents** ~~for listing~~ **have been listed** in the Orange Book **.** ~~, the FDA may decline to list the patent, or a manufacturer~~ **Manufacturers** of generic drugs may challenge the listing. If ~~imetelstat is approved for commercial sale and~~ an appropriate patent covering ~~imetelstat~~ **RYTELO** is not listed in the Orange Book or is subsequently removed from the Orange Book, a manufacturer of generic drugs would not be required to provide advance notice to us of any abbreviated NDA filed with the FDA to obtain permission to sell a generic version of ~~imetelstat~~ **RYTELO** . Any of the foregoing could harm our competitive position, business, financial condition, results of operations and prospects ~~stock~~ **imetelstat** .Many companies have encountered significant problems in protecting and defending intellectual property rights in jurisdictions outside the U.S.The legal systems of certain countries,particularly certain developing countries,do not favor the enforcement of patents,trade secrets and other intellectual property protection,particularly those relating to biotechnology and pharmaceutical products,which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally.For example,many countries outside the U.S.have compulsory licensing laws under which a patent owner must grant licenses to third parties.Proceedings to enforce our patent rights in jurisdictions outside the U.S.could result in substantial costs and divert our efforts and attention from other aspects of our business,and could put our patents at risk of being invalidated or interpreted narrowly . Changes in U. S. or international patent law or interpretations of such patent laws could diminish the value of our patents in general, thereby impairing our ability to protect our technologies and ~~imetelstat~~ **RYTELO** . The patent positions of pharmaceutical and biopharmaceutical companies, including ours, are highly uncertain and involve complex legal and technical questions. In particular, legal principles for biotechnology and pharmaceutical patents in the U. S. and in other countries are evolving, and the extent to which we will be able to obtain patent coverage to protect our technologies and ~~imetelstat~~ **RYTELO** , or enforce or defend issued patents, is uncertain. The U. S. has enacted and implemented wide- ranging patent reform legislation, including the Leahy- Smith America Invents Act, or the AIA, signed into law on September 16, 2011. The U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Depending on actions by Congress, the federal courts, and the **USPTO** ~~Patent Office~~ , the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents or patents that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce our existing patents or patents that we may obtain in the future. Occurrence of these events and / or significant impairment of our ~~imetelstat~~ **RYTELO** patent rights ~~would~~ **could** severely and adversely affect our financial results, business and business prospects ~~, and the future of imetelstat~~ , which might cause us to cease operations. As a result of the AIA, in March 2013, the U. S. transitioned to a first- inventor- to- file system under which, assuming the other requirements for patentability are met, the

first inventor to file a patent application is entitled to the patent. However, since the publication of discoveries in scientific or patent literature tends to lag behind actual discoveries by at least several months and sometimes several years, we are not able to be certain upon filing a patent application that the persons or entities that we name as inventors or applicants in our patent applications were the first to invent the inventions disclosed therein, or the first to file patent applications for these inventions. Thus, our ability to protect our patentable intellectual property depends, in part, on our ability to be the first to file patent applications with respect to our inventions, or inventions that were developed by our former collaboration partner and assigned to us, for the future development, commercialization and manufacture of ~~imetelstat~~ **RYTELO** . As a result, if we are not the first inventor- to- file, we may not be able to obtain patents for discoveries that we otherwise would consider patentable and that we consider to be significant to the future success of ~~imetelstat~~ **RYTELO** . Delay in the filing of a patent application for any purpose, including further development or refinement of an invention, may result in the risk of loss of patent rights. In 2012, the European Patent Package, or EU Patent Package, was approved and included regulations with the goal of providing for a single pan- European Unitary Patent, and a new European Unified Patent Court, or UPC, for litigation of European patents. The EU Patent Package was ratified in February 2023 and currently covers certain EU states. As of June 1, 2023, all European patents, including those issued prior to ratification, by default automatically fall under the jurisdiction of the UPC and allow for the possibility of obtaining pan- European injunctions and ~~be~~ **are** at risk of central revocation at the UPC in participating UPC states. Under the EU Patent Package, patent holders are permitted to " opt out " of the UPC on a patent- by- patent basis during an initial seven year transitional period after June 1, 2023. Owners of European patent applications who receive notice of grant after the EU Patent Package came into effect could, for the UPC contracting states, either obtain a Unitary Patent or validate the patent nationally and file an opt- out demand. The EU Patent Package may increase the uncertainties and costs surrounding the enforcement or defense of our issued European patents and pending applications. The full impact on future European patent filing strategy and the enforcement or defense of our issued European patents in member states and / or the UPC is not known. Filing, prosecuting, maintaining, defending and enforcing patents for ~~imetelstat~~ **RYTELO** and our technologies in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U. S. are less extensive than those in the U. S. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover ~~imetelstat~~ **RYTELO** and our technologies. We may not be able to protect our intellectual property rights in the U. S or worldwide and challenges to our owned or licensed patent rights would result in costly and time-consuming legal proceedings that could prevent or limit development or ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO** . Our patents or those patent rights we have licensed, including patent rights that we may seek with respect to inventions made by past or future collaborators, may be challenged through administrative or judicial proceedings, which could result in the loss of important patent rights. For example, where more than one party seeks U. S. patent protection for the same technology in patent applications that are subject to the law before the implementation of the AIA, the **USPTO** ~~Patent Office~~ may declare an interference proceeding in order to ascertain the party to which the patent should be issued. Patent interferences are typically complex, highly contested legal proceedings, subject to appeal. They are usually expensive and prolonged and can cause significant delay in the issuance of patents. Our pending patent applications or our issued patents, or those we have licensed and may license from others, may be drawn into interference proceedings or be challenged through post- grant review procedures or litigation, any of which could delay or prevent the issuance of patents, or result in the loss of issued patent rights. We may not be able to obtain from our past or future collaborators the information needed to support our patent rights which could result in the loss of important patent rights. Under the AIA, interference proceedings between patent applications filed on or after March 16, 2013, have been replaced with other types of proceedings, including derivation proceedings. The AIA also includes post- grant review procedures subjecting U. S. patents to post- grant review procedures similar to European oppositions, such as inter partes review, or IPR, covered business method post- grant reviews and other post- grant reviews. This applies to all our U. S. patents and those we have licensed and may license from others, even those issued before March 16, 2013. A third party could attempt to use the **USPTO** ~~Patent Office~~ procedures to invalidate patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. U. S. patents owned or licensed by us may therefore be subject to post-grant review procedures, as well as other forms of review and re- examination. In addition, the IPR process under the AIA permits any person, whether they are accused of infringing the patent at issue or not, such as entities associated with hedge funds, to challenge the validity of certain patents. Significant impairment of our ~~imetelstat~~ **RYTELO** patent rights ~~would~~ **could** severely and adversely affect our financial results, business and business prospects ~~, and the future of imetelstat~~ , which might cause us to cease operations. Certain jurisdictions, such as Europe, **China, Japan,** New Zealand and Australia, permit **third parties to file** oppositions ~~to be filed~~ **or invalidation trials** against granted patents or patents proposed to be granted. Because we seek to enable potential global commercialization of ~~imetelstat~~ **RYTELO** , securing both proprietary protection and freedom to operate outside of the U. S. is important to our business. ~~Opposition~~ **Third party** proceedings **such as oppositions and invalidation trials** require significant time and costs, and if we are unsuccessful or are unable to commit these types of resources to protect our ~~imetelstat~~ **RYTELO** patent rights, we could lose our patent rights and we could be prevented or limited in the development and commercialization of **RYTELO** imetelstat. Many companies have encountered significant..... risk of being invalidated or interpreted narrowly . As more groups become engaged in scientific research and product development in the areas of telomerase biology and hematologic malignancies, the risk of our patents, or patents that we have in- licensed, being challenged through patent interferences, derivation proceedings, IPRs, post- grant proceedings, oppositions **, invalidation trials** , re- examinations, litigation or other means will likely increase. Challenges to our patents through these procedures would be extremely expensive and time- consuming, even if the outcome was favorable to us. An adverse outcome in a patent dispute could severely harm our ability to further develop or commercialize ~~imetelstat~~ **RYTELO** , or could otherwise have a material adverse effect on our business, and might cause us to cease operations, by: • causing us to lose patent rights in the relevant

jurisdiction (s); • subjecting us to litigation, or otherwise preventing us from commercializing ~~imetelstat~~ **RYTELO** in the relevant jurisdiction (s); • requiring us to obtain licenses to the disputed patents; • forcing us to cease using the disputed technology; or • requiring us to develop or obtain alternative technologies. We may be subject to infringement claims that are costly to defend, and such claims may limit our ability to use disputed technologies and prevent us from pursuing research, development, manufacturing or commercialization of ~~imetelstat~~ **RYTELO** . The commercial success of ~~imetelstat~~ **RYTELO** will depend upon our ability to research, develop, manufacture, market and sell ~~imetelstat~~ **RYTELO** without infringing or otherwise violating the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, and many pharmaceutical companies, including potential competitors, have substantial patent portfolios. Since we cannot be aware of all intellectual property rights potentially relating to ~~imetelstat~~ **RYTELO** and its uses, we do not know with certainty that ~~imetelstat~~ **RYTELO** , or the ~~intended~~ commercialization thereof, does not and will not infringe or otherwise violate any third party' s intellectual property. For example, we are aware that certain third parties have or may be prosecuting patents and patent estates that may relate to ~~imetelstat~~ **RYTELO** , and while **these patents have expired, or** we believe ~~these patents will expire before imetelstat is able to be commercialized and / or~~ that ~~these patents~~ **a reasonable court should find they** are invalid and / or would not be infringed by the manufacture, use or sale of ~~imetelstat~~ **RYTELO** , it is possible that the owner (s) of these patents will assert claims against us in the future. In the event our technologies infringe the rights of others or require the use of discoveries and technologies controlled by third parties, we may be prevented from pursuing research, development, manufacturing or commercialization of ~~imetelstat~~ **RYTELO** , or may be required to obtain unblocking licenses from such third parties, develop alternative non- infringing technologies, which we may not be able to do at an acceptable cost or on acceptable terms, or at all, or cease the **commercialization and continued** development of ~~imetelstat~~ **RYTELO** . If we are unable to resolve an infringement claim successfully, we could be subject to an injunction that would prevent us from ~~potentially~~ commercializing ~~imetelstat~~ **RYTELO** and could also require us to pay substantial damages. In addition, while our past collaboration agreements have terminated, we are still subject to indemnification obligations to certain collaborators, including with respect to claims of third- party patent infringement. In addition to infringement claims, in the future we may also be subject to other claims relating to intellectual property, such as claims that we have misappropriated the trade secrets of third parties ~~. Provided that we are successful in continuing the development of imetelstat, we expect to see more efforts by others to obtain patents that are positioned to cover imetelstat~~ . Our success therefore depends significantly on our ability to operate without infringing patents and the proprietary rights of others. We may become aware of discoveries and technologies controlled by third parties that are advantageous or necessary to further develop or manufacture ~~imetelstat~~ **RYTELO** . Under such circumstances, we may initiate negotiations for licenses to other technologies as the need or opportunity arises. We may not be able to obtain a license to a technology required to pursue the research, development, manufacturing or commercialization of ~~imetelstat~~ **RYTELO** on commercially favorable terms, or at all, or such licenses may be terminated on certain grounds, including as a result of our failure to comply with any material obligations under such licenses. If we do not obtain a necessary license or if such a license is terminated, we may need to redesign such technologies or obtain rights to alternative technologies, which may not be possible, and even if possible, could cause further delays in the development efforts for ~~imetelstat~~ **RYTELO** and could increase the development and / or production costs of ~~imetelstat~~ **RYTELO** . In cases where we are unable to license necessary technologies, we could be subject to litigation and prevented from pursuing research, development, manufacturing or commercialization of ~~imetelstat~~ **RYTELO** , which would materially and adversely impact our business. Failure by us to obtain rights to alternative technologies or a license to any technology that may be required to pursue research, development, manufacturing or commercialization of ~~imetelstat~~ **RYTELO** would further delay current and potential future clinical trials of ~~imetelstat~~ **RYTELO** and any applications for regulatory approval, impair our ability to sell **RYTELO** ~~imetelstat, if approved~~ , and therefore result in decreased sales of ~~imetelstat~~ **RYTELO** for us. Occurrence of any of these events ~~would~~ **could** materially and adversely affect our business and might cause us to cease operations. We ~~are seeking~~ **have a** registered ~~trademarks~~ **trademark, RYTELO,** for **our product and failure to maintain such trademark could adversely affect our business. We have** a **registered trademark, RYTELO, which is the** commercial trade name for imetelstat **, in a number of countries and regions, including** in the U. S. and **Europe** ~~jurisdictions outside of the U~~ . ~~S. and failure to secure and maintain such registrations could adversely affect our business. We have secured a global trademark for a commercial trade name for imetelstat. During trademark registration proceedings, we may receive rejections or fail to maintain such registrations. Although we are given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, opposition~~ **Opposition** or cancellation proceedings **, however,** may be filed against our trademarks, and our trademarks may not survive such proceedings. If our United States **trademark** application which forms the basis for our international registration, or IR, for our commercial trade name is ~~refused,~~ withdrawn ~~,~~ or abandoned within the first 5 years of our IR **,** we will lose our IR registrations which could adversely affect our business. **We may be unable to maintain or enforce our current and future trademarks, and if we fail to satisfy the applicable regulatory requirements, we may not have enforceable trademark rights or registrations in such jurisdictions.** Our product trademark **, RYTELO,** is approved by ~~the EMA and provisionally approved by the FDA. If the FDA or EMA should reject the trademark, we may be required to expend additional time and resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to~~ the FDA and the EMA. We may become involved in disputes with past or future collaborator (s) over intellectual property inventorship, ownership or use, and publications by us, or by investigators, scientific consultants, research collaborators or others. Such disputes could impair our ability to obtain patent protection or protect our proprietary information, which, in either case, could have a significant impact on our business. Inventions discovered under research, material transfer or other collaboration agreements may become jointly owned by us and the other party to such agreements in some cases and may be the exclusive property of either party in other cases. Under some circumstances, it may be difficult to determine who invents and

owns a particular invention, or whether it is jointly owned, and disputes can arise regarding inventorship, ownership and use of those inventions. These disputes could be costly and time- consuming, and an unfavorable outcome could have a significant adverse effect on our business if we are not able to protect or license rights to these inventions. In addition, clinical trial investigators, scientific consultants and research collaborators generally have contractual rights to publish data and other proprietary information, subject to review by the trial sponsor. Publications by us, or by investigators, scientific consultants, previous employees, research collaborators or others, either with permission or in contravention of the terms of their agreements with us or with our past or future collaborators, may impair our ability to obtain patent protection or protect proprietary information which ~~would~~ **could** have a material adverse effect on our business, and might cause us to cease operations. Much of the information and know- how that is critical to our business is not patentable, and we may not be able to prevent others from obtaining this information and establishing competitive enterprises. We rely on trade secrets to protect our proprietary technology, especially in circumstances in which we believe patent protection is not appropriate or available. We attempt to protect our proprietary technology in part by confidentiality agreements with our employees, consultants, collaborators and contractors. However, we cannot provide assurance that these agreements will not be breached, that we would have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors, any of which would harm our business significantly. In May 2016, the Defend Trade Secrets Act of 2016, or the DTSA, was enacted, providing a federal cause of action for misappropriation of trade secrets. Under the DTSA, an employer may not collect enhanced damages or attorney fees from an employee or contractor in a trade secret dispute brought under the DTSA, unless certain advanced provisions are observed. We cannot provide assurance that our existing agreements with employees and contractors contain notice provisions that would enable us to seek enhanced damages or attorneys' fees in the event of any dispute for misappropriation of trade secrets brought under the DTSA. Risks Related to Managing Our Growth and Other Business Operations We may be unable to successfully retain or recruit key personnel to support the **commercialization and further** development ~~and potential future commercialization~~ of ~~imetelstat~~ **RYTELO** or to otherwise successfully manage our growth. Our ability to successfully **commercialize RYTELO in the U. S. for lower- risk MDS and in any other jurisdiction or indication for which it is approved, and to continue to** develop ~~imetelstat~~ **RYTELO** in ~~the~~ **other myeloid hematologic malignancies** ~~future and to potentially commercialize imetelstat~~ depends to a significant extent on the skills, experience and efforts of our executive officers and key members of our staff. In addition, we need to recruit, maintain, motivate and integrate additional personnel with expertise and experience in **sales, marketing, market access, commercial operations, pricing,** clinical science, biostatistics, clinical operations, pharmacovigilance, quality, manufacturing, regulatory affairs, medical affairs, legal affairs, **and** compliance ~~, market access, pricing, commercial operations, sales, and marketing,~~ to enable us to further **commercialize and further** develop **RYTELO** ~~and potentially commercialize imetelstat~~. We face intense competition for qualified individuals from numerous pharmaceutical, biopharmaceutical and biotechnology companies, as well as academic and other research institutions, and competition in our geographic regions is particularly intense. The substantial risks and uncertainties related to our **commercialization and further** development ~~and the potential approval and commercialization~~ of ~~imetelstat~~ **RYTELO**, and the risks and uncertainties regarding our future business viability could have an adverse impact on our ability to retain and recruit qualified personnel. We may also face higher than expected personnel costs in order to attract new personnel due to shortages in qualified applicants, or to maintain our current management and personnel due to the increased number of opportunities in the biotechnology sector. If we are unable to successfully retain, motivate and incentivize our existing personnel, or to attract, assimilate and retain other highly qualified personnel in the future on acceptable terms, our ability to **commercialize and** further develop **RYTELO** ~~and potentially commercialize imetelstat~~ will be impaired, and our business and the price of our common stock would be adversely impacted. In addition, our personnel are currently performing their duties in multiple jurisdictions, and if we are unable or fail to comply with employment, tax, benefits and other laws in such jurisdictions, we may face penalties, fines or litigation. Our future financial performance and our ability to develop, manufacture and commercialize **RYTELO** ~~imetelstat will depend~~ **depends**, in part, on our ability to effectively manage any future growth. Our management may have to divert financial and other resources, as well as devote a substantial amount of time, to managing growth activities, such as enhancing operational, financial and management processes and systems. If we do not effectively manage the expansion of our operations, we could experience weaknesses in our infrastructure and ability to comply with applicable legal and regulatory requirements and regulations, operational mistakes or shortcomings, loss of business opportunities, loss of employees and reduced productivity among remaining employees. If we seek to establish potential future collaborative arrangements for ~~imetelstat~~ **RYTELO**, we may be unable to establish such collaborative arrangements on acceptable terms, or at all, and may have to delay, alter or abandon **commercialization** ~~our~~ **or** ~~imetelstat~~ **further** development **of RYTELO** ~~and commercialization plans~~. We intend to develop ~~imetelstat~~ **RYTELO** broadly for hematologic malignancies, and to **commercialize, market and sell RYTELO in the U. S. for certain patients with lower- risk MDS and** potentially **in the EU for certain patients with lower- risk MDS. We may seek to self-** commercialize **or** ~~, market and sell imetelstat in the U. S. and the EU. We may~~ seek a collaborative partner or partners, at an appropriate time, to assist us in the potential development and commercialization of **RYTELO** ~~imetelstat, especially in the EU and other regions~~ outside the U. S., and to provide funding for such activities. We face significant competition in seeking appropriate collaborative partners, and these potential collaborative arrangements are complex and time consuming to negotiate, document and implement. Our ability to seek and establish potential collaborative arrangements may be impacted by delays in marketing approvals of ~~imetelstat~~ **RYTELO** in lower- risk MDS in the ~~U. S. and / or~~ EU and in reporting results from IMpactMF, as well as the period of the patent **protection** ~~term for our intellectual property portfolio~~ and market exclusivity for ~~imetelstat~~ **RYTELO. In addition, the terms of our Pharmakon Loan Agreement may limit our ability to enter into certain collaborative arrangements and any future debt agreements may continue or further limit our ability to enter into such agreements**. We may not be able to establish collaborative arrangements on acceptable terms, or at all. In this regard, collaborative arrangements with third parties may

require us to relinquish material rights, including revenue from ~~potential~~ commercialization, or assume material ongoing development obligations that we would have to fund or otherwise support. If we are unable to negotiate collaborative arrangements, we may have to: • delay ~~or~~ **,** curtail **or abandon** the additional development of ~~imetelstat~~ **RYTELO** ; • ~~further~~ delay **, curtail** or abandon the ~~potential~~ commercialization of **RYTELO in jurisdictions where it is approved** ~~imetelstat outside of the U. S.~~ ; • reduce the scope of potential future sales or marketing activities; or • increase our expenditures and undertake development or commercialization activities at our own expense, which will require additional capital than our current resources. We have established subsidiaries in the United Kingdom and the Netherlands, which exposes us to additional costs and risks. The wholly- owned subsidiaries we have established in the U. K. and the Netherlands subject us to certain additional costs and risks associated with doing business outside the U. S., including: • the increased complexity and costs inherent in managing international operations in geographically disparate locations; • challenges and costs of complying with diverse regulatory, financial and legal requirements, which are subject to change at any time; • potentially adverse tax consequences, including changes in applicable tax laws and regulations; • potentially costly trade laws, tariffs, export quotas, custom duties or other trade restrictions, and any changes to them **, including in connection with new Trump administration changes** ; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations; • natural disasters, political and economic instability, including terrorism and civil and political unrest, outbreak of health epidemics, ~~including any resurgence of COVID- 19,~~ and the resulting global economic and social impacts; and ~~In addition, our international operations in the U. K. and the Netherlands expose us to fluctuations in currency exchange rates between the British pound, the Euro and the U. S. dollar. Given the volatility of currency exchange rates, there is no assurance that we will be able to effectively manage currency transaction and / or conversion risks. To date, we have not entered into derivative instruments to offset the impact of foreign exchange fluctuations, which fluctuations could have an adverse effect on our financial condition and results of operations.~~ We may not be able to obtain or maintain sufficient insurance on commercially reasonable terms or with adequate coverage against potential liabilities in order to protect ourselves against **claims such as** product liability **or personal injury** claims **arising from** ~~or~~ **our commercialization of RYTELO,** claims related to clinical trial conduct, or claims related to data protection. Our business exposes us to potential product liability and other risks that are inherent in the testing, manufacturing and marketing of human therapeutic products. We may become subject to product liability **or personal injury** claims **related to the commercialization of RYTELO,** or claims related to clinical trial conduct ~~or the potential commercialization of imetelstat, if any~~ , including if the use of ~~imetelstat~~ **RYTELO** is alleged to have injured patients, such as injuries alleged to arise from any hepatotoxicity or hemorrhagic event associated with the use of ~~imetelstat~~ **RYTELO** . We currently have ~~limited~~ product liability and clinical trial liability insurance **that we believe is adequate, but we may experience losses in excess of our coverage or that are not covered by our insurance** , and we may not be able to maintain this type of insurance for the ~~potential~~ commercialization of **RYTELO** ~~imetelstat, if any~~ , or any of our current or potential future clinical trials of ~~imetelstat~~ **RYTELO** . In addition, this type of insurance may become too expensive for us to afford because of the highly risky and uncertain nature of ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO** , clinical trials generally and the high cost of insurance for our business activities. We may be unable to obtain or maintain clinical trial insurance in all of the jurisdictions where we conduct current or potential future clinical trials. In addition, business liability, product liability and cybersecurity insurance are becoming increasingly expensive, particularly for biotechnology and pharmaceutical companies, and the pool of insurers offering insurance coverage to biotechnology and pharmaceutical companies generally is becoming smaller, making it more difficult to obtain insurance for our business activities at a reasonable price, or at all. Being unable to obtain or maintain product liability, clinical trial liability, cybersecurity or other insurance for our business activities in the future on acceptable terms or with adequate coverage against potential liabilities would have a material adverse effect on our business, and could cause us to **limit or** cease our **commercialization and further** development of ~~imetelstat~~ **RYTELO** . In the past, we and certain of our officers have been named as defendants in securities class action lawsuits and shareholder derivative lawsuits. Potential similar or related lawsuits that may be filed in the future, could result in substantial damages, divert management' s time and attention from our business, and have a material adverse effect on our results of operations. Any such lawsuits, or other lawsuits to which we are subject, will be costly to defend or pursue and are uncertain in their outcome. **We are not currently a party to any material pending legal proceedings. However,** ~~Securities~~ **securities** ~~- related~~ class action lawsuits and / or derivative lawsuits have often been brought against companies, including biotechnology and biopharmaceutical companies, that experience volatility in the market price of their securities. This risk is especially relevant for us because we often experience significant stock price volatility in connection with our activities. In 2020, three securities class action lawsuits were filed against us and certain of our officers. One of the lawsuits was voluntarily dismissed ~~. The~~ **, and final judgment with respect to the** other two lawsuits ~~, filed in the U. S. District Court for the Northern District of California, were consolidated by the Court. In September 2022, the parties agreed to a settlement and entered into a Stipulation and Agreement of Settlement, which was subject to court approval. The Court granted final approval of the settlement on September 28, 2023 and final judgment~~ was entered ~~on~~ **in** October ~~3,~~ 2023. In 2020 and 2021, seven shareholder derivative actions were filed in a number of courts, naming as defendants certain of our then current officers and certain of our then current and former members of our board. **All seven** ~~On May 17, 2023, the Delaware Court~~ of ~~Chancery approved a settlement of~~ the **shareholder** derivative **actions** ~~case pending before it, and the case was dismissed with prejudice. Subsequently, each of the remaining derivative cases~~ were dismissed with prejudice. While we ~~have~~ settled these lawsuits, it is possible that additional lawsuits might be filed, or allegations might be received from stockholders, with respect to these same or other matters and also naming us and / or our officers and directors as defendants. Such lawsuits and any other related lawsuits are subject to inherent uncertainties, and the actual defense and disposition costs will depend upon many unknown factors. ~~The outcome of such lawsuits is necessarily uncertain.~~ We could be forced to expend significant resources in

the defense of any additional lawsuits, and we may not prevail ~~. In addition, we have and may continue to incur substantial legal fees and costs in connection with such lawsuits~~. Monitoring, initiating and defending against legal actions is time- consuming for our management, is likely to be expensive and may detract from our ability to fully focus our internal resources on our business activities. We could be forced to expend significant resources in any potential future lawsuits, and we may not prevail in such lawsuits. Additionally, we may not be successful in having any such lawsuits dismissed or settled within the limits of our insurance coverage. A decision adverse to our interests in **any legal proceedings** ~~similar or related litigation~~, could result in the payment of substantial damages, or possibly fines, and could have a material adverse effect on our business, our stock price, cash flow, results of operations and financial condition. We may be subject to third- party litigation, and such litigation would be costly to defend or pursue and uncertain in its outcome. Our business may bring us into conflict with our licensees, licensors, or others with whom we have contractual or other business relationships, or with our competitors or others whose interests differ from ours. **Our commercial launch of RYTELO may result in product or personal injury disputes, or other disputes with health care providers, patients or other third parties as a result of our commercialization efforts.** We may experience employment- related disputes ~~as we seek to expand our personnel resources~~. We may become involved in performance or other disputes with the CROs we have retained to support our ~~imetelstat~~ clinical development activities, or with other third parties such as service providers, vendors, manufacturers, suppliers or consultants ~~, which could result in a further delay or cessation of current and potential future clinical trials and otherwise significantly further delay our ability to develop or potentially commercialize imetelstat~~. If we are unable to resolve those conflicts on terms that are satisfactory to all parties, we may become involved in litigation brought by or against us. Lawsuits are subject to inherent uncertainties, and defense and disposition costs depend upon many unknown factors. Despite the availability of insurance, we may incur substantial legal fees and costs in connection with litigation. Lawsuits could result in judgments against us that require us to pay damages, enjoin us from certain activities, or otherwise negatively affect our legal or contractual rights, which could have a significant adverse effect on our business. In addition, the inherent uncertainty of such litigation could lead to increased volatility in our stock price and a decrease in the value of our stockholders' investment in our securities. We are subject to U. S. and certain foreign export and import controls, sanctions, embargoes, anti- corruption laws, and anti- money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business. We are subject to export control and import laws and regulations, and other state and national anti- bribery and anti- money laundering laws in the countries in which we conduct activities. Anti- corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and / or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. Risks Related to Competitive Factors If our..... sales of imetelstat, if approved. RISKS RELATED TO INFORMATION TECHNOLOGY SYSTEMS, DATA SECURITY AND DATA PRIVACY If our information technology systems or data, or those of third parties ~~upon which~~ **with whom** we ~~rely~~ **work**, are or were compromised, we could experience adverse consequences resulting from such compromise, including ~~, but not limited to,~~ regulatory investigations or actions; litigation; fines and penalties; a disruption of our business operations, including our clinical trials; reputational harm; loss of revenue and profits; and other adverse consequences. In the ordinary course of our business, we (and third parties ~~upon which~~ **with whom** we ~~rely~~ **work**) collect, receive, store, use, transfer, make accessible, protect, secure, dispose of, transmit, disclose, or otherwise process (commonly known as processing) proprietary, confidential, and sensitive data, including personal data (such as health- related data and participant study related data), intellectual property, and trade secrets (collectively, sensitive information). In addition, we rely on third- party service providers to establish and maintain appropriate information technology and data security protections **, including disaster recovery and business continuity procedures,** over the information technology systems they provide us to operate our critical business systems, including cloud- based infrastructure and systems, employee email, and data storage and management systems. However, except for contractual duties and obligations, we have limited ability to control or monitor third parties' safeguards and actions related to such matters, and these third parties may not have adequate information security measures in place. Furthermore, while we may be entitled to damages if our third- party service providers fail to satisfy their privacy or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. Most of our employees work remotely, resulting in **increased risks of loss or theft of company devices as well as** increased risks to our information technology systems and data, as employees utilize network connections, computers, and devices outside our premises and networks, including working at home and while in transit and in public locations. Additionally, the prevalent use of mobile devices that access our sensitive information increases the risk of security incidents. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. Our information technology systems, including in our remote work environment, and those of the third parties ~~upon which~~ **with whom** we ~~rely~~ **work**, **have been in the past and** may **continue to** be vulnerable to evolving threats. These threats are prevalent, continue to increase, and

come from a variety of sources such as traditional “ hackers, ” threat actors, **“** ~~""~~ hacktivist, ~~"~~ **”** organized criminal threats actors, or internal bad actors, personnel (such as through theft, error or misuse), sophisticated nation states and nation- state- supported actors. These threats include, but are not limited to, social- engineering attacks, **targeted phishing campaigns,** malicious code or malware, unauthorized intrusions, denial- of- service attacks, personnel misconduct or errors, ransomware attacks, supply- chain attacks, software bugs, computer viruses, server malfunctions, software, hardware or data center failures, loss of data or other information technology assets, natural disasters, terrorism, war, telecommunication and electrical failures and attacks enhanced or facilitated by artificial intelligence, or AI, and other similar threats. In particular, ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions in operations, loss of **sensitive** data and income, reputational harm, and diversion of funds. If we were to experience such an attack, extortion payments might alleviate the negative impact of a ransomware attack, but we might be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. Similarly, supply- chain attacks and attacks on clinical trial sites as well as regulatory and health authorities have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain or our third- party partners’ supply chains, or of clinical trial sites and regulatory and health authorities, have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems ~~(including those related to imctelstat)~~ or the third- party information technology systems that support us and the services provided to us **, or remediate and recover compromised systems in a timely manner. For example, in February 2024, one of our service providers that processes clinical trial data experienced a security incident that resulted in certain of the service provider’ s information systems being unavailable for a limited period of time. Based on the service provider’ s forensic investigation findings that were shared with us, we believe that this incident did not have a material impact on us, our clinical trials or clinical trial participants. As another example, in March 2024, we learned about another security incident, involving another service provider, that processes personnel data for our limited number of UK personnel and directors of Geron UK Ltd. Following the service provider’ s forensic investigation, the service provider informed us that it did not determine the specific data involved or the incident’ s impact. While we believe that this incident did not have a material impact on us, out of an abundance of caution, we submitted a notification to the UK Information Commissioner’ s Office and notified potentially affected personnel and directors of the incident** . Any of these **or similar incidents or** threats may result in unauthorized, unlawful or accidental loss, corruption, access, modification, destruction, alteration, acquisition or disclosure of sensitive information, such as clinical trial data or information, intellectual property, proprietary business data and personal data. The costs to us to attempt to protect against such security incidents could be significant, including potentially requiring us to modify our business, and while we have implemented security measures **, policies and procedures** designed to protect our information technology systems **from cybersecurity threats** and to identify and remediate vulnerabilities, such measures may not be **fully implemented, complied with or** successful **in protecting our systems and information** . We may expend significant resources or modify our business activities (including our clinical trial activities) to try to protect against security incidents. We may be unable in the future to detect **cybersecurity threats or** vulnerabilities in our information technology systems because such threats and techniques change frequently, are sophisticated in nature, and may not be detected until after a security incident has occurred. **We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.** Unremediated high risk or critical vulnerabilities pose material risks to our business **, particularly due to the reliance on software vendors to adequately patch and implement fixes to address critical or high- risk vulnerabilities in a timely manner. Further, we may be materially impacted by software updates applied by our software vendors if such updates cause significant downtime to our systems** . If we or third parties ~~upon which~~ **with whom** we ~~rely~~ **work** experience or are perceived to have experienced a breach, we may experience **material** adverse consequences. These consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits, and inspections), interruptions in our operations, including disruption of our ~~imctelstat~~ **commercialization and** development ~~program~~ **efforts** , interruptions or restrictions on processing sensitive data (which could result in delays in obtaining, or our inability to obtain, regulatory approvals and significantly increase our costs to recover or reproduce the data), reputational harm, litigation (including class action claims), indemnification obligations, negative publicity, financial loss, and other harms. In addition, such a breach may require public notification of the breach **, or we may choose to voluntarily notify relevant stakeholders, or take other actions, such as providing credit monitoring and identity theft protection services, and we have done so in the past** . Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Additionally, sensitive information of the Company could be leaked, disclosed, or revealed as a result of or in connection with our employees’, personnel’ s, or vendors’ use of generative AI technologies. Many of our contracts with relevant stakeholders include obligations relating to the safeguard of sensitive information, and a breach could lead to claims against us by such stakeholders. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities, damages, or claims relating to our data privacy and security obligations. In addition, failure to maintain effective internal accounting controls related to data security breaches and cybersecurity in general could impact our ability to produce timely and accurate financial statements and could subject us to regulatory scrutiny. **If we fail to successfully implement or upgrade our enterprise resource planning and other information systems, our business and results of operation could be adversely impacted.** We **periodically implement or upgrade new or enhanced enterprise resource planning, or ERP, and other business systems in order to better manage**

our business operations. Implementation or upgrade of new business processes and information systems requires the commitment of significant personnel, training and financial resources, and entails risks to our business operations. If we do not successfully implement ERP and other information systems improvements, or if there are delays or difficulties in implementing these systems, we may not realize anticipated productivity improvements or cost efficiencies, and we may experience operational difficulties and challenges in effectively managing our business, all of which could result in quality issues, reputational harm, lost market and revenue opportunities, and otherwise adversely affect our business, financial condition and results of operations. For example, in 2024 we implemented a new ERP and other information systems to help us manage our operations and financial reporting. This project required, and may continue to require, investment of capital and human resources, the re- engineering of processes of our business, and the attention of many employees who would otherwise be focused on other aspects of our business. Costs and risks inherent in implementing new systems, such as the ERP that we implemented in 2024, may include disruptions to business continuity, administrative and technical problems, interruptions or delays in sales, expenditure overruns, delays in paying our suppliers and employees, and data migration issues. If we do not properly address or mitigate these issues, this could result in increased costs and diversion of resources, negatively impacting our operating results and ability to effectively manage our business. Additionally, if the ERP system that we implemented in 2024 does not operate as intended, the effectiveness of our internal control over financial reporting could be negatively affected. We and third parties with whom we work are subject to stringent and changing U. S. and foreign laws, regulations, rules, contractual obligations, industry standards, policies and other obligations related to data privacy and security. Our **(or the third parties with whom we work)** actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue and profits; and other adverse business impacts. In the ordinary course of business, we process personal data and other sensitive data, including proprietary and confidential business data, trade secrets, intellectual property, clinical trial participant data, and other sensitive third- party data. We are therefore subject to or affected by numerous data privacy and security obligations, such as federal, state, local and foreign laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts, and other obligations governing the processing of personal data. These obligations may change, are subject to differing interpretations and may be inconsistent among jurisdictions or conflict. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business; affect us or our collaborators', service providers' and contractors' ability to operate in certain jurisdictions or to collect, store, transfer, use and share personal data; necessitate the acceptance of more onerous obligations in our contracts; result in liability; or impose additional costs on us. These obligations may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. In addition, these obligations may require us to change our business model. Outside the U. S., an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, the European Union' s General Data Protection Regulation ~~(GDPR) (EU) 2016 / 679~~, or the EU GDPR, **and the United Kingdom' s GDPR, or the UK GDPR (collectively, the " GDPR "),** ~~imposes~~ **impose** strict requirements on the processing of personal data. **For example,** ~~Under~~ **under** ~~the EU~~ GDPR, government regulators may impose temporary or definitive bans on data processing, ~~as well as~~ fines **of up to 20 million Euros under the EU GDPR, 17. 5 million pounds sterling under the UK GDPR or,** in **each case, 4 % of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent** ~~the~~ **their interests** ~~event of violations~~. In addition, we may be unable to transfer personal data from the EEA **, the UK** and other jurisdictions to the U. S. or other countries due to data localization requirements or limitations on cross- border data flows. The EEA and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the EEA and the UK ~~,~~ have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross- border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the U. S. in compliance with law, such as the EEA and UK' s standard contractual clauses, the UK' s International Data Transfer Agreement / Addendum, and the EU- U. S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U. S.- based organizations who self- certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the U. S. If there is no lawful manner for us to transfer personal data from the EEA, the UK, or other jurisdictions to the U. S., or if the requirements for a legally- compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. **Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups, and** ~~Some~~ **some** EEA regulators have prevented companies from transferring personal data out of the EEA for allegedly violating the **EU** GDPR' s cross- border data transfer limitations. Likewise, we expect that there will continue to be new proposed laws, regulations and industry standards relating to data privacy and security in the U. S. For example, HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health data. Additionally, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020, or CPRA, collectively CCPA, imposes obligations on businesses to which it applies. These obligations include, but are not limited to, providing

specific disclosures in privacy notices and affording California residents certain rights related to their personal data. The CCPA allows for statutory fines for noncompliance. While the CCPA contains limited exceptions for clinical trial data, the CCPA' s implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. In addition, the CPRA establishes a California Privacy Protection Agency to implement and enforce the CPRA, which could increase the risk of an enforcement action, and applies to personal ~~information~~ **data** of business representatives and employees. Other states have also enacted data privacy and security laws. For example, Virginia passed the Consumer Data Protection Act, and Colorado passed the Colorado Privacy Act, both of which differ from the CPRA and became effective in 2023. If we become subject to new data privacy and security laws, at the state level or otherwise, the risk of enforcement action against us could increase because we may become subject to additional obligations, and the number of individuals or entities that can initiate actions against us may increase. Our employees and personnel use generative AI technologies to perform their work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages. In addition to data privacy and security laws, we **are** ~~may be~~ contractually subject to industry standards adopted by industry groups and **we are, and** may become **in the future,** subject to such obligations ~~in the future~~. We ~~may~~ **are** also be bound by other contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. We may publish privacy policies, marketing materials, **white papers,** and other statements, such as **statements relating to** compliance with certain certifications or self- regulatory principles **concerning** ~~, regarding~~ data privacy and security. ~~If~~ **Regulators in the United States are increasingly scrutinizing these statements, and if** these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, **misleading** or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences. It is possible that, in the future, we may fail or be perceived to have failed to comply with applicable data privacy and security obligations. Moreover, despite our best compliance efforts, we may not be successful in achieving compliance if our personnel or third parties **with** whom we **work** ~~rely on~~ fail to comply with such obligations, which could negatively impact our business operations and compliance posture. If we or the third parties ~~on which~~ **with whom** we ~~rely~~ **work** fail, or are perceived to have failed, to address or comply with data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions; litigation; additional reporting requirements and / or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including ~~but not limited to~~: interruptions or stoppages in our business operations including, as relevant, clinical trials; inability to process personal data or to operate in certain jurisdictions; limited ability to **continue to** develop or commercialize ~~imetelstat~~ **RYTELO** ; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations. Moreover, clinical trial participants or research subjects about whom we or our vendors obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Risks Related to Our Common Stock ~~AND~~ **and** Financial Reporting Historically, our stock price has been extremely volatile and your investment may suffer a decline in value. Historically, our stock price has been extremely volatile. Between January 1, 2014 and December 31, ~~2023~~ **2024** , our stock has traded as high as $ 6. 38 per share and as low as $ 0. 89 per share. Between January 1, ~~2023~~ **2024** and December 31, ~~2023~~ **2024** , the price has ranged between a high of $ ~~3~~ **5** . ~~84~~ **34** per share and a low of $ 1. ~~68~~ **64** per share. The significant market price fluctuations of our common stock have been due to and may in the future be influenced by a variety of factors, including: • **the level of RYTELO sales in the U. S.; •** announcements regarding ~~the potential~~ regulatory approval or non- approval of ~~imetelstat and~~ **RYTELO in any** ~~the~~ **other** ~~timing thereof~~ **jurisdictions or indications** , **or** specific label indications for **RYTELO;** or restrictions, warnings or limitations in its use ~~, or delays in the regulatory review and commercialization process~~ ; • announcements regarding the **further** research and development of ~~imetelstat~~ **RYTELO** , or adverse efficacy or safety results of, further delays in the commencement, enrollment or conduct of, discontinuation of, or further modifications or refinements to any current ~~clinical trials of imetelstat, as well as for~~ **or** ~~our expanded access program or for~~ potential future clinical trials ~~of imetelstat~~ , for any reason, or our inability, for any reason, to successfully continue the development of ~~imetelstat~~ **RYTELO** ; • our ability to obtain additional capital **if and** when needed to further advance ~~the imetelstat~~ **our development** program; • changes in laws or regulations applicable to ~~imetelstat~~ **RYTELO** , including ~~but not limited to~~ **laws or regulations concerning the commercialization of RYTELO or** clinical trial requirements for approval or other regulatory developments related to ~~imetelstat~~ **RYTELO** ; • announcements of technological innovations, new commercial products, or clinical progress or lack thereof by us, potential future collaborative partners or our competitors; • adverse developments concerning our manufacturers, including our inability to obtain adequate product supply for ~~imetelstat~~ **RYTELO** or inability to do so at acceptable prices; • the size and growth of the market **opportunity** for ~~our lead imetelstat~~ **RYTELO in its currently approved and any potential future approved** indications ~~of lower- risk MDS and relapsed / refractory MF~~ ; • disputes or other developments relating to ~~imetelstat~~ **RYTELO** proprietary rights, including patents, litigation matters and our ability to obtain, enforce and defend patent protection **and maintain regulatory exclusivity** for **RYTELO and** our technologies; • the terms and timing of any future collaboration agreements for the **further** development and ~~potential~~ commercialization of ~~imetelstat~~ **RYTELO** that we may establish; • announcements of significant acquisitions, strategic partnerships, collaborations, joint ventures or capital commitments by us or our competitors; • the demand in the market for our common stock; • increased or continuing operating losses; • general domestic and international market conditions or market conditions relating to the biopharmaceutical and pharmaceutical industries, especially given the volatility caused by macroeconomic or other global conditions, such as inflation, rising interest rates, prospects of a recession, government shutdowns **, further changes in tariffs and other trade restrictions** ,

bank failures and other disruptions to financial systems, civil or political unrest, military conflicts, pandemics or other health crises and supply chain and resource issues; • perceptions of the biotechnology and pharmaceutical industry by the public, legislature, regulators and the investment community; • our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public; • publication of commentary, articles or research reports about us or our industry, or positive or negative recommendations or withdrawal of research coverage, by securities analysts, bloggers, news media or other third parties; • large stockholders increasing or exiting their position in our common stock or an increase in the short interest in our common stock **; • sales of stock by our officers and directors** ; • announcements of or developments concerning any litigation; • actions instituted by activist shareholders or others; • the issuance of common stock to partners, vendors or investors to raise additional capital or as a result of option or warrant exercises; • other events or factors that are beyond our control; and • the occurrence of any other risks and uncertainties discussed under the heading " Risk Factors. " Provisions in our charter, bylaws and Delaware law may inhibit potential acquisition bids for us, which may adversely affect the market price of our common stock and / or prevent holders of our common stock from benefiting from what they believe may be the positive aspects of acquisitions and takeovers. Provisions of our charter documents and bylaws may make it substantially more difficult for a third party to acquire control of us and may prevent changes in our management, including provisions that: • prevent stockholders from taking actions by written consent; • divide the board of directors into separate classes with terms of office that are structured to prevent all of the directors from being elected in any one year; and • set forth procedures for nominating directors and submitting proposals for consideration at stockholders' meetings. In addition, our certificate of incorporation provides our board of directors with the authority to issue up to 3, 000, 000 shares of undesignated preferred stock and to determine or alter the rights, preferences, privileges and restrictions granted to or imported upon these shares without further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction without further action by our stockholders. As a result, the market price of our common stock may be adversely affected. If in the future, we issue preferred stock that has preference over our common stock with respect to the payment of dividends or upon our liquidation, dissolution or winding up, or if we issue preferred stock with voting rights that dilute the voting power of our common stock, the rights of holders of our common stock or the market price of our common stock could be adversely affected. Provisions of Delaware law may also inhibit potential acquisition bids for us or prevent us from engaging in business combinations. In addition, we have individual severance agreements with our executive officers and a company-wide severance plan, either of which could require a potential acquirer to pay a higher price. Either collectively or individually, these provisions may prevent holders of our common stock from benefiting from what they may believe are the positive aspects of acquisitions and takeovers, including the potential realization of a higher rate of return on their investment from these types of transactions. The exclusive forum provisions in our amended and restated bylaws could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or any of our directors, officers, or employees, or the underwriters of any offering giving rise to such claim, which may discourage lawsuits with respect to such claims. Our amended and restated bylaws provide that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for: • any derivative claim or cause of action or proceeding brought on our behalf; • any claim or cause of action for breach of a fiduciary duty owed by any of our current or former directors, officers or other employees, or our stockholders, to us or to our stockholders; • any claim or cause of action against us or any of our current or former directors, officers or other employees, or our stockholders, arising pursuant to any provision of the General Corporation Law of the State of Delaware, our certificate of incorporation, or our bylaws; • any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; • any claim or cause of action as to which the General Corporation Law of the State of Delaware confers jurisdiction on the Court of Chancery of the State of Delaware; or • any claim or cause of action against us or any of our current or former directors, officers or other employees, or our stockholders, governed by the internal affairs doctrine or otherwise related to our internal affairs. In addition, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act of 1933, as amended, or the Securities Act, or the rules and regulations thereunder. Our amended and restated bylaws provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision, including for all causes of action asserted against any defendant named in such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. The application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court, and our stockholders cannot waive compliance with the federal securities laws and the rules and regulations thereunder. While the Delaware courts have determined that such choice of forum provisions are facially valid and several state trial courts have enforced such provisions and required that suits asserting Securities Act claims be filed in federal court, there is no guarantee that courts of appeal will affirm the enforceability of such provisions, and a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such an instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions, which costs could be borne by stockholders, and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions. Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to the

exclusive forum provisions in our amended and restated bylaws, including the Federal Forum Provision. These provisions could limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, or our stockholders or the underwriters of any offering giving rise to such claims, which may discourage lawsuits with respect to such claims. Furthermore, if a court were to find the exclusive forum provisions contained in our bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could have a material and adverse impact on our business and our financial condition. We do not intend to pay cash dividends on our common stock in the foreseeable future. We do not anticipate paying cash dividends on our common stock in the foreseeable future. Any payment of cash dividends will depend upon our financial condition, results of operations, capital requirements and other factors, and will be at the discretion of our board of directors. In addition, the terms of our **Pharmakon** Loan Agreement ~~prevent us from paying~~ **restrict our ability to pay** dividends and any future debt agreements may continue to ~~preclude us from paying~~ **or further restrict our ability to pay** dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future. Our employees, independent contractors, principal investigators, clinical trial sites, contract research organizations, consultants or vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We are exposed to the risk that our employees, independent contractors, principal investigators, clinical trial sites, CROs, consultants or vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct or disclosure of unauthorized activities to us that violate the FDA' s or similar international regulatory authorities' regulations, including those laws requiring the reporting of true, complete and accurate information; manufacturing standards; healthcare fraud and abuse laws and regulations; or laws that require the true, complete and accurate reporting of financial information or data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our non- clinical studies or clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by our employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could adversely affect our business, financial condition, results of operations or prospects through: • the imposition of civil, criminal and administrative penalties, damages and monetary fines **; • possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs** ; • contractual damages; • diminished potential profits and future earnings; and **Our business could be negatively impacted by environmental, social and corporate governance, or ESG, matters or our reporting of such matters. There is an increasing focus from certain investors, employees, partners, and other stakeholders concerning ESG matters. We may be, or be perceived to be, not acting responsibly in connection with these matters, which could negatively impact us. Moreover, the SEC has proposed, and may continue to propose, certain mandated ESG reporting requirements, such as the SEC' s final rules designed to enhance and standardize climate-related disclosures, which, if such climate- related disclosure rules ultimately go into effect, would significantly increase our compliance and reporting costs and may also result in disclosures that certain investors or other stakeholders deem to impact our reputation negatively and / or that harm our stock price. We currently do not report our environmental emissions and absent a legal requirement to do so we currently do not plan to report our environmental emissions, and lack of reporting could result in certain investors declining to invest in our common stock. Furthermore, the criteria by which our ESG practices, including our initiatives and public goals, are assessed may change due to the evolution of the sustainability landscape, which could result in greater expectations of us and may cause us to undertake costly initiatives to satisfy new criteria. If we are unable to respond effectively to these changes to the sustainability landscape, governments, customers, and investors may conclude that our policies and / or actions with respect to ESG matters are inadequate. If we fail or are perceived to have failed to achieve previously announced public goals or to accurately disclose our progress on such goals or initiatives, our reputation, business, financial condition and results of operations could be adversely impacted.** Failure to achieve and maintain effective internal controls in accordance with Section 404 of the Sarbanes- Oxley Act of 2002 could have a material adverse effect on our business and stock price. Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, requires that we establish and maintain an adequate internal control structure and procedures for financial reporting. Our Annual Reports on Form 10- K must contain an annual assessment by management of the effectiveness of our internal control over financial reporting and must include disclosure of any material weaknesses in internal control over financial reporting that we have identified. In addition, our independent registered public accounting firm must provide an opinion annually on the effectiveness of our internal control over financial reporting. The requirements of Section 404 are ongoing and also apply to future years. We expect that our internal control over financial reporting will continue to evolve as our business develops, including **in connection with our** ~~as we prepare to potentially launch and commercialize~~ **commercialization** ~~imetelstat~~ **of RYTELO** . Although we are committed to continue to improve our internal control processes and we will continue to diligently and vigorously review our internal control over financial reporting in order to ensure compliance with Section 404 requirements, any control system, regardless of how well designed, operated and evaluated, can provide only reasonable, not absolute, assurance that its objectives will be met **. Moreover, in 2024 we implemented a new ERP and other information systems to help us manage our operations and financial reporting. However, there is an**

increased risk that changing controls may be ineffective in connection with the implementation of the new ERP and this ERP system may place additional burdens on employees to learn and adapt our processes to effectively operate under the ERP system. If the ERP system that we implemented in 2024 does not operate as intended, the effectiveness of our internal control over financial reporting could be negatively impacted . Therefore, we cannot assure you that material weaknesses or significant deficiencies will not exist or otherwise be discovered in the future, particularly in light of our increased reliance on personnel working remotely. If material weaknesses or other significant deficiencies occur, such weaknesses or deficiencies could result in misstatements of our results of operations, restatements of our financial statements, a decline in our stock price, or other material adverse effects on our business, reputation, results of operations, financial condition or liquidity. Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations. New income, sales, use, excise or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could affect the tax treatment of our domestic and foreign sales and earnings. Any new taxes could adversely affect our domestic and international business operations and our business and financial condition. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. Future guidance from the U. S. Internal Revenue Service and other tax authorities with respect to such legislation may adversely affect us, and certain aspects of such legislation could be repealed or modified in the future, which could have an adverse effect on us. For example, the Inflation Reduction Act **of 2022** ~~includes~~ **included** provisions that ~~will impact~~ **impacted** the U. S. federal income taxation of corporations, including imposing a minimum tax on the book income of certain large corporations and an excise tax on certain corporate stock repurchases that **is** ~~would be~~ imposed on the corporation repurchasing such stock. Changes in corporate tax rates, the realization of net deferred tax assets relating to our U. S. operations, the taxation of earnings from other countries, and the deductibility of expenses or future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one- time charges in the current or future taxable years, and could increase our future U. S. tax expense. For example, **under the Tax Cuts and Jobs Act of 2017,** effective January 1, 2022, research and experimental expenses must be capitalized for tax purposes and amortized over five years for research activities conducted in the United States and over fifteen years for research activities conducted outside the United States, instead of being deducted in the year incurred. Unless this provision is ~~deferred,~~ modified ~~,~~ or repealed by Congress, or the U. S. Department of the Treasury issues regulations narrowing its application, our future tax obligations could be increased, which could harm our operating results. The impact of this provision will depend on multiple factors, including the amount of research and experimental expenses we incur, whether we achieve sufficient income to fully utilize such deductions and whether we conduct our research and experimental activities inside or outside the United States. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. Our net operating loss carryforwards attributable to tax years beginning before January 1, 2018 could expire unused and be unavailable to offset future income tax liabilities. In addition, under current U. S. federal income tax law, federal net operating losses incurred in taxable years beginning after December 31, 2017, can be carried forward indefinitely, but the deductibility of such federal net operating losses **in a taxable year** is limited to 80 % of taxable income **in such year** . Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an " ownership change, " generally defined as a greater than 50 percentage point cumulative change (by value) in its equity ownership over a three- year period, the corporation' s ability to use its pre- change net operating loss carryforwards and other pre- change tax attributes (such as research and development tax credits) to offset its post- change taxable income or taxes may be limited. Changes in our stock ownership **have occurred in the past, and future ownership changes** , some of which ~~are~~ **may be** outside ~~of~~ our control, **could occur** ~~may have resulted~~ in ~~, or other~~ -- **the** future ~~changes could~~ **, as a** result **of shifts** in ~~, an~~ **our stock** ownership ~~change~~ . If a limitation were to apply, utilization of a portion of our domestic net operating loss and tax credit carryforwards could be limited in future periods, and a portion of the carryforwards may expire before being available to reduce future income tax liabilities, which could adversely impact our financial position. At the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. **For example, in June 2024, California enacted legislation that, with certain exceptions, suspends the use of California net operating losses to offset California income and limits the use of California business tax credits to offset California taxes, for taxable years beginning after 2023 and before 2027.** It is also uncertain if and to what extent various states will conform to current U. S. federal income tax law.