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

**Legend:** **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

Our ~~business is~~ **operations and financial results are** subject to ~~numerous~~ **various** risks and uncertainties, including those described **below** ~~in Part I~~ , ~~Item 1A~~ **which could adversely affect our business, financial condition, results of operations, cash flows, and the trading price of our common stock** ~~" Risk Factors " in this Annual Report~~ **Additional risks and uncertainties that we currently do not know about or that we currently believe to be immaterial may also impair our business** . You should carefully consider ~~these~~ -- **the** risks **described below** and ~~uncertainties when investing~~ **the other information** in **this Annual Report on Form 10- K for the period ended December 31, 2024 (the " Annual Report "), including** our ~~common stock~~ **audited condensed consolidated financial statements and the related notes thereto, and " Management' s Discussion and Analysis of Financial Condition and Results of Operations** . **"** ~~The principal risks~~ **Risks Related to Our Financial Position** and **Need for Capital** ~~uncertainties affecting our business include the following: ● We~~ are a commercial ~~-stage~~ biopharmaceutical company with a limited operating history **and** ~~. To date, we~~ have **not** generated **significant revenue** ~~approximately $ 97. 0 million~~ from product sales. We have incurred significant operating losses since our inception, anticipate that we will incur continued losses for the foreseeable future and may never achieve profitability. ~~● We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations. ● Our Revenue Interest Financing Agreement with Healthcare Royalty Partners, and our other agreements, could restrict our ability to commercialize IMCIVREE, limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations. ● We have only one approved product, which is still in clinical development in additional indications, and we may not be successful in any future efforts to identify and develop additional product candidates. ● The successful commercialization of IMCIVREE and any other product candidates will depend in part on the extent to which governmental authorities, private health insurers, and other third- party payors provide coverage and adequate reimbursement levels. Failure to obtain or maintain coverage and adequate reimbursement for setmelanotide or our other product candidates, if any and if approved, could limit our ability to market those products and decrease our ability to generate revenue. ● Positive results from early clinical trials of setmelanotide may not be predictive of the results of later clinical trials of setmelanotide. If we cannot generate positive results in our later clinical trials of setmelanotide, we may be unable to successfully develop, obtain regulatory approval for and commercialize additional indications for setmelanotide. ● The number of patients suffering from each of the MC4R pathway deficiencies is small and has not been established with precision. If the actual number of patients with any of these conditions is smaller than we had estimated, our revenue and ability to achieve profitability will be materially adversely affected. Moreover, our ability to recruit patients to our trials may be materially adversely affected. Patient enrollment may also be adversely affected by competition and other factors. ● Failures or delays in the commencement or completion of our planned clinical trials of setmelanotide could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business. ● Changes in regulatory requirements and, guidance in the United States or abroad, or unanticipated events during our clinical trials of setmelanotide may occur, which may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline. Additionally, it may be necessary to validate different or additional instruments for measuring subjective symptoms, and to show that setmelanotide has a clinically meaningful impact on those endpoints in order to obtain regulatory approval. ● Even if we complete the necessary clinical trials, the regulatory and marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining additional approvals for the commercialization of setmelanotide beyond FDA approval for obesity due to Bardet- Biedl syndrome or proopiomelanocortin, or POMC, proprotein convertase subtilisin / kexin type 1, or PCSK1, or leptin receptor, or LEPR, deficiencies in the United States. We depend entirely on the success of setmelanotide, and we cannot be certain that we will be able to obtain additional regulatory approvals for, or successfully commercialize, setmelanotide. If we~~ are ~~not able to obtain, or if there are delays in obtaining, required additional regulatory approvals, we will not be able to commercialize setmelanotide in additional indications in the United States or in foreign jurisdictions, and our ability to generate revenue will be materially impaired. ● Our approach to treating patients with MC4R pathway deficiencies requires the identification of patients with unique genetic subtypes, for example, POMC genetic deficiency. The FDA or other equivalent competent authorities in foreign jurisdictions could require the clearance, approval or CE marking of an in vitro companion diagnostic device to ensure appropriate selection of patients as~~ a **global** ~~condition of approving 4setmelanotide in additional indications. The requirement that we obtain clearance~~ , ~~approval or CE mark of an in vitro companion diagnostic device will require substantial financial resources, and could delay or prevent the receipt of additional regulatory approvals for setmelanotide, or adversely affect those we have already obtained. ● Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the~~ commercial ~~profile of an approved labeling or result in significant negative consequences following marketing approval, if any. ● We may fail to realize the anticipated benefits of our acquisition of Xinvento B. V., those benefits may take longer to realize than expected, and we may encounter significant integration difficulties. ● If the third parties we rely on, and will continue to rely on, do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain additional regulatory approvals for or continue to commercialize setmelanotide and our business could be substantially hard. ● Our industry is intensely competitive. If we are not able to compete effectively against current and future competitors, we may not be able to generate sufficient revenue from the sale of IMCIVREE, our business will not grow~~

and our financial condition and operations will suffer. ● If we are unable to adequately protect our proprietary technology or maintain issued patents that are sufficient to protect setmelanotide, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects. ● Global events, such as the COVID- 19 pandemic and the economic slowdown, have and may continue to adversely impact our business, including our preclinical studies, clinical trials and other commercialization prospects. ● We have identified a material weakness in our internal controls over financial reporting and may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, which may result in material misstatements of our consolidated financial statements or cause us to fail to meet our periodic reporting obligations. PART IItem 1. BusinessOverviewWe are a global, commercial- stage biopharmaceutical company dedicated to transforming the lives of patients and their families living with rare neuroendocrine diseases **a limited operating history on which to base your investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk** . We are **were incorporated in February 2013. Our operations to date have been primarily** focused on **developing and commercializing** advancing our melanocortin- 4 receptor (MC4R) agonists, including our lead asset, IMCIVREE ® (setmelanotide) , as a precision medicine designed to treat **patients living with** hyperphagia and severe obesity caused by rare MC4R pathway diseases. While obesity affects hundreds of millions of people worldwide **Our business activities have included acquiring rights to intellectual property** , **business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and conducting research and development activities, including clinical trials, for setmelanotide. To date** we are developing therapies for a subset of individuals who have **generated approximately $ 227** hyperphagia, a pathological hunger, and severe obesity due to an impaired MC4R pathway, which may be caused by traumatic injury or genetic variants . **6 million of revenue from product sales** The MC4R pathway is an endocrine pathway in the brain that is responsible for regulating hunger, caloric intake and energy expenditure, which consequently affect body weight . **In** IMCIVREE, an MC4R agonist for which we hold worldwide rights, is the first- ever therapy developed for patients with certain rare diseases that is approved or authorized in the United States, European Union (EU), Great Britain, Canada and other countries and regions. IMCIVREE is approved **to reduce excess body** by the U. S. Food and Drug Administration (FDA) for chronic weight management **and maintain weight reduction long term** in adult and pediatric patients 6 **aged 2** years of age and older with **syndromic or** monogenic or syndromic obesity due to : **Bardet- Biedl syndrome** ( i **BBS** ) **or pro-** proopiomelanocortin --- **opiomelanocortin** (POMC), proprotein convertase subtilisin / kexin type 1 (PCSK1) **,** or leptin receptor (LEPR) deficiency as determined by an FDA- approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of 5uncertain - **uncertain** significance (VUS ); or (ii) Bardet- Biedl syndrome (BBS ). The European Commission (EC) and Great Britain **the United Kingdom** ' s Medicines & Healthcare Products Regulatory Agency (MHRA) have **has** authorized IMCIVREE for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. Including the United States and Canada, we have achieved market access for IMCIVREE for BBS or POMC and LEPR deficiencies, or both, in 14 countries, and we continue to collaborate with authorities to achieve access in additional markets. In addition to our ongoing commercial efforts of setmelanotide, we are advancing what we believe is the most comprehensive clinical research program ever initiated in MC4R pathway diseases, with multiple ongoing and planned clinical trials. Our MC4R pathway program is designed to expand the total number of patients who would benefit from setmelanotide therapy or who we believe could be addressed by one of our new drug candidates, such as RM- 718, which is designed to be a more selective MC4R agonist with weekly administration, or LB54640, an investigational oral small molecule MC4R agonist now in Phase 2 clinical trials. With setmelanotide, we have completed enrollment in our Phase 3 trial in patients with hypothalamic obesity. Our Phase 3 EMANATE trial, comprised of four independent substudies evaluating setmelanotide in genetically caused MC4R pathway diseases, and our Phase 2 DAYBREAK trial evaluating setmelanotide in additional genetic indications, are ongoing. In our recently completed Phase 3 pediatrics trial in 12 patients between the ages of 2 and younger than 6 with BBS or POMC or LEPR deficiency obesities, setmelanotide achieved the primary endpoint with a 3. 04 mean reduction in BMI- Z score (a measure of body mass index deviations from what is considered normal) and 18. 4 percent mean reduction in BMI. We are seeking regulatory approval in the United States and Europe to expand the label for IMCIVREE to treat patients as young as 2 with these diseases based on these data. With RM- 718, we anticipate beginning Phase 1 in- human trials in the first half of 2024, including a multiple- ascending dose study in patients with hypothalamic obesity. We are leveraging what we believe is the largest known DNA database focused on obesity- with almost 80, 000 sequencing samples as of December 31, 2023- to improve the understanding, diagnosis and care of people living with severe obesity due to certain variants in genes associated with the MC4R pathway. Our sequencing- based epidemiology estimates show that each of these genetically- defined MC4R pathway deficiencies are considered rare diseases, according to established definitions based on patient populations. Our epidemiology estimates are approximately 4, 600 to 7, 500 for U. S. patients in initial FDA- approved indications, including obesity due to biallelic POMC, PCSK1 or LEPR deficiencies, and BBS. We estimate the epidemiology for patients with hypothalamic obesity to be between 5, 000 and 10, 000 in the United States, based on our analysis of published literature. Our epidemiology estimates for the indications being studied in our Phase 3 EMANATE trial suggest that approximately 53, 000 U. S. patients with one of these genetically driven obesities have the potential to respond well to setmelanotide. Similarly, our epidemiology estimates for patients with genetic indications who demonstrated an initial response in our Phase 2 DAYBREAK trial is approximately 65, 300. All these patients face similar challenges as other patients with rare diseases, namely lack of awareness, resources, tests, tools and especially therapeutic options. We are working to expand access to IMCIVREE globally. Our disease awareness and patient finding efforts are aligned with a singular focus on building a community of caregivers and healthcare providers focused on transforming the treatment of these diseases. We have multiple field teams in the United States and Europe engaging with

physicians who treat patients with severe obesity. We continue to bring together health care providers, patients and families with educational and awareness events. Our genetic testing programs fuel MC4R pathway research, disease education and awareness and patient finding. With 226 employees in the United States and Europe as of February 1, 2024, a rapidly expanding network of key opinion leaders, and an increasing number of identified, diagnosed and treated patients, we are focused on changing the paradigm for the treatment of rare MC4R pathway diseases. Our focused disease awareness and patient finding efforts fuel the key elements of our strategy, including: ● Increase global access to IMCIVREE: With access for IMCIVREE achieved in 14 countries for BBS and / or POMC and LEPR deficiencies, we are now focused on community building programs, disease awareness and education efforts, patient finding and securing reimbursement. We continue to seek market access for IMCIVREE on a country- by- country basis in Europe and additional international markets. 6 ● Execute on clinical development programs: Our clinical development programs are designed to expand the overall market for and reach of setmelanotide as a potential treatment for additional MC4R pathway diseases. In addition to our pivotal trial in hypothalamic obesity, our Phase 3 EMANATE trial and our Phase 2 DAYBREAK trial are ongoing. We will continue to expand our genetic testing effort focusing on clinical trial enrollment and commercialization efforts. ● Lifecycle management and pipeline expansion: In parallel with clinical development plans to expand the reach of setmelanotide, we are advancing RM- 718, an investigational, MC4R- specific agonist designed for weekly administration and LB54640, an investigational, oral MC4R agonist — both of which are designed not to cause hyperpigmentation — in the clinic. In addition, we are advancing towards the clinic with new therapies for congenital hyperinsulinism (CHI), a rare genetic disease. 7Market OverviewSevere Obesity, Hyperphagia, and the MC4R PathwayRare MC4R pathway diseases are distinct from general obesity. The hallmark characteristics of rare MC4R pathway diseases are severe obesity and hyperphagia, a pathological and insatiable hunger that drives a severe preoccupation with food and extreme food- seeking behaviors. Lifestyle interventions are not therapeutic in patients with these diseases because they fail to address the underlying genetic or acquired impairment of central energy regulation and satiety. Accordingly, the discovery that the MC4R pathway regulates both energy intake (hunger) and energy expenditure has made it an important target for therapeutics. Studies have shown that injuries to the hypothalamus region of the brain in patients with certain tumors impair MC4R signaling, leading to increased hunger, reduced energy expenditure and rapid onset of severe obesity. In addition to obesity due to POMC, PCSK1 or LEPR deficiencies and BBS, recent advances in genetic studies have identified several diseases characterized at least in part with early- onset, severe obesity and hyperphagia that are the result of genetic variants affecting the MC4R pathway, including certain variants of the POMC, PCSK1, LEPR, SRC1 and SH2B1 genes, as well as MC4R deficiency obesity and deficiencies in many additional genes with strong or very strong relevance to the MC4R pathway. With a deeper understanding of this critical signaling pathway, we are taking a different approach to drug development by focusing on specific genetic variants and acquired injury affecting the MC4R pathway. We believe that this approach has the potential to provide clinically- meaningful improvements in obesity and hyperphagia by re- establishing lost function in the MC4R pathway. Rare MC4R Pathway DiseasesThe MC4R pathway has been the focus of extensive scientific investigation for many years. This neuro- endocrine pathway in the hypothalamus is a key signaling pathway responsible for regulating hunger, food or calorie intake, and energy expenditure, which consequently affects body weight. It is known to be a critical component in the regulation of energy balance. The critical role of the MC4R pathway in weight regulation is supported by the observation that single gene variants at many points in this pathway result in early- onset, severe obesity. The MC4R pathway is illustrated in the figure below. Under normal conditions, POMC neurons are activated by adiposity and satiety signals, including those resulting from the hormone leptin acting through the LEPR. POMC neurons produce a protein, which is processed by the PCSK1 enzyme, into melanocyte stimulating hormone, or MSH, the natural ligand, or activator of the MC4R. When upstream genetic variants, traumatic injuries or lesions disrupt this pathway, it can lead to insufficient MC4R activation and downstream signaling; the result of which is hyperphagia, reduced energy expenditure and severe obesity. 8The figure below also illustrates some of the genes that are upstream of the MC4R and the potential effect variants in those genes may have on the activation of the MC4R, which regulates food intake and energy expenditure. Setmelanotide Development Targets: Upstream Deficiencies Affecting the MC4R PathwayAgRP, agouti- related protein; LEPR, leptin receptor; MC4R, melanocortin- 4 receptor; MSH, melanocyte- stimulating hormone; ACTH, adrenocorticotropic hormone; PCSK1, proprotein convertase subtilisin / kexin- type 1; POMC, proopiomelanocortin. Reference: Yazdi FT et al. PeerJ. 2015; 3: e856. We are focused on developing setmelanotide as a precision treatment for rare MC4R pathway diseases. In addition to acquired hypothalamic obesity, we are evaluating setmelanotide in Phase 2 and 3 trials for the treatment of obesity due to variants in one of a number of genes associated with the MC4R pathway. Setmelanotide has the potential to restore lost function in this pathway by activating the intact MC4R- expressing neuron downstream of the genetic impairment. In this way, we believe setmelanotide acts as restorative therapy, to restore lost signaling of the MC4R pathway. Epidemiology Estimates of Rare MC4R Pathway DiseasesWhile obesity is a global epidemic, we are focused on rare MC4R pathway diseases. Impairment of the MC4R pathway is characterized by hyperphagia and rapid- onset obesity or the presence of early- onset, severe obesity. Of the tens of millions of individuals with obesity in the United States, the U. S. Center for Disease Control (CDC) estimates that there are approximately 5 million individuals whose severe obesity had onset between the ages of 2 and 5 years old. The tables below summarizes the estimated population sizes for indications currently approved or under pivotal clinical investigation. These calculations rely on internal and proprietary sequencing data and current estimated responder rates to setmelanotide therapy, and they assume a U. S. population of 327 million, of which 1. 7 % have early- onset, severe obesity (Hales et al in JAMA — April 2018: Trends in Obesity and Severe Obesity Prevalence in US Youth and Adults by Sex and Age, 2007- 2008 to 2015- 2016). 9Approved by the U. S. FDA and authorized by the EC and Great Britain' s MHRAaEstimated U. S. populationEstimated European populationBardet- Biedl syndrome4, 000 – 5, 000b4, 000 – 5, 000b Obesity due to POMC or LEPR deficiency caused by biallelic variants in the POMC, PCSK1 or LEPR genes – 600 – 2, 500Similar prevalence as U. S. c a. Authorized by the EC and MHRA for use in patients six years of age and older. Approved by the FDA for use in patients six years of age and older with monogenic or syndromic

obesity. b. For BBS, prevalence estimates vary between populations, from 1 in 100, 000 in northern European populations with higher prevalence rates in some additional regions throughout the world. We estimate the number of patients with BBS in the United States is between 4, 000 and 5, 000, with a similar number in continental Europe and the United Kingdom (UK). These estimates are based on our patient identification efforts in the United States and Europe and our proprietary genetic sequencing data, as well as our belief that BBS, like most rare diseases, is underdiagnosed. We believe the BBS health care provider network in EU member states and the UK is particularly well established and more advanced than in the United States, and based on field work, we believe there are approximately 1, 500 patients diagnosed and being cared for at academic centers in Europe. Applying these population- adjusted identified patient populations to the United States and other countries with comparable population genetics supports our epidemiology estimates. c. For POMC or LEPR deficiencies, we estimate European prevalence is similar to the United States. While our sequencing data include patients from the United States and Europe, we do not have comparable sequencing data from European countries and these estimates are therefore based on applying relative population percentages to the Rhythm- derived estimates described above. Separately, in Canada, where our new drug submission for the treatment of obesity and control of hunger in BBS or biallelic POMC, PSCK1 or LEPR deficiency is under review, we estimate there are approximately 300 – 400 individuals with BBS. This is based on data on file, a range of prevalence estimates for BBS in Canada between 1 in 125, 000 to 1 in 160, 000, and a population in Canada of 38, 929, 902 as of July 1, 2022, according to StatsCan. Also, our prevalence estimate accounts for a reported founder effect in province of Newfoundland, where estimated prevalence is approximately 1 in 17, 500 (Forsythe E, Beales PL. Eur J Hum Genet. 2013; 21 (1): 8- 13.) The prevalence of POMC, PCSK1, and LEPR deficiency obesity is not well characterized as very little data are available. 10Setmelanotide currently being evaluated in Phase 3 trialsEstimated U. S. populationEstimated European populationAcquired hypothalamic obesity 5, 000 – 10, 000d3, 500 – 10, 000e Obesity due to POMC insufficiency caused by heterozygous variants in the POMC or PCSK1 genes6, 000f Similar prevalence as U. S. fObesity due to LEPR insufficiency caused by heterozygous variants in the LEPR gene4, 000 f Similar prevalence as U. S. fObesity due to SRC1 deficiency caused by a variant in the NCOA1 gene (SRC1 deficiency obesity) ~ 20, 000 f Similar prevalence as U. S. fObesity due to SH2B1 deficiency caused by a variant in the SH2B1 gene or 16p11. 2 deletion encompassing the SH2B1 gene (SH2B1 deficiency obesity) ~ 23, 000 f Similar prevalence as U. S. fSetmelanotide currently being evaluated in Phase 2 DAYBREAK trial Obesity due a deficiency in the MC4R pathway caused by variants in the SEMA3 family, PHIP, TBX3 or PLXNA family ~ 65, 300f, g Similar prevalence as U. S. f d. For hypothalamic obesity in the United States, our internal Company estimates are based on reported incidence of hypothalamic obesity following craniophryngioma and long- term survival rates, (Zacharia, et al., Neuro-Oncology 14 (8): 1070 – 1078, 2012. doi: 10. 1093 / neuonc / nos142; and Muller, et al., Neuro- Oncology 17 (7), 1029 – 1038, 2015 doi: 10. 1093 / neuonc / nov044.) e. Our European prevalence estimate for hypothalamic obesity is limited to the EU4 (Germany, France, Spain, Italy), UK and the Netherlands. The total 2020 population estimates for the six key countries (EU4, the Netherlands, and UK) of 339, 295, 304 was used to reach a final prevalence of 0. 1- 0. 3 in 10, 000 patients. f. For patients with genetic variants of the MC4R pathway, the rarity and the genetic pathophysiology of our target indications means that there is no comprehensive patient registry or other method of establishing with precision the actual number of patients. As a result, we have had to rely on other available sources to derive clinical prevalence estimates for these monogenic indications. For the four rare MC4R pathway diseases we are studying on the Phase 3 EMANATE trial (POMC insufficiency, LEPR insufficiency, SRC1 deficiency and SH2B1 deficiency), we believe that the patient populations in continental Europe and UK are at least as large as those in the United States. While our sequencing data include patients from the United States and Europe, we do not have comparable sequencing data from European countries and these estimates are therefore based on applying relative population percentages to the Rhythm- derived estimates described above. We recently updated our prevalence estimates in 2021 based on sequencing data from individuals with obesity, and rates of response to setmelanotide in our exploratory Phase 2 Basket study. Because the published epidemiology studies for these genetic deficiencies are based on relatively small population samples, and are not amenable to robust statistical analyses, it is possible that these projections may significantly under- or overestimate the addressable 11population. While our projected estimates of the aggregate total addressable population continues to expand with the addition of new genes, the addressable population faces the challenges of a rare disease population. g. As announced on December 6, 2023, during our ' Update on MC4R Pathway Programs' event for investors and analysts. U. S. prevalence estimates based on results from our URO genetic testing program with samples from more than 36, 000 participants, classification of variants for pathogenic, likely pathogenic and 20 % of VUS and applied to established estimate of approximately 5 million people in the US with early- onset obesity; 1. van der Klaauw et al. Cell. 2019; 176: 729- 742. e18. 2. Marenne et al. Cell Metab. 2020; 31: 1107- 1119. e12. 3. Bamshad et al. Am J Hum Genet. 1999; 64: 1550- 1562. 4. Ackinci et al. J Clin Res Pediatr Endocrinol. 2019; 11: 341- 349. Limitations of Current TherapiesAlthough drugs approved for general obesity potentially can be used in patients with obesity and rare MC4R pathway diseases, all currently available products have limited efficacy and treat symptoms without addressing the underlying biology of MC4R impairment. For example, drugs which delay gastric emptying may cause a patient to feel full and eat less, but are also often associated with nausea and vomiting as a consequence of the delayed emptying. In the case of individuals with rare MC4R pathway diseases, these therapies also do not specifically address the impaired signaling in this central energy regulating pathway. Similarly, bariatric surgery which has been shown to be quite effective in the general population with obesity, may be unsuccessful in patients with rare MC4R pathway diseases for the same reason. MC4R Pathway ProgramIMCIVREE ® (setmelanotide) IMCIVREE is approved by the FDA for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to: (i) POMC, PCSK1 or LEPR deficiency as determined by an FDA- approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or VUS; or (ii) BBS. The EC and Great Britain' s MHRA have authorized setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults

and children 6 years of age and above. IMCIVREE also was approved by Health Canada, where it is indicated in adults and pediatric patients 6 years of age and older with impairments in the MC4R pathway due to genetic diseases, for the treatment of obesity and control of hunger in BBS or biallelic POMC, PCSK1, or LEPR deficiency. IMCIVREE is the only therapeutic specifically approved for patients with these diseases. As an MC4R agonist, IMCIVREE is designed to restore impaired MC4R pathway activity arising due to genetic impairments upstream of the MC4R. IMCIVREE contains setmelanotide acetate, a MC4R agonist. Setmelanotide is an 8 amino acid cyclic peptide analog of endogenous melanocortin peptide α- MSH. The chemical name for setmelanotide acetate is acetyl- L- arginyl- L- cysteinyl- D- alanyl- L- histidinyl- D- phenylalanyl- L- arginyl- L- tryptophanyl- L- cysteinamide cyclic (2 → 8)- disulfide 12acetate. Its molecular formula is C49H68N18O9S2 (anhydrous, free- base), and molecular mass is 1117. 3 Daltons (anhydrous, free- base). The chemical structure of setmelanotide is: IMCIVREE injection is a sterile, clear to slightly opalescent, colorless to slightly yellow solution. Each 1 mL of IMCIVREE contains 10 mg of setmelanotide provided as setmelanotide acetate, which is a salt with 2 to 4 molar equivalents of acetate, and the following inactive ingredients: 100 mg N- (carbonyl- methoxypolyethylene glycol 2000)- 1, 2- distearoyl- glycero- 3- phosphoethanolamine sodium salt, 8 mg carboxymethylcellulose sodium (average MWt 90, 500), 11 mg mannitol, 5 mg phenol, 10 mg benzyl alcohol, 1 mg edetate disodium dihydrate, and Water for Injection. The pH of IMCIVREE is 5 to 6. Obesity due to POMC, PCSK1 or LEPR deficiency are ultra- rare diseases caused by variants in POMC, PCSK1 or LEPR genes that impair the MC4 receptor pathway. People living with obesity due to POMC, PCSK1 or LEPR deficiency struggle with hyperphagia, an extreme, insatiable hunger, beginning at a young age and resulting in early- onset, severe obesity. Pivotal Phase 3 Clinical Trials Evaluating Setmelanotide in POMC and LEPR Deficiency Obesities We assessed the safety and efficacy of IMCIVREE in two pivotal trials that were identically designed: one- year, open- label studies, each with an eight- week, double- blind withdrawal period. The studies enrolled patients with homozygous or presumed compound heterozygous pathogenic, likely pathogenic variants, or VUS, for either the POMC, PCSK1 or LEPR gene. In both studies, adult patients had a body mass index (BMI) of ≥ 30 kg / m2. Weight in pediatric patients was ≥ 95th percentile using growth chart assessments. Efficacy analyses were conducted in 21 patients who had completed at least one year of treatment at the time of a pre- specified data cutoff. Of the 21 patients included in the efficacy analysis in both pivotal studies, 62 % were adults and 38 % were aged 16 years or younger. In Study 1, 50 % of patients were female, 70 % were White, and the median baseline BMI was 40. 0 kg / m2 (range: 26. 6- 53. 3). In Study 2, 73 % of patients were female, 91 % were White, and the median baseline BMI was 46. 6 kg / m2 (range: 35. 8- 64. 6). In the POMC / PCSK1 study, 80 % of patients with obesity due to POMC or PCSK1 deficiency met the primary endpoint, achieving a ≥ 10 % weight loss after one year of treatment with IMCIVREE. In the LEPR study, 46 % of patients with obesity due to LEPR deficiency met the primary endpoint by achieving a ≥ 10 % weight loss after 1 year of treatment with IMCIVREE. Bardet- Biedl syndromeBardet- Biedl syndrome (BBS) is a life- threatening, ultra- rare orphan disease. BBS is a disease that causes hyperphagia and severe obesity beginning in early childhood, as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. For patients with BBS, hyperphagia and obesity can have significant health consequences. BBS is part of a class of disorders called ciliopathies, or disorders associated with the impairment of cilia function in cells. 13Cilia are hair- like cellular projections that play a fundamental role in the regulation of several biological processes, including satiety signaling. Cilia dysfunction in the hypothalamus, including in the MC4R pathway, is thought to contribute to hyperphagia and obesity in BBS. BBS is a genetically heterogeneous disease that has been associated with mutations in 29 genes, to date. All result in a similar syndrome of clinical manifestations. Recent scientific studies identify deficiencies affecting the MC4R pathway as a potential cause of the hyperphagia and obesity associated with BBS, and demonstrate that an MC4R agonist can directly impact these symptoms. Pivotal Phase 3 Clinical Trial Evaluating Setmelanotide in BBS Approvals and marketing authorizations for BBS in the United States, European Union, Great Britain and Canada were based on data from our pivotal Phase 3 clinical trial of setmelanotide in patients with BBS. As we first reported in December 2020, the trial met its primary endpoint and all key secondary endpoints, with statistically significant and clinically meaningful reductions in weight and hunger at 52 weeks on therapy. The pivotal data that formed the basis for IMCIVREE' s approvals in BBS were published in the peer- reviewed journal The Lancet Diabetes and Endocrinology in November 2022. As previously disclosed, treatment with setmelanotide resulted in significant weight and hunger reductions after one year of treatment among patients with BBS. The primary endpoint was achieved by 32. 3 % (95 % confidence interval (CI), 16. 7 %, 51. 4 %; p = 0. 0006) of patients ≥ 12 years old, all of whom were patients with BBS. Data highlights among patients with BBS (n = 32) after 52 weeks of setmelanotide include: • Fifteen (15) patients ≥ 18 years achieved a mean (SD) percent reduction in BMI of - 9. 1 % (6. 8 %; 95 % CI, − 13. 4 %, − 4. 8 %); • Fourteen (14) patients < 18 years achieved a mean (SD) change in BMI Z- score of − 0. 8 (0. 5; 95 % CI, − 1. 0, − 0. 5), and 12 patients (85. 7 %) achieved ≥ 0. 2- point reduction in BMI Z; and • Fourteen (14) patients ≥ 12 years who reported hunger scores achieved reduction of - 30. 5 % in maximal hunger score. The safety results observed in this study were consistent with that observed with setmelanotide in previous clinical trials in patients with other rare MC4R pathway diseases. Skin hyperpigmentation (n = 23; 60. 5 %) was the most common adverse event (AE). Two patients experienced serious AEs, neither of which was considered related to setmelanotide treatment. Label Expansion Opportunity for Patients Between 2 Years Old and Younger than 6 The hyperphagia and severe obesity of rare genetically- caused MC4R pathway diseases can present early in life. Therefore, we believe access to treatment earlier in life will lead to better outcomes for children. That is why we are seeking to expand the label for IMCIVREE to include patients between the ages of 2 years **of** old and younger than 6. On December 6, 2023, we presented new data from our 52- week, Phase 3 pediatrics trial demonstrating that setmelanotide met the primary endpoint and achieved clinically meaningful weight reduction in patients within this age range. This trial was a multi- center, one- year, open- label trial in pediatric patients with obesity due to biallelic POMC, PCSK1 or LEPR deficiency or a clinical diagnosis of BBS with genetic confirmation. The primary efficacy endpoint was a responder analysis, based on the proportion of patients who experience a decrease from baseline in BMI- Z score of ≥ 0. 2. Highlights from the data include: • 83. 3 percent of all patients (10 of 12) achieved ≥ 0. 2 reduction in BMI- Z score from baseline to week 52; • 18. 4 percent mean reduction from

baseline in BMI at week 52 (N = 12); • 3. 04 mean reduction from baseline in BMI- Z score at week 52 (N = 12); 14 • 11 patients completed the trial, and all remain on therapy, as of Dec. 5, 2023; one patient discontinued and was lost to follow- up; and • The safety profile is consistent with past trials evaluating setmelanotide. Based on these data, we submitted a Type II variation application to the EMA seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hunger in pediatric patients between 2 and younger than 6 years old with BBS or POMC, PCSK1 or LEPR deficiency in the European Union. We anticipate submitting a supplementary New Drug Application to the FDA in the first half of 2024 seeking a similar label expansion. Development of Setmelanotide for Additional IndicationsHypothalamic ObesityWe also are developing setmelanotide as a treatment for hypothalamic obesity, a severe obesity that arises from mechanical hypothalamic injury, for which there are no approved therapies. In 2022, setmelanotide demonstrated potential to transform the care of individuals living with the rapid onset of extreme weight gain of hypothalamic obesity with clinical data that suggested setmelanotide treatment resulted in significant, durable weight loss. On the basis of these results, we requested, and setmelanotide received, Breakthrough Therapy Designation from the FDA for the treatment of hypothalamic obesity in 2022. Lesions of the hypothalamus can derive from various types of tumors (e. g., craniopharyngiomas, gliomas, pituitary adenomas, hamartomas) or may be caused by surgeries and / or radiotherapies for the treatment of these same tumor types. These hypothalamic lesions, whether caused by the tumor itself and / or the treatment of the tumor, can disrupt the MC4R pathway. Moreover, patients with hypothalamic obesity display a high degree of hyperleptinemia and hyperinsulinemia. Alpha- melanocortin stimulating hormone (MSH) can be detectable in blood, and its levels can change depending on different energy states; however, in patients with craniopharyngioma or post- surgical treatment for it, α- MSH levels are significantly reduced. Reduced serum α- MSH levels may suggest melanocortin pathway deficiency, which might explain obesity in these patients. Rhythm completed enrollment in its global Phase 3 trial of setmelanotide in hypothalamic obesity with patients aged 4 years or older with hypothalamic obesity randomized 2: 1 to setmelanotide therapy or placebo for a total of 60 weeks, including up to eight weeks for dose titration, with over 140 patients consented and screened by end of December 2023. As of February 2024, all 120 patients who will comprise the pivotal patient cohort have been dosed. As agreed to with both the FDA and the EMA, Rhythm' s regulatory submissions would be based on data from this cohort. The primary endpoint is the percent change in BMI after 52 weeks on a therapeutic regimen of setmelanotide versus placebo. We expect to report top- line study results in the first half of 2025. On February 22, 2024, we announced our clinical development plan to support the potential approval of setmelanotide for hypothalamic obesity in Japan, where we believe there is a higher per- capita incidence and prevalence rate of this disease than in Europe and the United States. We estimate there are approximately 5, 000 to 8, 000 patients in Japan with hypothalamic obesity. Following constructive discussions with Japan' s Pharmaceuticals and Medical Devices Agency (PMDA), we agreed to a development plan to add a cohort of 12 Japanese patients to the ongoing Phase 3 clinical trial of setmelanotide for patients with hypothalamic obesity. Pending successful completion of the trial, we plan to use these data as part of our registration package seeking approval from Japan' s Ministry of Health, Labor and Welfare. In addition to efficacy data, we will collect and submit PK data from Japanese patients, expediting the typical pathway of collecting such data from an earlier- stage trial in Japanese subjects. We anticipate dosing the first Japanese subject in this trial in the third quarter of 2024. The pivotal Phase 3 trial follows positive efficacy results from our 16- week Phase 2 trial, as well as data demonstrating durable and deepening weight loss in patients who transitioned from the Phase 2 trial to our open- label, long- term extension trial. The Phase 2 trial enrolled 18 patients with hypothalamic obesity caused by structural hypothalamic damage secondary to craniopharyngioma or other benign brain tumor types, surgical resection, and / or chemotherapy. Patients were between 6 and 40 years old with a BMI ≥ 95th percentile (children 6 to < 18 years) or ≥ 35 15kg / m2 (adults ≥ 18 years). The primary endpoint was the proportion of patients who achieved a 5 percent or greater reduction in BMI after 16 weeks of treatment. Hunger was also assessed daily, as self- reported by individual patients. Highlights from the data as presented at ObesityWeek 2022 include: ● 89 percent (16 of 18) patients evaluable for assessment had ≥ 5 % reduction in BMI (P < 0. 0001; confidence interval, 69 %- 98 %); ● 78 percent (14 of 18) patients had a 10 % or greater reduction in BMI at 16 weeks; ● 14. 5 mean percent reduction in BMI (N = 18) at Week 16 from baseline; ● 12. 6 mean percent reduction body weight (N = 18) at Week 16 from baseline; ● Mean (standard deviation [ SD ]) BMI Z score at Week 16 was 2. 7 (1. 3) (n = 13 pediatric patients), a reduction of 1. 3 (1. 0) points from baseline; and ● Mean (SD) most hunger score at baseline was 6. 6 (1. 6), compared with 3. 7 (2. 5) at Week 16, for a reduction of − 2. 9 (2. 3) points or 45 % for patients ≥ 12 years of age (n = 11). Consistent with prior clinical experience in other rare MC4R pathway diseases, setmelanotide was observed to be generally well tolerated. The most common adverse events (AEs) included nausea (61. 1 %), vomiting (33. 3 %), skin hyperpigmentation (33. 3 %), diarrhea (22. 2 %), and COVID- 19 (22. 2 %). Two patients discontinued due to AEs and a third patient discontinued from the study due to non- compliance. On October 17, 2023 at ObesityWeek, we reported 12- month data from patients with hypothalamic obesity who enrolled in our long- term extension trial. Twelve patients who enrolled in Rhythm' s open- label, 16- week Phase 2 trial and who also enrolled in the long- term extension trial and reached one year or more on setmelanotide were included in the one- year data analysis. With a data cutoff date of June 13, 2023, highlights from the data include: ● 25. 5 % reduction in mean BMI from baseline in patients with hypothalamic obesity (n = 12) at one year; ● Mean reduction of- 1. 1 in BMI Z score from baseline in pediatric patients (n = 11) at one year on therapy; ● Three of 11 pediatric patients achieved normal weight at one year, as defined by the U. S. National Institutes of Health (NIH) and World Health Organization (WHO) (> 5th to < 85th BMI percentile); ● Eleven of 12 patients (91. 7 %) improved by one or more weight classes based on BMI or BMI percentile as defined by the NIH and WHO; and ● Body composition changes were favorable, with larger percent decreases in total fat mass compared with lean muscle mass. There were no serious adverse events (AE), no AEs that led to study discontinuation during the trial, and no new safety concerns were observed. Additional MC4R Pathway Genetic VariantsWe also are advancing a broad clinical development program evaluating setmelanotide in several ongoing clinical trials, and we are leveraging the largest known DNA database focused on obesity- with almost 80, 000 sequencing samples as of December 2023- to improve the understanding, diagnosis and care of people living with hyperphagia

and severe obesity due to certain variants in genes associated with the MC4R pathway. There remains a significant unmet need with no effective therapeutic options for patients with these rare MC4R pathway diseases, and we believe setmelanotide has the potential to address the hyperphagia and severe obesity associated with these rare genetic diseases. We have two ongoing trials evaluating setmelanotide as a therapy for patients with hyperphagia and early- onset, severe obesity: the Phase 3 EMANATE trial and the Phase 2 DAYBREAK trial. Phase 3 EMANATE TrialThe ongoing pivotal Phase 3 EMANATE clinical trial is a randomized, double- blind, placebo- controlled trial, designed to evaluate setmelanotide in four independent sub- studies in patients with obesity due to: a heterozygous variant 16of the POMC / PCSK1 genes or LEPR gene, certain variants of the SRC1 gene or the SH2B1 gene. The epidemiology estimates for the indications being studied in our Phase 3 EMANATE trial suggest that approximately 53, 000 U. S. patients with one of these genetic deficiencies have the potential to respond to setmelanotide. POMC, PCSK1 and LEPR are core genes of the MC4R pathway. Heterozygous variants in POMC, PCSK1 and LEPR have been associated with clinical obesity that may be due to MC4R pathway dysfunction. Obesity due to rare variants in the SRC1 gene is an autosomal dominant disorder that is characterized by early- onset severe obesity and hyperphagia, as SRC1 variants found in individuals with severe obesity significantly impaired leptin- induced POMC expression (Yang et al 2019, Nat Comm. 10, Article 1718). Specifically, SRC1 is a transcriptional coactivator that has links to both the leptin receptor and to POMC. When the leptin receptor is activated, SRC1 is activated through a cascade of events that then drives the expression of POMC. Individuals who have heterozygous loss- of- function variants in their SRC1 genes can have insufficient leptin receptor activation of the MC4R pathway as a result of decreased POMC expression. This decreases the amount of available MSH to activate the MC4R, consequently resulting in hyperphagia and obesity in these individuals. Obesity due to variants in the SH2B1 gene is a rare genetic disease that is characterized by early- onset severe obesity, hyperphagia, hyperinsulinemia, and reduced final height. SH2B1 variants can arise through either DNA variants in the SH2B1 gene or through chromosomal deletions (chromosome 16) that encompass the SH2B1 gene. In both cases, dysfunction / loss of only one copy of the SH2B1 gene is sufficient to give rise to obesity and hyperphagia. The SH2B1 protein has been shown to have direct links to the MC4R- pathway. Specifically, SH2B1 is an adapter protein that amplifies the signal coming through the leptin receptor. In individuals who carry heterozygote loss of function mutations in SH2B1 or a chromosomal deletion that removes the SH2B1 from the chromosome, individuals may have insufficient leptin receptor activity activation of their MC4R pathway. This gives rise to a well- documented form of severe early- onset obesity and hyperphagia. We expect to complete enrollment in two or more substudies in the Phase 3 EMANATE trial in the second half of 2024. Proof of Concept Achieved in Exploratory Phase 2 Basket StudyIn January 2021, we announced proof- of- concept data from our exploratory Phase 2 Basket Study in multiple patient cohorts of patients with severe obesity due to a variant in one of the two alleles in the POMC, PCSK1, or LEPR genes (PPL HET obesity), as well as the SRC1 and SH2B1 genes. We provided subsequently furnished updated data in multiple presentations at medical meetings throughout 2021. The Phase 2 Basket Study was an open label study designed to evaluate setmelanotide in patients with obesity defined as BMI ≥ 30 kg / m2 for patients 16 years of age or older or BMI ≥ 95th percentile for age and gender for patients between 6 and 16 years old. Patients were stratified by cohort according to their genetic variant. The primary endpoint of the study was the percent of patients in each subgroup showing at least a 5 % loss of body weight over three months (" clinical responders "). PPL HET Obesity (POMC, LEPR, PCSK1) highlights included: ● Overall, 12 of 35 patients (34. 3 %) achieved the primary endpoint. This full analysis includes six patients who withdrew early; ● Mean reduction from baseline in body weight over three months across all 35 patients was- 3. 7 %, which includes both clinical responders and non- responders; and ● Among the 12 patients who achieved the primary endpoint (responder group), the mean reduction from baseline in body weight over three months was- 10. 1 %. In our analyses, we are applying variant classification guidelines from the American College of Medical Genetics, or ACMG (as described in Richards, et al., 2015), to patient cohort stratification. Specific variants of the POMC, LEPR, PCSK1, SRC1 or SH2B1 gene may be classified based on published data as being pathogenic, likely pathogenic, likely benign or benign, or classified as a variant of unknown significance or VUS. As genetics of obesity remains an emerging field, the vast majority of variants in genes associated with the MC4R pathway are classified as VUS. Our hypothesis was 17that patients with genetic variants that indicate a higher degree of pathogenicity would be more likely to have impaired pathway signaling and therefore more likely to respond to setmelanotide. ● Patients with PPL HET obesity were stratified into three pre- specified cohorts by classification of their genetic variants according to ACMG guidelines; ● Four of eight patients (50. 0 %) with a pathogenic or likely pathogenic variant achieved greater than 5 % weight loss over three months; ● Four of eight patients (50. 0 %) with the N221D variant of the PCSK1 gene achieved greater than 5 % weight loss over three months; and ● Four of 19 patients (21. 1 %) with a variant of unknown significance (VUS) achieved greater than 5 % weight loss over three months. In September 2021, we presented updated interim data from the SRC1 and SH2B1 cohorts at the at the 59th Annual European Society for Paediatric Endocrinology (ESPE) Meeting. The data presented were based on an interim analysis of patients who completed 12 weeks of therapy. These presentations included analyses that showed setmelanotide achieved clinically meaningful weight loss or BMI Z reduction in 30 % (9 of 30) of study participants with obesity due to variants of the SRC1 gene and clinically meaningful weight loss or BMI Z reduction in 43 % (15 of 35) of study participants with obesity due to variants of the SH2B1 gene, including 16p11. 2 chromosomal deletions. Specifically in the SRC1 cohort, a total of 30 patients with obesity and deficiency in the SRC1 gene were enrolled in the full analysis set of this study. These patients had a mean BMI of 45. 4 kg / m2 or BMI Z of 3. 0 at baseline. Highlights of these data, as of a cut- off date of March 16, 2021, include: ● Nine of 30 (or 30 %) of patients achieved a clinically meaningful response to setmelanotide at three months, as defined by weight loss of 5 % or greater from baseline, or for patients under 18 years old, a reduction of at least 0. 15 in BMI Z score: oIn adult patients 18 years or older, six of 20 (or 30 %) achieved 5 % or greater weight loss at three months; oIn patients younger than 18 years, three of 10 (or 30 %) achieved a BMI Z reduction of 0. 15 % or more at three months. ● Across all enrolled patients, the mean overall weight loss from baseline to three months among patients 18 years and older (a sample of 20) was- 4. 0 % (a standard deviation of 3. 3 %), and the mean overall BMI Z score reduction from baseline to

three months among patients younger than 18 years (n = 10) was- 0. 21 (a standard deviation of 0. 23). In addition, these interim data showed a clear separation between patients who responded to setmelanotide treatment at three months and those who did not: ● The mean body weight reduction for adult patients who responded (n = 6) was 7. 9 % (90 % confidence interval (CI), − 9. 7 to − 6. 0), as compared to 2. 3 % (90 % CI, − 3. 2 to − 1. 4) for adult patients who did not respond (a sample of 14); ● The mean BMI Z reduction for patients younger than 18 years who responded (n = 3) was 0. 48 (90 % CI, − 0. 95 to − 0. 01), as compared to 0. 09 (90 % CI, − 0. 11 to − 0. 07) for those who did not respond (n = 7). 18In the SH2B1 cohort, a total of 35 patients with obesity and 16p11. 2 deletions that include the SH2B1 gene or deficiency in the SH2B1 gene were enrolled in the full analysis set of this study. These patients had a mean BMI of 47. 2 kg / m2 or BMI Z of 3. 6 at baseline. Highlights of these interim data, as of a cut- off date of March 16, 2021, include: ● Fifteen of 35 (or 42. 9 %) of patients achieved a clinically meaningful response to setmelanotide at three months, as defined by weight loss of 5 % or greater from baseline, or for patients under 18 years old, a reduction of at least 0. 15 in BMI Z score: oIn patients 18 or older, eight of 22 (or 36. 4 %) achieved 5 % or greater weight loss at three months; oIn patients younger than 18 years, seven of 13 (or 53. 8 %) achieved a BMI Z reduction of 0. 15 % or more at three months. Across all enrolled patients, the mean overall weight loss from baseline to three months among patients 18 years and older (n = 22) was- 3. 1 % (a standard deviation of 3. 9 %), and the mean overall BMI Z score reduction from baseline to three months among patients younger than 18 years (n = 13) was- 0. 15 (a standard deviation of 0. 13). In addition, the interim data showed a clear separation between patients who responded to setmelanotide treatment at three months and those who did not: ● The mean body weight reduction for adult patients who responded (n = 8) was 7. 2 % (90 % CI, − 8. 6 to − 5. 8), as compared to 0. 8 % (90 % CI, − 1. 9 to 0. 3) for adult patients who did not respond (n = 14); ● The mean BMI Z reduction for patients younger than 18 years who responded (n = 7) was 0. 25 (90 % CI, − 0. 29 to − 0. 21), as compared to 0. 03 (90 % CI, − 0. 08 to 0. 02) patients younger than 18 years who did not respond (n = 7). Consistent with prior clinical experience, setmelanotide was generally well tolerated in each of these rare genetic diseases of obesity as of the cutoff date. The most common treatment- emergent adverse events, or TEAEs, included mild injection site reactions, hyperpigmentation, and nausea and vomiting, which occurred early in the treatment course. There were no SAEs related to treatment with setmelanotide. Phase 2 DAYBREAK trial Our ongoing Phase 2 DAYBREAK trial is a signal- finding study with a two- stage design. We designed it to evaluate setmelanotide in patients who carry a confirmed variant in one or more genes with strong or very strong relevance to the MC4R pathway. The first stage of the study consisted of a 16- week open- label treatment period; patients 18 years or older who achieved a body mass index (BMI) at least 3 % less than the Baseline BMI at the end of Stage 1 and patients < 18 years old who achieved a BMI at least 3 % less than the Baseline BMI or a decrease in BMI Z- score of at least 0. 05 at the end of Stage 1 were eligible for enrollment in the second stage of the study. Stage 2 is a 24- week, double- blind, placebo- controlled, randomized, withdrawal study, in which patients will be randomized 2: 1 to receive setmelanotide or placebo. The primary efficacy endpoint is a responder analysis by gene, based on the proportion of patients who enter Stage 2 who are responders compared to placebo. During our " Update on MC4R Pathway Program " event on December 6, 2023, we announced data from the Stage 1 or open- label part of DAYBREAK that demonstrate potential efficacy in patients in multiple genetically- defined cohorts. We presented data from the full analysis set for DAYBREAK, which includes164 patients. A total of 112 patients completed the 16- week Stage 1 of the Phase 2 trial, with 52 patients who discontinued. The rates of response from Stage 1 of the trial were: 19 ● 30 % of patients (12 of 40) with variants in the SEMA3 gene cohort; ● 35. 6 % of patients (16 of 45) with variants in the PLXNs gene cohort; ● 56. 3 % of patients (9 of 16) with variants in the PHIP gene cohort; ● 40 % of patients (2 of 5) with variants in the TBX3 gene cohort; ● 30 % of patients (3 of 10) with variants in the MAGEL2 gene cohort; and ● 25 % of patients (5 of 20) with variants in the SIM1 gene cohort. For those who completed Stage 1, the rates of response of patients who achieved a BMI reduction of greater than 5 % from a post- hoc analysis were: ● 44. 4 % of patients (12 of 27) with variants in the PLXNs gene cohort; ● 61. 5 % of patients (16 of 26) with variants in the SEMA3 gene cohort; and ● 69. 2 % of patients (9 of 13) with variants in the PHIP gene cohort. A total of 49 patients who completed Stage 1 with a response to setmelanotide were randomized into Stage 2 of the trial. Stage 2 is a 24- week, double- blind, placebo- controlled withdrawal study. These patients were stratified into genetically defined cohorts and randomized 2: 1 to receive setmelanotide or placebo. We anticipate announcing DAYBREAK Stage 2 data in the second half of 2024. Weekly Formulation of SetmelanotideIn collaboration with Camurus AB, or Camurus, we have developed a once- weekly, long- acting formulation of setmelanotide using FluidCrystal ® technology. When injected subcutaneously, aqueous body fluid may be absorbed by the excipient lipid phase, which may then form a gel- like depot consisting of liquid crystals formed in situ leading to slow diffusion of setmelanotide from the depot. While we believe that this formulation may be more convenient and less burdensome than setmelanotide, which is a once- daily administration, for patients and their families, we have paused development in favor of advancing RM- 718. In the event RM- 718 shows positive efficacy and safety results, we will discontinue development of the weekly formulation of setmelanotide. We have completed one Phase 3 trial evaluating the weekly formulation of setmelanotide in patients with rare MC4R pathway diseases. This weekly switch trial was a randomized, double- blind switch trial in patients with obesity due to biallelic or heterozygous POMC, PCSK1 or LEPR deficiency or a clinical diagnosis of BBS with genetic confirmation, who were previously enrolled in our long- term, open- label extension trial. Patients were randomized 1: 1 to receive once- weekly setmelanotide and once- daily placebo, or once- daily setmelanotide and once- weekly placebo for 13 weeks. Following the 13- week randomized treatment period, patients crossed over to an open- label, 13- week study in which all patients will receive once- weekly setmelanotide. The study is intended to provide detailed pharmacokinetic characterization of the weekly formulation. We anticipate announcing pharmacokinetics (PK) data from approximately 10 patients who completed this Phase 3 trial in 2024. Safety and Tolerability ResultsHistorically, clinical data with other MC4R therapies suggested that MC4R- mediated side effects may include changes in blood pressure and heart rate, increased erections in males, changes in libido and sexual function in females, and nausea and vomiting. It is noteworthy that the pattern of effects differed among each of the other MC4R therapies, underscoring the complex physiology of MC4R. With setmelanotide, there has been little, if any, evidence of

blood pressure or heart rate changes, preliminarily supporting an important differentiation of setmelanotide from previous MC4R therapies. Monitoring for blood pressure and heart rate changes, as well as other potential adverse events, or AEs, is included in all setmelanotide clinical trials. Because of these first-generation MC4R therapy failures, the setmelanotide program employed an intensive preclinical screening program to assess clinical candidates for blood pressure and heart rate effects, along with efficacy. The cornerstone of this preclinical screening program was a significant investment in obese primate studies which 20validated setmelanotide as a promising compound for clinical development. More recently, new research supporting a unique mechanism of action of setmelanotide, compared to earlier MC4R agonists and the endogenous ligand MSH, was published in May 2018 in Nature Medicine. Setmelanotide was generally well tolerated in our Phase 1, Phase 2 and Phase 3 clinical trials to date. Overall, except as outlined below, the number and patterns of AEs were generally low, and the intensity of the AEs was generally mild, and infrequently led to clinical trial discontinuation. Over the course of our clinical development program, a total of 926 patients who participated in our trials have received the daily or weekly formulation of setmelanotide, including 20 patients who had been on setmelanotide therapy for more than five years, as of November 24, 2023 (excluding commercial therapy): Duration of Setmelanotide Therapy Number of patients < 1 year 701 > 1 year 225 > 2 years 151 > 3 years 92 > 4 years 44 > 5 years 20 Total 926 In the majority of our trials, we observed a small increase in frequency of penile erections in male patients, as well as signs of sexual arousal in a small number of female patients. These symptoms were infrequent, generally mild, not painful, and short- lived. Most often these symptoms were reported in the first week of treatment. There was a small incidence of nausea and vomiting, as well as injection site reactions, both of which usually were reported as mild, early in treatment, and short- lived. A small number of patients had dose reductions and / or discontinued treatment due to nausea and vomiting. We also noted darkening of skin and skin lesions, such as moles and freckles, in approximately half of the patients who received setmelanotide. This was likely caused by activation of the closely related MC1 receptor, the receptor that mediates skin darkening in response to sun exposure. This was observed generally after one to two weeks of treatment, most often plateaued by two to four weeks of treatment, and like sun- related tanning, generally returned to baseline after cessation of exposure. Overall, the most common AEs reported among setmelanotide treated patients have been skin hyperpigmentation, injection site reactions, nausea, headache, vomiting, decreased appetite, and diarrhea. Life- Cycle Management and Preclinical DevelopmentLB54640, an oral MC4R agonist On January 4, 2024, we announced that we entered into a global licensing agreement with LG Chem, Ltd. (" LG Chem"), a leading global company headquartered in South Korea that specializes in life sciences as one of its core 21businesses, for LB54640, an investigational oral small molecule MC4R agonist now in Phase 2 clinical trials. The development of an effective oral therapy for treating MC4R pathway diseases has been a major goal for the industry and the early data from LG Chem suggest they have identified a candidate that could address MC4R pathway diseases without hyperpigmentation or cardiovascular side effects. We believe our deep developmental experience and global commercial presence uniquely positions us to move this molecule forward with the goal of offering a full portfolio of treatment options to patients struggling with hyperphagia and severe obesity and ensuring they get the treatment that is right for them. In a Phase 1 trial in healthy overweight adults, LB54640 demonstrated dose- dependent weight reduction. LB54640 also demonstrated favorable safety resultsin the trial, with no changes in blood pressure or heart rate observed and no hyperpigmentation observed. In addition, LB54640 has received orphan drug designation from FDA for the treatment of LEPR deficiency and POMC deficiency. We assumed sponsorship of two Phase 2 studies designed to evaluate weight loss efficacy, safety, tolerability and pharmacokinetics of LB54640. The SIGNAL trial is a randomized, placebo- controlled, double- blind study designed to enroll and evaluate approximately 28 patients with acquired hypothalamic obesity. Participants will receive one of three doses of LB54640 by oral administration once daily for up to 52 weeks, and the primary endpoint of the study is the change from baseline in body mass index after 14 weeks of treatment. The open- label, single- arm, 52- week ROUTE trial is designed to enroll five patients with POMC, LEPR, or PCSK1 deficiency obesity. Participants will receive LB54640 by oral administration once daily for up to 52 weeks, and the primary endpoint of the study is the change from baseline in body mass index after 14 weeks of treatment. RM- 718, the next generation of MC4R agonists We have designed a new MC4R agonist for weekly administration. A new chemical entity, RM- 718, we believe has demonstrated the potential to reduce body weight and hunger, with favorable safety results observed in preclinical studies. RM- 718 is designed to be more highly targeted and MC1R sparing with the potential to not cause hyperpigmentation. In a series of pre- clinical studies, RM- 718 reduced overall body weight, body weight gain and food consumption in animal models. Our investigational new drug application (IND) has been accepted by the FDA, and we expect to initiate Phase 1 in- human trials in the first half of 2024, including a multiple- ascending dose study in patients with hypothalamic obesity. RM- 718 is an investigational, synthetic, cyclic heptamer (7- amino acid- containing) peptide, and is designed as a selective and potent MC4R agonist that spares other melanocortin receptors. The RM- 718 formulation is a sustained release depot designed for once weekly (QW), subcutaneous (SC) injection, consisting of RM- 718 and excipients. The major components are phospholipids (PL) that are a natural part of the cell membrane and, once injected into tissue and coming into contact with aqueous body fluids and tissues, can precipitate and trap a co- administered drug to form a drug- PL co- precipitate (nanometer- sized phospholipid particles) that functions as a depot. Over time, this depot slowly diffuses into the surrounding tissue and / or is degraded by local phospholipase (slowly hydrolyzing phospholipids) resulting in a slow and controlled release of RM- 718 over time. Nonclinical studies of RM- 718 in obese rats over 3 weeks of treatment demonstrated significant and stable reduction of body weight (- 12. 9 %) and body weight gain, reduced food, and water consumption (- - 25 %) and improvement in insulin sensitivity without any pharmacological effects on the cardiovascular and respiratory systems. Studies in rodents (diet induced obese rats and mice including obese Zucker rats and Sprague Dawley rats) and monkeys also demonstrated that RM- 718 suppressed food intake and weight gain. Nonclinical toxicology studies of RM- 718 administered for 28 days were conducted in rats and cynomolgus monkeys with doses up to 30 mg / kg. RM- 718 was well tolerated in rats and monkeys, with no evidence of systemic toxicity. RM- 718- related clinical observations of hyperpigmentation of skin on the muzzle in monkeys were rare (observed in only one monkey at the 30 mg / kg dose).

Microscopic analysis showed minimal to moderate increased pigment of the epidermis of the skin of the muzzle at ≥ 10 mg / kg / doses, and we believe this result is probably species- specific and the result of MC1R stimulation. 22In safety pharmacology studies evaluating potential adverse effects on the cardiovascular and respiratory systems in cynomolgus monkeys, RM- 718 produced no treatment- related changes in effects on heart rate, blood pressure, electrocardiographic changes, or respiratory parameters up to the 30 mg / kg weekly dose. Moreover, when compared to an MC4R agonist LY2112688 (formulated by Eli Lilly and Company), continuous SC infusion for 3 days of LY2112688 at 0. 5 and 1 mg / kg / day, resulted in a slight increase in blood pressure at the 1 mg / kg / day dose level, relative to the reference item (saline), with effects being more pronounced during the night cycle, with no definitive effect on heart rate. These changes were not noted following continuous administration of RM- 718 at doses of 1 and 5 mg / kg / day for 3 days, with heart rate and blood pressure remaining comparable to the reference item (saline) up to 96 hours post start of infusion. A slight, non- dose dependent decrease in body temperature was seen in all test article- treated groups over the course of the study, all within normal variation for monkeys and it was not considered adverse. Congenital Hyperinsulinism Program In February 2023, we completed the acquisition of Xinvento B. V., or Xinvento, a Dutch private limited liability company based in the Netherlands, through our wholly- owned subsidiary Rhythm Pharmaceuticals Netherlands B. V., a Dutch private limited liability company. Xinvento was founded in 2021 by Claudine van der Sande and is developing novel investigational therapeutic candidates designed to improve the care of patients and families living with CHI. Ms. Van der Sande joined Rhythm as a vice president and head of our CHI program following the acquisition. CHI is a rare disease that we believe is well aligned with our corporate strategy and broadens our focus into an adjacent endocrine indication with a high unmet need. CHI is the most frequent cause of severe, random and persistent hypoglycemia in newborns and children. Hypoglycemia results from an over- secretion of insulin, which causes blood sugar levels to fall dangerously low. Without proper and immediate treatment, children with CHI may suffer seizures, coma, or even death and, longer term, patients may experience developmental delays, epilepsy, cerebral palsy, and other neurological damage. Available treatments are suboptimal in terms of safety, tolerability and effectiveness. Patient and family surveys conducted by Congenital Hyperinsulinism International, a global patient advocacy organization, demonstrate that hypoglycemic low blood sugar levels are occurring one or more times per day in 30 % and one or more times per week in an additional 22 % of patients despite being on standard of care. In the United States, the estimated incidence rate for CHI is 1: 29, 000 to 1: 31, 000, according to the literature. With the acquisition, Rhythm acquired a suite of assets designed to treat patients with this disease. We are focused on identifying and nominating a lead compound to advance into pre- clinical testing. We anticipate nominating a candidate by the end of 2024. Genetic Sequencing and Patient FindingWe continue to expand our sequencing efforts in individuals living with early- onset, severe obesity to support research, patient finding and community building efforts to better understand rare genetic diseases of obesity. Our obesity DNA database contains sequencing data from almost 80, 000 individuals, as of December 31, 2023. Our sequencing data has come from four distinct sources in recent years: the Genetic Obesity ID | Genotyping Study, a global network of collaborations with obesity researchers with individual sample collections, institutional biobanks and Uncovering Rare Obesity (URO) or Rare Obesity Advanced Diagnosis (ROAD) programs. More than 90 % of our DNA sequencing database is derived from the U. S. population. Therefore, our estimates of patient populations in Canada and Europe are more preliminary, but we believe prevalences of these genetic diseases are similar to those in United States. By bringing additional awareness to these rare genetic diseases of obesity, our sequencing efforts have the potential to help foster patient communities and drive medical action in these populations. URO, our free genetic testing program designed to help determine if individuals have an underlying genetic cause of their severe obesity, is the primary driver of how we collect sequencing samples and identify patients in the North America region. As obesity has reached epidemic levels in the United States, we are focused on identifying people with early- onset obesity that may be caused by certain rare genetic variants. As part of these efforts, we have launched Uncovering Rare Obesity in order to increase access to genetic testing. This program complements several initiatives designed to advance the understanding of genetic causes of severe obesity, and Uncovering Rare Obesity broadens these efforts and brings access to genetic testing into the community 23setting. Currently available physician- ordered genetic testing panels are often cost prohibitive, while many consumer genetic tests are incomplete when it comes to genetic disorders of obesity. This makes it difficult to confirm an underlying genetic cause of severe obesity. We believe the program marks an important step in the understanding of these disorders that might help patients and their families find new diagnosis and treatment strategies in the years ahead. Our U. S. partner, Prevention Genetics, a subsidiary of Exact Sciences Corp., a Clinical Laboratory Improvement Amendments- College of American Pathologists of CLIA / CAP- certified independent laboratory, conducts the genetic testing for Uncovering Rare Obesity. This program covers the cost of the test and excludes office visit, copay, sample collection, and any other related costs to a participant. In addition, as part of the program, licensed genetic counselors from PWN Health, a leading provider of professional guidance for diagnostic and genetic testing, are available to advise participating individuals. The ROAD program mirrors the URO program as it is designed to increase awareness on rare MC4R pathway diseases caused by genetic variants and support patient identification in the International region. We collect samples from individuals with severe obesity from seven countries, including Spain, Italy, Ireland, Israel, Turkey and Germany. Our partner CGC Genetics Unilabs conducts the genetic testing for ROAD. This program covers the cost of the test, the kit and shipment. As of the end of 2023 and excluding third- party sources, we have collected samples from approximately 40, 000 individuals with severe obesity through our URO and ROAD programs, which now are our primary source of sequencing samples. Commercial Efforts for IMCIVREE We are focused on developing the global infrastructure to make IMCIVREE available in as many markets as possible. IMCIVREE, an MC4R agonist for which we hold worldwide rights, is the first- ever precision medicine developed for patients with certain rare diseases that is approved or authorized in the United States, EU, Great Britain, Canada and other countries and regions. IMCIVREE is approved by the FDA for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to: (i) POMC, PCSK1 or LEPR deficiency as determined by an FDA- approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are

interpreted as pathogenic, likely pathogenic, or VUS; or (ii) BBS. The EC and Great Britain' s MHRA have authorized IMCIVREE for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. We are seeking regulatory approval in the United States and Europe to expand the label for IMCIVREE to treat patients as young as 2 with these diseases. Including the United States and Canada, we have achieved market access for IMCIVREE for BBS or POMC and LEPR deficiencies, or both, in 14 countries, and we continue to collaborate with authorities to achieve access in additional markets. While we are focused on commercial access for IMCIVREE for BBS and POMC and LEPR deficiencies, we are working with the broader community of patients and families, physicians, scientists and more to engage with them on the impact of hyperphagia and severe obesity caused by rare MC4R pathway diseases. Individually, populations with each of these MC4R pathway diseases are rare, and affected patients face many of the same challenges as any classically rare disease patient populations. There is little or no awareness about rare MC4R pathway diseases, and the patients suffering from them are lost in the health care system, with limited educational resources and no effective treatments for their condition. All our efforts and services described above are designed to address the challenges of rare diseases and lay the groundwork for potential future launches, with a focus on scalability. 24CompetitionThe biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors with general obesity medications in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop compounds that could make setmelanotide obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to setmelanotide. If we are not able to compete effectively against our current and future competitors, our business will not grow, and our financial condition and operations will suffer. Currently, IMCIVREE is the only approved treatment for weight management in patients with obesity due to BBS or POMC, PCSK1 or LEPR deficiencies, and there are no other approved treatments for addressing hyperphagia related behaviors of patients with rare MC4R pathway diseases. Bariatric surgery is not an appropriate treatment option for these MC4R pathway diseases because the severe obesity and hyperphagia associated with these diseases are considered to be risk factors for bariatric surgery. Also, existing therapies indicated for general obesity and those in clinical development for the same, including glucagon- like peptide- 1 (GLP- 1) receptor agonists, such as Wegovy ®, and glucose- dependent insulinotropic polypeptide (GIP) and glucagon- like peptide- 1 (GLP- 1) agonists, such as tirzepatide, do not specifically restore function impaired by genetic deficiencies and trauma to the hypothalamus that disrupt MC4R pathway signaling, which we believe is a root cause of hyperphagia and obesity in patients with these diseases. Studies such as the SURMOUNT- 1 study, which served as the basis of the FDA approval of tirzepitide for obesity, specifically excluded patients with: " obesity induced by other endocrinologic disorders or monogenetic or syndromic forms of obesity." Courage Therapeutics and Confo Therapeutics each have early- stage programs that are exploring MC4R agonism, and Palatin Technologies is evaluating bremelanotide in obesity as an adjunct therapy to GLP- 1. Licensing AgreementsIpsen Pharma S. A. S. Pursuant to a license agreement with Ipsen Pharma S. A. S., or Ipsen, we have an exclusive, sublicensable, worldwide license to certain patents and other intellectual property rights to research, develop, and commercialize compounds that were discovered or researched by Ipsen in the course of conducting its MC4R program or that otherwise were covered by the licensed patents. Rights under the license included the right to research, develop and commercialize setmelanotide. Pursuant to the license, we have a non- exclusive, sublicensable, worldwide license to certain patents and other intellectual property rights that were licensed by Ipsen from a third- party or that Ipsen may develop in the future to research, develop, and commercialize any of the compounds exclusively licensed by Ipsen pursuant to the license. Under the terms of the Ipsen license agreement, Ipsen is eligible to receive payments of up to $ 40. 0 million upon the achievement of certain development and commercial milestones in connection with the development, regulatory approval and commercialization of applicable licensed products, and royalties on future sales of the licensed products. Substantially all of the aggregate payments under the Ipsen license agreement are for milestones that may be achieved no earlier than first commercial sale of the applicable licensed product, and as of December 31, 2023, we have paid $ 4. 0 million in clinical and regulatory milestones and $ 9. 0 million in commercial milestones. Royalties in the mid- single digits on future sales of the applicable licensed products will be due under the Ipsen license agreement on a licensed product- by- licensed product and country- by- country basis until the later of the date when sales of a licensed product in a particular country are no longer covered by patent rights licensed pursuant to the Ipsen license agreement and the tenth anniversary of the date of the first commercial sale of the applicable licensed product in the applicable country. The term of the Ipsen license agreement continues until the expiration of the applicable royalty term on a country- by- country and product- by- product basis. Upon expiration of the term of the agreement, the licensed rights granted to us under the agreement, to the extent they remain in effect at the time of expiration, will thereafter become irrevocable, perpetual and fully paid- up licenses that survive the expiration of the term. We have a right to terminate the license agreement at any time during the 25term for any reason on 180 days' written notice to Ipsen. Ipsen has a right to terminate the agreement prior to expiration of its term for our material breach of the agreement, our failure to initiate or complete development of a licensed product or our bringing an action seeking to have an Ipsen license patent right declared invalid. Upon any early termination of the license agreement not due to Ipsen' s material breach, all licensed rights granted under the license agreement will terminate. CamurusIn January 2016, we entered into a license agreement for the use of Camurus' drug delivery technology, FluidCrystal, to formulate setmelanotide with Camurus. Under the terms of the agreement, Camurus granted us a worldwide license to the FluidCrystal technology to formulate setmelanotide and to develop, manufacture, and commercialize this new formulation for once- weekly dosing, administered as a SC injection. The license granted to us is specific to the FluidCrystal technology incorporating setmelanotide.

Under the terms of the license agreement, we are responsible for manufacturing, development, and commercialization of the setmelanotide FluidCrystal formulation worldwide. Camurus received a non- refundable and non- creditable upfront payment of $ 0. 5 million in January 2016, and is eligible to receive progressive payments of approximately $ 65. 0 million, of which the majority are sales milestones. As of December 31, 2023, we have made $ 2. 3 million of milestone payments to Camurus. In addition, Camurus is eligible to receive tiered, mid to mid- high, single- digit royalties on future sales of the product. The term of the agreement continues until the expiration of the applicable royalty term on a country- by- country and product- by- product basis. Upon expiration of the term of the agreement, the licensed rights granted to us under the agreement, to the extent they remain in effect at the time of expiration, will thereafter become irrevocable, perpetual and fully paid- up licenses that survive the expiration of the term. We have a right to terminate the license agreement at any time during the term for any reason upon 90 days' written notice to Camurus. Camurus has a right to terminate the agreement prior to expiration of its term for our material breach of the agreement, if we voluntarily or involuntarily file for bankruptcy, or for our bringing an action seeking to have a Camurus license patent right declared invalid. Upon any early termination of the license agreement not due to Camurus' material breach, all licensed rights granted under the license agreement will terminate. RareStone Group Ltd. In December 2021, we entered into an Exclusive License Agreement with RareStone, or the RareStone License. Pursuant to the RareStone License, we granted to RareStone an exclusive, sublicensable, royalty- bearing license under certain patent rights and know- how to develop, manufacture, commercialize and otherwise exploit any pharmaceutical product that contains setmelanotide in the diagnosis, treatment or prevention of conditions and diseases in humans in China, including mainland China, Hong Kong and Macao. RareStone has a right of first negotiation in the event that Rhythm chooses to grant a license to develop or commercialize the licensed product in Taiwan. According to the terms of the RareStone License, RareStone has agreed to seek local approvals to commercialize IMCIVREE for the treatment of obesity and hyperphagia due to POMC, PCSK1, or LEPR deficiency, as well as Bardet- Biedl and Alström syndromes. Additionally, RareStone agreed to fund efforts to identify and enroll patients from China in Rhythm' s global EMANATE trial, a Phase 3, randomized, double- blind, placebo- controlled trial to evaluate setmelanotide in four independent sub- studies in patients with obesity due to a heterozygous variant of POMC / PCSK1 or LEPR; certain variants of the SRC1 gene, and certain variants of the SH2B1 gene. According to the terms of the RareStone License, RareStone made an upfront payment to Rhythm of $ 7. 0 million and issued Rhythm 1, 077, 586 ordinary shares. Rhythm will be eligible to receive development and commercialization milestones of up to $ 62. 5 million, as well as tiered royalty payments on annual net sales of IMCIVREE. On October 28, 2022, we delivered written notice, or the Notice, to RareStone that we have terminated the RareStone License for cause. In accordance with the Notice, we maintain that RareStone has materially breached its obligations under the RareStone License to fund, perform or seek certain key clinical studies and waivers, including with respect to our global EMANATE trial, among other obligations. On December 21, 2022, RareStone provided written notice to us that it objects to the claims in the Notice, including our termination of the RareStone License for cause. On March 16, 2023, we provided written notice, or the March Notice, to RareStone reaffirming our position that RareStone has materially breached its obligations under the RareStone License and that we have terminated the RareStone License 26for cause, and also requested documentation supporting RareStone' s purported dispute notice objecting to the claims in the Notice. On May 10, 2023, RareStone provided written notice to us reaffirming its objections to the claims in our October Notice and March Notice, including to our termination of the RareStone License for cause. On November 29, 2023, RareStone wrote to us seeking to negotiate and execute a commercial supply agreement as contemplated under the Exclusive License Agreement, and on January 19, 2024, we responded in writing again reaffirming our position that RareStone has materially breached its obligations under the RareStone License and that we have terminated the RareStone License for cause. LG Chem In January 2024, we entered into a license agreement and share issuance agreement with LG Chem, Ltd. Under the terms of the license agreement, we obtained worldwide rights to exploit LGC' s proprietary compound LB54640 and will assume sponsorship of two ongoing LGC Phase 2 studies designed to evaluate safety, tolerability, pharmacokinetics and weight loss efficacy of LB54640. The SIGNAL trial is a randomized, placebo- controlled, double- blind study designed to enroll and evaluate approximately 28 patients with acquired hypothalamic obesity. Participants will receive one of three doses of LB54640 by oral administration once daily for up to 52 weeks, and the primary endpoint of the study is the change from baseline in body mass index after 14 weeks of treatment. The open- label, single- arm, 16- week ROUTE trial is designed to enroll five patients with POMC or LEPR deficiency obesity. We paid LGC $ 40. 0 million in cash and issued shares of our common stock with an aggregate value of $ 20. 0 million. The shares were issued at a per share price equal to the ten- day volume weighted- average closing price for our common stock, calculated as of the trading day immediately prior to January 4, 2024. We also agreed to make a $ 40. 0 million payment in cash 18 months after the effective date of the license agreement. In addition and subject to the completion of Phase 2 development of LB54640, the Company has agreed to pay LGC royalties of between low- to- mid single digit percent of net revenues from its MC4R portfolio, including LB54640, commencing in 2029 and dependent upon achievement of various regulatory and indication approvals, and subject to customary deductions and anti- stacking. Royalties may further increase to a low double digit percent royalty, though such royalty would only be applicable on net sales of LB54640 in a region if LB54640 is covered by a composition of matter or method of use patent controlled by LGC in such region and the Company' s MC4R portfolio is not covered by any composition of matter or method of use patents controlled by the Company in such region. Such increased rate would only apply on net sales of LB54640 for the limited remainder of the royalty term in the relevant region. Patents and Proprietary RightsOur MC4R portfolio of licensed and exclusively owned patent families, which includes setmelanotide, consists of 16 patent families currently being prosecuted or maintained, which include applications and patents directed to compositions of matter, formulations and methods of treatment using setmelanotide. As of January 26, 2024, the portfolio for the MC4 program consists of 19 issued United States patents and 347 issued non- United States patents across 12 of the 18 families. There also 13 pending United States patent applications and 130 pending non- United States applications in 40 jurisdictions. In the patent family directed to selected MC4R receptor agonists, including the

composition of matter for setmelanotide, we have 10 issued United States patents and 191 issued non- United States patents, including Australia, Canada, China, Europe, Hong Kong, India, Israel, Japan, Korea, New Zealand, Russia and Singapore. The standard 20- year term for patents in this family would expire in 2026, but two of the United States patents are expected to expire in 2027 due to patent term adjustments. Patent term extensions for delays in marketing approval may also extend the terms of patents in this family, and we have filed for patent term extension in the United States that, if granted, would extend the composition of matter patent protection to 2032. In addition to the patents and patent applications discussed above, we co- own one patent family with Charité- Universitätsmedizin Berlin, which has been filed in 21 jurisdictions and yielded 1 issued United States patent and 2 non- United States patents. We also co- own one patent family with the University of Strasbourg and the French National 27Institute of Health and Medical Research, which has been filed in 4 jurisdictions. Both of these patent families relate to the melanocortin program. We have also in- licensed a patent portfolio consisting of 20 patent families from LG Chem directed to the compositions of matter and methods of use of the oral MC4R agonist LB54640 and related compounds. Intellectual Property Protection StrategyWe currently seek, and intend to continue seeking, patent protection whenever commercially reasonable for any patentable aspects of setmelanotide and related technology or any new products or product candidates we acquire in the future. Where our intellectual property is not protected by patents, we may seek to protect it through other means, including maintenance of trade secrets and careful protection of our proprietary information. Our license from Ipsen for the melanocortin program require Ipsen, subject to certain exceptions and upon consultation with us, to prosecute and maintain its patent rights as they relate to the licensed compounds and methods. If Ipsen decides to cease prosecution or maintenance of any of the licensed patent rights, we have the option to take over prosecution and maintenance of those patents and Ipsen will assign to us all of its rights in such patents. For those patent rights that we own exclusively, we control all prosecution and maintenance activities. The patent positions of biopharmaceutical companies are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether the product candidate we in- license will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction, and furthermore, we cannot determine whether the claims of any issued patents will provide sufficient proprietary protection to protect us from competitors, or will be challenged, circumvented or invalidated by third parties. Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. This potential issue is exacerbated by the fact that, prior to March 16, 2013, in the United States, the first to make the claimed invention may be entitled to the patent. On March 16, 2013, the United States transitioned to a " first to file " system in which the first inventor to file a patent application may be entitled to the patent. For applications filed prior to the institution of the " first to file " system, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or PTO, or a foreign patent office to determine priority of invention. Moreover, we may have to participate in other proceedings declared by the United States PTO or a foreign patent office, such as post- grant proceedings and oppositions, that challenge the validity of a granted patent. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us. Although we currently have issued patents directed to a number of different attributes of our products, and pending applications on others, there can be no assurance that any issued patents would be held valid by a court of competent jurisdiction. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using specific compounds or technology. To the extent prudent, we intend to bring litigation against third parties that we believe are infringing our patents. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non- provisional patent application. In the United States, a patent' s term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States PTO in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent with an earlier expiration date. As mentioned above, in the United States, the patent term of a patent that covers an FDA- approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. Setmelanotide has received FDA approval and we have filed for patent term extension on that product. In the future, if and when our other pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term adjustments and extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable 28authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such adjustments or extensions. To protect our rights to any of our issued patents and proprietary information, we may need to litigate against infringing third parties, or avail ourselves of the courts or participate in hearings to determine the scope and validity of those patents or other proprietary rights. These types of proceedings are often costly and could be very time- consuming to us, and we cannot be certain that the deciding authorities will rule in our favor. An unfavorable decision could result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications. Any such decision could result in our key technologies not being protectable, allowing third parties to use our technology without being required to pay us licensing fees or may compel us to license needed technologies from third parties to avoid infringing third- party patent and proprietary rights. Such a decision could even result in the invalidation or a limitation in the scope of our patents or could cause us to lose our rights under existing issued patents or not to have rights granted under our pending patent applications. We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, no assurance can be given that others will not

independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual' s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual will be our exclusive property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information. ManufacturingWe currently contract with various third parties for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into process development and manufacturing service agreements with our CMOs, Corden Pharma Brussels S. A, or Corden (formerly Peptisyntha SA prior to its acquisition by Corden), PolyPeptide Group, Braine L' Alleud, or Polypeptide, Neuland Laboratories, and Recipharm Monts S. A. S for certain process development and manufacturing services for regulatory starting materials and / or drug substance, or API, and drug product in connection with the manufacture of setmelanotide. We have also entered into commercial supply agreements with both Polypeptide and Recipharm. Under our agreements, we pay these third parties for services and / or manufacture of setmelanotide in accordance with the terms of mutually agreed upon work orders, which we may enter into from time to time. We may need to engage additional third- party suppliers to manufacture our clinical and commercial drug supplies in the future. In connection with our commercialization of setmelanotide or any future product candidate, we have engaged and could need to engage other third parties to assist in manufacturing and / or supply chain related aspects. While there are a limited number of companies that can produce raw materials and API in the quantities and with the quality and purity that we require for our product, based on our diligence to date, we believe our current network of manufacturing partners are able to fulfill these requirements, and are capable of continuing to expand capacity as needed. Additionally, we have, and will continue to evaluate further relationships with additional suppliers to increase overall capacity as well as further reduce risks associated with reliance on a limited number of suppliers for manufacturing. Under the current agreements, each party is subject to customary indemnification provisions. Our contract manufacturing agreements give us visibility into the expected future cost of producing setmelanotide at commercial scale. Based upon a range of prices of currently- marketed therapies indicated for orphan diseases, we believe that our cost of goods for setmelanotide will be highly competitive. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for clinical supplies to support our activities through regulatory approval and commercial manufacturing, the CMOs with whom we currently work may need to increase scale of production or we expect that we 29may need to secure additional capacity or seek alternate suppliers. We believe that our current suppliers and CMOs are able to scale production to meet our clinical and commercial demands. Because we rely on these CMOs, we have personnel with pharmaceutical development and manufacturing experience who are responsible for maintaining our CMO relationships. Setmelanotide is distributed in the U. S. through our specialty pharmacy and in the EU / UK through third- party service providers that deliver the medication to patients. We plan to continue building out our network for commercial distribution in jurisdictions in which setmelanotide is approved. Regulatory MattersGovernment RegulationGovernment authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record- keeping, promotion, advertising, distribution, marketing and export and import of drug products. A new drug must be approved by the FDA through NDA process or by comparable foreign regulatory authorities through similar applications before it may be legally marketed in the United States and in foreign jurisdictions. We, along with any third- party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval of our products and product candidates. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. U. S. Drug Development ProcessIn the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. The process required by the FDA before a drug may be marketed in the United States generally involves the following: ● completion of preclinical laboratory tests, animal studies and formulation studies, certain of which must be conducted in accordance with FDA' s Good Laboratory Practice requirements and other applicable regulations; ● submission to the FDA of an IND, which must become effective before human clinical trials may begin; ● approval by an independent Institutional Review Board (IRB) or ethics committee at each clinical site before each trial may be initiated; ● performance of adequate and well- controlled human clinical trials in accordance with good clinical practices (GCPs), to establish the safety and efficacy of the proposed drug for its intended use; ● preparation of and submission to the FDA of an NDA after completion of all pivotal trials; ● a determination by the FDA within 60 days of its receipt of an NDA to file the application for review ● satisfactory completion of an FDA advisory committee review, if applicable; ● satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice (cGMP) requirements to assure that the facilities, methods and controls are adequate to preserve the drug' s identity, strength, quality and purity, and potential inspection of selected clinical investigation sites to assess compliance with GCPs; and30 ● FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States. Prior to beginning the first clinical trial with a product candidate in the United States, a sponsor must submit an IND to the FDA. An IND is a request for allowance from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol (s) for clinical studies. The IND also includes results

of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30- day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA allowance to begin a clinical trial. Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which among other things, include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB' s requirements or if the drug has been associated with unexpected serious harm to patients. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries. Human clinical trials are typically conducted in three sequential phases that may overlap or be combined: ● Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. ● Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials. 31 ● Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk / benefit ratio of the investigational product and to provide an adequate basis for product approval. In some cases, the FDA may require, or sponsors may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so- called Phase 4 studies, may be conducted after initial marketing approval, and may be used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life. U. S. Review and Approval ProcessAssuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, including results from preclinical and other non- clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. Data can come from company- sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by independent investigators. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non- orphan indication. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is

cGMP- compliant to assure and preserve the product' s identity, strength, quality and purity. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the filing date to complete a standard review of an NDA for a drug that is a new molecular entity. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a " filing " decision after it the application is submitted. The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP and adequate to assure consistent production of the product within required specifications. Additionally, before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. 32After the FDA evaluates an NDA and conducts inspections of manufacturing facilities where the investigational product and / or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the NDA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections and / or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the NDA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and / or require post- marketing testing and surveillance to monitor safety or efficacy of a product. If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a Risk Evaluation and Mitigation Strategy (REMS) to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. The FDA may also require one or more Phase 4 post- market studies and surveillance to further assess and monitor the product' s safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post- marketing studies. In addition, the Pediatric Research Equity Act (PREA) requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non- compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation. Expedited Development and Review ProgramsThe FDA offers a number of expedited development and review programs for qualifying product candidates. For example, the Fast Track program is intended to expedite or facilitate the process for reviewing new products that are intended to treat a serious or life- threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a Fast Track product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the application may be eligible for priority review. An NDA for a Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. A product candidate intended to treat a serious or life- threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance 33beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers. Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track designation and / or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review. An NDA is eligible for priority review if the product candidate is designed to treat a serious or life- threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For new- molecular- entity NDAs, priority review designation means the FDA' s goal is to take action on the marketing application within six months of the 60- day filing date.

Additionally, depending on the design of the applicable clinical trials, product candidates studied for their safety and effectiveness in treating serious or life- threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well- controlled confirmatory clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit, and may require that such confirmatory studies be underway prior to granting any accelerated approval. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory studies in a timely manner or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval do not change the standards for approval, but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Orphan Drug Designation and ExclusivityUnder the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200, 000 individuals in the United States, or a patient population greater than 200, 000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee. A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity 34or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Post- approval RequirementsDrug products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record- keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third- party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post- market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things: ● restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls; ● fines, warning letters, or untitled letters; ● clinical holds on clinical studies; ● refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals; ● product seizure or detention, or refusal to permit the import or export of products; ● consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; ● mandated modification of promotional materials and labeling and the issuance of corrective information; ● the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or ● injunctions or the imposition of civil or criminal penalties. The FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. Failure to comply with these requirements can

result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in 35the product's labeling and that differ from those approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA- approved labelling. Marketing ExclusivityExclusivity provisions authorized under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five- year period of non- patent data exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application (ANDA), or an NDA submitted under Section 505 (b) (2) (505 (b) (2) NDA), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non- infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA alternatively provides three years of non- patent exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three- year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505 (b) (2) NDAs for drugs containing the active agent for the original indication or condition of use. Five- year and three- year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any preclinical studies and adequate and well- controlled clinical trials necessary to demonstrate safety and effectiveness. Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to existing periods of regulatory exclusivity or patent terms if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven- year period of marketing exclusivity, except in certain circumstances. FDA Approval and Regulation of Companion DiagnosticsIf safe and effective use of a therapeutic product depends on an in vitro diagnostic medical device, then the FDA generally will require approval or clearance of that diagnostic, known as an in vitro companion diagnostic device, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and in vitro companion diagnostic devices. According to the guidance, for novel drugs, an in vitro companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. If the FDA determines that an in vitro companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the in vitro companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the in vitro companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. Under the FDCA, in vitro diagnostics, including in vitro companion diagnostic devices, are generally regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, 36premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post- market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510 (k) clearance, and premarket approval, or PMA approval. The FDA has stated that it generally requires in vitro companion diagnostic devices intended to select the patients who will respond to a drug to obtain a PMA for that diagnostic simultaneously with approval of the drug. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well- controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements. PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time- consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the

deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post- approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained or problems are identified following initial marketing. After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer' s manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States. Regulation of Combination Products in the United StatesCertain product are comprised of components, such as drug components and device components, that would normally be subject to different regulatory frameworks by the FDA and frequently regulated by different centers at the FDA. These products are known as combination products. Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The determination of which center will be the lead center is based on the " primary mode of action " of the combination product. Thus, if the primary mode of action of a drug- device combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established the Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory 37review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute. A combination product with a primary mode of action attributable to the drug component generally would be reviewed and approved pursuant to the drug approval processes set forth in the FDCA. In reviewing the NDA for such a product, however, FDA reviewers would consult with their counterparts in the device center to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the QSR applicable to medical devices. Foreign RegulationIn addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of setmelanotide to the extent we choose to sell any setmelanotide outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by equivalent competent authorities in foreign jurisdictions before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post- approval regulatory requirements, such as those regarding product manufacture, marketing, pharmacovigilance, promotion, advertising or distribution would apply to any product that is approved outside the United States. Regulation and Procedures Governing Marketing Authorization of Medicinal Products in the European UnionNon- clinical studies and clinical trialsSimilarly to the United States, the various phases of non- clinical and clinical research in the EU are subject to significant regulatory controls. Non- clinical studies are performed to demonstrate the health or environmental safety of new biological substances. Non- clinical (pharmaco- toxicological) studies must be conducted in compliance with the principles of good laboratory practice (GLP) as set forth in EU Directive 2004 / 10 / EC (unless otherwise justified for certain particular medicinal products, e. g., radio- pharmaceutical precursors for radio- labeling purposes). In particular, non- clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non- clinical studies. These GLP standards reflect the Organization for Economic Co- operation and Development requirements. Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines on good clinical practices (GCP) as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide " no fault" compensation to any study subject injured in the clinical trial. The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation (CTR), which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database. 38While the EU Clinical Trials Directive required a separate clinical trial application (CTA) to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application for multi- center trials. The CTR allows sponsors to make a single submission to

both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the EU Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Medicines used in clinical trials must be manufactured in accordance with Good Manufacturing Practice (GMP). Other national and EU- wide regulatory requirements may also apply. Marketing AuthorizationsIn the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, (MA). To obtain regulatory approval of a product candidate in the EU, we must submit a marketing authorization application, (MAA). The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs: ● " Centralized MAs " are issued by the European Commission (EC) through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) and are valid throughout the EU. The centralized procedure is mandatory for certain types of products, such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal products, (iii) advanced therapy medicinal products (ATMPs) such as gene therapy, somatic cell- therapy or tissue- engineered medicines, and (iv) medicinal products containing a new active substance indicated for the treatment certain diseases, such as HIV / AIDS, cancer, neurodegenerative diseases, diabetes, auto- immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for any products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or for which the granting of a MA would be in the interest of public health in the EU. ● " National MAs " are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state. A MA has an initial validity for five years in principle. The MA may be renewed after five years on the basis of a re- evaluation of the risk- benefit balance by the EMA or by the competent authority of the EU member state. To this end, the MA holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the MA was granted, at least six months before the 39MA ceases to be valid. The European Commission or the competent authorities of the EU member states may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five year period of MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market or on the market of the authorizing EU member state (s) within three years after authorization ceases to be valid (the so- called " sunset clause "). Under the centralized procedure, the maximum timeframe for the evaluation of an MAA by the CHMP is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. In exceptional cases, the CHMP might perform an accelerated review of a MAA in no more than 150 days (not including clock stops). Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U. S. In March 2016, the EMA launched an initiative, the Priority Medicines (PRIME) scheme, a voluntary scheme aimed at enhancing the EMA' s support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA' s committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. Moreover, in the EU, a " conditional " MA may be granted in cases where all the required safety and efficacy data are not yet available. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and has to be renewed annually until fulfillment of all the conditions. Once the pending studies are provided, it can become a " standard " MA. However, if the conditions are not fulfilled within the timeframe set by the EMA, the MA ceases to be renewed. Furthermore, MA may also be granted " under exceptional circumstances " when the applicant can show that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. This may arise in particular when the intended indications are very rare and, in the present state of scientific knowledge, it is not possible to provide comprehensive

information, or when generating data may be contrary to generally accepted ethical principles. This MA is close to the conditional MA as it is reserved for medicinal products to be approved for severe diseases or unmet medical needs and the applicant does not hold the complete data set legally required for the grant of a MA. However, unlike the conditional MA, the applicant does not have to provide the missing data and will never have to. Although the MA " under exceptional circumstances " is granted definitively, the risk- benefit balance of the medicinal product is reviewed annually and the MA is withdrawn in case the risk- benefit ratio is no longer favorable. Data and marketing exclusivityThe EU also provides opportunities for market exclusivity. Upon receiving MA, reference product candidates generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents applicants generic or biosimilar applicants from relying on the pre- clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. During the market exclusivity period, an application for a generic or biosimilar MA can be submitted and a related MA may be granted, and the innovator' s data may be referenced, but no generic or biosimilar can be placed on the EU market until 10 years have elapsed from the initial MA of the reference product in the EU. The overall ten- year period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU' s regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. 40Orphan Medicinal ProductsThe criteria for designating an " orphan medicinal product " in the EU are similar in principle to those in the United States. Regulation (EC) No. 141 / 2000, as implemented by Regulation (EC) No. 847 / 2000 provides that a medicinal product can be designated as an orphan if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition; (2) either (a) such condition affects not more than five in ten thousand persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. In the EU, an application for designation as an orphan product can be made any time prior to the filing of the application for MA. Orphan designation entitles a party to incentives such fee reductions or fee waivers, protocol assistance, and access to the centralized procedure. Once authorized, orphan medicinal products are entitled to a ten- years period of market exclusivity for the approved therapeutic indication, which means that the competent authorities cannot accept another MAA, or grant a MA, or accept an application to extend a MA for a similar product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan (PIP). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The orphan exclusivity period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan destination, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time if: (i) the second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior, (ii) inability of the applicant to supply sufficient quantities of the orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. A company may voluntarily remove a product from the orphan register. Pediatric DevelopmentIn the EU, MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a PIP agreed with the EMA' s Pediatric Committee (PDCO). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all member states and study results are included in the product information, even when negative, the product is eligible for a six- months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted. Post- Approval RequirementsSimilar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the EC and / or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance (QPPV) who is responsible for the establishment and maintenance of that system, and oversees the safety profiles of medicinal products and any emerging safety concerns. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (PSURs). 41All new MAA must include a risk management plan (RMP) describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk- minimization measures or post- authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post- authorization safety studies. The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative

advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off- label promotion is prohibited. Direct- to- consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another. The aforementioned EU rules are generally applicable in the European Economic Area (EEA) which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland. Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti- corruption 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 MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties. Regulation of Combination Products in the European UnionThe EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug- device combination product. EU guidance has been published to help manufacturers select the right regulatory framework. Drug- delivery products intended to administer a medicinal product where the medicinal product and the device form a single integral product are regulated as medicinal products in the EU. The EMA is responsible for evaluating the quality, safety and efficacy of MAAs submitted through the centralized procedure, including the safety and performance of the medical device in relation to its use with the medicinal product. The EMA or the EU member state national competent authority will assess the product in accordance with the rules for medicinal products described above but the device part must comply with the EU Medical Devices Regulation (including the general safety and performance requirements provided in Annex I). MAA must include — where available — the results of the assessment of the conformity of the device part with the EU Medical Devices Regulation contained in the manufacturer' s EU declaration of conformity of the device or the relevant certificate issued by a notified body. If the MAA does not include the results of the conformity assessment and where for the conformity assessment of the device, if used separately, the involvement of a notified body is required, the competent authority must require the applicant to provide a notified body opinion on the conformity of the device. By contrast, in case of drug- delivery products intended to administer a medicinal product where the device and the medicinal product do not form a single integral product (but are e. g. co- packaged), the medicinal product is regulated in accordance with the rules for medicinal products described above while the device part is regulated as a medical device and will have to comply with all the requirements set forth by the EU Medical Devices Regulation. The characteristics of non- integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co- packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MAA for the medicinal product on the characteristics of the medical device (s) that may impact on the quality, safety and / or efficacy of the medicinal product. 42The requirements regarding quality documentation for medicinal products when used with a medical device, including single integral products, co- packaged and referenced products, are outlined in the EMA guideline of July 22, 2021, which became effective on January 1, 2022. The aforementioned EU rules are generally applicable in the EEA. Regulation of Companion Diagnostics in the European UnionIn the EU, in vitro diagnostic medical devices were regulated by Directive 98 / 79 / EC (IVDD) which regulated the placing on the market, the CE marking, the essential requirements, the conformity assessment procedures, the registration obligations for manufactures and devices as well as the vigilance procedure. In vitro diagnostic medical devices had to comply with the requirements provided for in the Directive, and with further requirements implemented at national level (as the case may be). The regulation of companion diagnostics is subject to further requirements since the in vitro diagnostic medical devices Regulation No 2017 / 746 (IVDR) became applicable on May 26, 2022. On October 14, 2021, the EC proposed a " progressive " roll- out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices. The European Parliament and Council adopted the proposed regulation on December 15, 2021. The IVDR fully applies since May 26, 2022 but there is a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the IVDR. The IVDR introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue an EU certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or a MAA for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent authorities or the EMA. The aforementioned EU rules are generally applicable in the EEA. Brexit and the Regulatory Framework in the United KingdomThe United Kingdom (UK) left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU- UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement (TCA) and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. EU

laws which have been transposed into UK law through secondary legislation continue to be applicable as " retained EU law ", however new EU legislation such as the EU CTR or in relation to orphan medicines is not be applicable. The UK government has passed the Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ' appropriate authority' to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) is the UK' s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain (GB); broadly, Northern Ireland will 43continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. On February 27, 2023, the UK Government and the European Commission reached a political agreement on the " Windsor Framework " which will revise the Protocol on Ireland / Northern Ireland in order to address some of the perceived shortcomings in its operation. Under the changes, Northern Ireland will be reintegrated under the regulatory authority of the MHRA with respect to medicinal products. The Windsor Framework was approved by the EU- UK Joint Committee on March 24, 2023, so the UK government and the EU will enact legislative measures to bring it into law. On June 9, 2023, the MHRA announced that the medicines aspects of the Windsor Framework will apply from January 1, 2025. The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150- day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt- out. After Brexit, companies established in the UK cannot use the centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post- Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. A new international recognition framework has been in place from January 1, 2024, whereby the MHRA will have regard to decisions on the approval of MAs made by the EMA and certain other regulators when determining an application for a new GB MA. There will be no pre- MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i. e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10, 000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB. Additionally, on June 26, 2022, the MHRA published its response to a 10- week consultation on the post- Brexit regulatory framework for medical devices and diagnostics. In this response the MHRA confirmed that it would bring forward legislative changes to the UK Medical Devices Regulations 2002 (which are based on EU legislation, primarily the EU Medical Devices Directive and the (EU) IVDD), in particular to create new access pathways to support innovation, create an innovative framework for regulating software and artificial intelligence as medical devices, reform in vitro diagnostic medical devices regulation, and foster sustainability through the reuse and remanufacture of medical devices. Regulations implementing the new regime were originally scheduled to come into force in July 2023, but have recently been postponed to July 2025. Devices bearing CE marks issued by EU notified bodies under the EU Medical Devices Regulation or EU Medical Devices Directive are now subject to transitional arrangements. The UK Government has introduced legislation that provides that CE- marked medical devices may be placed on the GB market on the following timelines: ● general medical devices compliant with the EU Medical Devices Directive or EU Active Implantable Medical Devices Directive with a valid declaration and CE marking can be placed on the GB market up until the sooner of expiry of the certificate or June 30, 2028; and ● general medical devices, including custom- made devices, compliant with the EU Medical Devices Regulation can be placed on the GB market up until June 30, 2030. Following these transitional periods, it is expected that all medical devices will require a UK Conformity Assessed (UKCA) mark. Manufacturers may choose to use the UKCA mark on a voluntary basis until June 30, 2023. However, UKCA marking will not be recognized in the EU. The rules for placing medical devices on the market in Northern Ireland, which is part of the UK, differ from those in the rest of the UK. Compliance with this legislation is a prerequisite to be able to affix the UKCA mark to our products, without which they cannot be sold or marketed in GB. Pharmaceutical Coverage and ReimbursementIn the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on Government and third- party payors to reimburse all or 44part of the associated healthcare costs. Patients are unlikely to use IMCIVREE unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales will depend, in part, on the extent to which third- party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, IMCIVREE and other product candidates we may develop and obtain approval for in the future. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third- party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost- effectiveness of medical products and services and imposing controls to manage costs. Third- party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication. In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost- effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, setmelanotide may not be considered medically necessary or cost effective. A decision by a third- party payor not to cover IMCIVREE or any of our product candidates, if approved, could reduce physician utilization of our products and have a material adverse effect on our

sales, results of operations and financial condition. Additionally, a payor' s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor' s determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third- party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost- containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost- containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company' s revenue generated from the sale of any approved products. Coverage policies and third- party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Outside the United States, ensuring adequate coverage and payment for setmelanotide will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of setmelanotide or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts. We are also enrolled in the Medicaid Drug Rebate Program and other governmental pricing programs, and have price reporting and payment obligations under these programs. In the EU, pricing and reimbursement schemes vary widely from one member state to another. Some member states may require the completion of additional studies that compare the cost- effectiveness of a particular medicinal product candidate to currently available therapies or so called Health Technology Assessments (HTA), in order to obtain reimbursement or pricing approval. For example, the EU provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. The downward pressure on healthcare costs in general, and particularly in relation to prescription only medicinal products, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. 45HTA of medicinal products is, however, becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including France, Germany, Ireland, Italy, Spain and Sweden. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost- effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies between EU member states. In addition, pursuant to Directive 2011 / 24 / EU on the application of patients' rights in cross- border healthcare, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU member states and in pricing and reimbursement decisions and may negatively affect price in at least some EU member states. Healthcare Laws and RegulationsWe are subject to healthcare regulation and enforcement by the federal government and the states where we conduct business. These laws include, without limitation, state and federal anti- kickback, antitrust, fraud and abuse, false claims, and physician and other healthcare provider payment transparency laws and regulations. Foreign governments also have comparable regulations. The federal Anti- Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The Anti- Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti- Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. Further, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation. The majority of states also have anti- kickback laws which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third- party payor, including commercial insurers. Additionally, the civil False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U. S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. Violations of the False Claims Act can result in very significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi- billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes.

We expect that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters. Similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation. The federal civil monetary penalties laws, impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to 46influence the beneficiary' s selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies. In addition, there has been increased federal and state regulation of payments made to physicians and other healthcare providers. The Physician Payments Sunshine Act imposes new reporting requirements on drug manufacturers for payments made by them to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiology assistants, and certified nurse midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Drug manufacturers must report such payments to the government by the 90th day of each calendar year. State and foreign laws and regulations restrict business practices in the pharmaceutical industry and complicate our compliance efforts. For example, some states require companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the federal government' s compliance guidance or otherwise restrict payments to healthcare providers and other potential referral sources. Some states require manufacturers to file reports relating to pricing and marketing information. Some state and local governments require the public registration of pharmaceutical sales representatives. Certain states also mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and / or require the tracking and reporting of gifts, compensation and other remuneration to physicians. Violation of any of such laws or any other governmental regulations that may apply to drug manufacturers may result in penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment. In the EU, interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self- regulation codes of conduct and physicians' codes of professional conduct in the individual EU member states. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU. The provision of benefits or advantages to physicians is also governed by national laws (including anti- bribery laws) of the EU member states. In the UK, the UK Bribery Act 2010 applies to any company incorporated in or " carrying on business ", irrespective of where in the world the alleged bribery activity occurs. This Act could have implications for our interactions with physicians in and outside the UK. Violation of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and / or approval by the physician' s employer, their competent professional organization, and / or the competent 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 individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment. Failure to comply with the EU legislation and national laws on medicinal products including on the promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices, statutory health insurance, bribery and anti- corruption or with other applicable regulatory requirements can result in enforcement action by the EU member state authorities, which may include any of the following: fines, imprisonment, orders forfeiting products or prohibiting or suspending their supply to the market, or requiring the manufacturer to issue public warnings, or to conduct a product recall. Data Privacy and Security LawsNumerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health- related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health- related and other personal information. In 47addition, certain foreign laws govern the privacy and security of personal data, including health- related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and / or criminal penalties and restrictions on data processing. Healthcare ReformA primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the Patient Protection and Affordable Care Act, or signed the ACA, was signed into law, which, among other things, included changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to IMCIVREE and our potential drug candidates are: ● an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications; ● expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133 % of the federal poverty level, thereby potentially increasing a manufacturer' s Medicaid rebate liability; ● expansion of manufacturers' rebate liability under the

Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of " average manufacturer price, " or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicaid managed care plans; ● expansion of the list of entity types eligible for participation in the Public Health Service 340B drug pricing program, or the 340B program, to include certain free- standing cancer hospitals, critical access hospitals, rural referral centers, and sole community hospitals, but exempting " orphan drugs, " such as IMCIVREE, from the 340B ceiling price requirements for these covered entities; ● established the Medicare Part D coverage gap discount program, which require manufacturers to provide a 70 % point- of- sale- discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; ● a Patient- Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and ● established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. 48In addition, other legislative and regulatory changes have been proposed and adopted in the United States since the ACA was enacted. These changes included an aggregate reduction in Medicare payments to providers, which went into effect on April 1, 2013 and will remain in effect through 2032, unless additional Congressional action is taken. In addition, the American Taxpayer Relief Act of 2012, which further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap, beginning January 1, 2024. The rebate was previously capped at 100 % of a drug' s AMP. Most significantly, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) into law. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations. HHS has issued and will continue to issue guidance implementing the IRA, although the Medicare drug price negotiation program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant. Moreover, the federal government and individual states in the United States have become increasingly active in developing proposals, passing legislation and implementing regulations designed to control drug pricing, including price or patient reimbursement constraints, discounts, formulary flexibility, marketing cost disclosure and transparency measures. These new laws and the regulations and policies implementing them, as well as other healthcare- related measures that may be adopted in the future, could materially reduce our ability to develop and commercialize IMCIVREETM and our product candidates, if approved. In the EU, on December 15, 2021, Regulation No 2021 / 2282 on HTA, amending Directive 2011 / 24 / EU, was adopted. While the regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation- related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non- clinical (e. g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement. Human CapitalOur employees are dedicated to our mission to transform the lives of patients and their families living with hyperphagia and severe obesity caused by rare MC4R pathway diseases by rapidly advancing care and precision medicines addressing the root cause. As of February 1, 2024, we had 226 employees, including 174 in the United States and Canada and 52 in 10 countries outside North America. We also work with consultants and contractors to provide both specific expertise and flexibility for our business needs. We believe that our future success largely depends upon our continued ability to attract, hire and retain highly skilled employees. We emphasize several measures and objectives in managing our human capital assets, including, among others, employee engagement, development and training, talent acquisition and retention, employee wellness, diversity, inclusion, and compensation and pay equity. We frequently assess the external market to provide our employees with competitive salaries, bonuses, opportunities for equity ownership, development opportunities that enable continued 49learning and growth and a robust employment package that promotes well- being across all aspects of their lives, including health care, retirement planning and paid time off. In addition, we regularly collect employee feedback to ensure open communication, measure employee engagement and identify opportunities for improvement. We maintain efforts to ensure our employees are enabled to take advantage of flexible working arrangements. We believe that developing a diverse and inclusive culture is critical to continuing to attract and retain the top talent necessary to deliver on our growth strategy. As such, we are investing in a work environment where our employees feel inspired and included; it is our policy to pursue the best talent and to not make

employment (including hiring, promotion, or compensation) or other contracting decisions on the basis of any legally protected characteristics. We continue to focus on extending our diversity and inclusion initiatives across our entire global workforce. In addition, we work to ensure our employees understand and embrace our commitment to our patient community and our focus on changing the paradigm for treatment of rare genetic diseases of obesity. We value our employees' courage to ask bold questions and their commitment to learning and collaboration, as each person brings a unique contribution to furthering our mission. Grounded in these guiding principles, we believe we have developed a collaborative environment where our colleagues feel respected, valued, and inspired to contribute to their fullest potential. Corporate InformationWe are a Delaware corporation organized in February 2013. We were originally incorporated under the name Rhythm Metabolic, Inc., and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Our principal executive offices are located at 222 Berkeley Street, 12th Floor, Boston, MA 02116, and our telephone number is (857) 264- 4280. Our website is www. rhythmtx. com. Information that is contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report, and you should not consider information on our website to be part of this Annual Report. Available InformationWe make available free of charge on the investor relations portion of our website our Annual Reports on Form 10- K, Quarterly Reports on Form 10- Q, Current Reports on Form 8- K, Proxy Statements for our annual meetings of stockholders, and amendments to those reports, as soon as reasonably practicable after we file such material with, or furnish it to, the Securities and Exchange Commission, or SEC. These filings are available for download free of charge on the investor relations portion of our website located at https: / / ir. rhythmtx. com. The SEC also maintains a website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that website is https: / / www. sec. gov. Item 1A. Risk Factors Our operations and financial results are subject to various risks and uncertainties, including those described below, which could adversely affect our business, financial condition, results of operations, cash flows, and the trading price of our common stock. Additional risks and uncertainties that we currently do not know about or that we currently believe to be immaterial may also impair our business. You should carefully consider the risks described below and the other information in this Annual Report, including our consolidated financial statements and the related notes thereto, and " Management' s Discussion and Analysis of Financial Condition and Results of Operations. " Risks Related to Our Financial Position and Need for CapitalWe are a commercial stage biopharmaceutical company with a limited operating history and have not generated significant revenue from product sales. We have incurred significant operating losses since our inception, anticipate that we will incur continued losses for the foreseeable future and may never achieve profitability. We are a commercial stage biopharmaceutical company with a limited operating history on which to base your investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in February 2013. Our operations to date have been primarily focused on developing and commercializing IMCIVREE ® (setmelanotide) to treat patients living with hyperphagia and severe obesity 50caused by rare MC4R pathway diseases. Our business activities have included acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and conducting research and development activities, including clinical trials, for setmelanotide. To date we have generated approximately $ 97. 0 million of revenue from product sales. In the United States, IMCIVREE is approved for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to POMC, PCSK1 or LEPR deficiency as determined by an FDA approved test demonstrating variants in POMC, PCSK1 or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, or BBS. The EC has authorized IMCIVREE for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. The MHRA authorized setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above . Health Canada has approved IMCIVREE for weight management in adult and pediatric patients 6 years of age and older with obesity due to BBS or genetically- confirmed POMC, PCSK1, or LEPR deficiency due to variants interpreted as pathogenic, likely pathogenic, or of uncertain significance. In total, to date we have achieved market access for - **or named patient sales of** IMCIVREE for BBS or POMC and LEPR deficiencies, or both, in 14 **more than 15** countries **outside the United States** , and we continue to collaborate with authorities to achieve access in additional markets . We have not obtained any other regulatory approvals for setmelanotide . We first commercialized IMCIVREE in the **United States** U. S. in the first quarter of 2021 and therefore do not have a long history operating as a commercial company. We are continuing to transition from a company with a research and development focus to a company capable of supporting commercial activities and we may not be successful in such transition. We are still at the early stages of demonstrating our ability to manufacture at commercial scale, or arrange for a third party to do so on our behalf, or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history. **In February 2023, in order to expand our pipeline and build on our focus on rare endocrinology diseases, we acquired Xinvento B. V., a Netherlands- based biotech company focused on developing therapies for congenital hyperinsulinism (CHI). Our CHI program remains in the discovery phase and we do not expect to derive revenue from our CHI program for many years, if at all. There can be no assurance that regulatory approvals will be received or if received that they will be received when anticipated and ultimately we may fail to realize the anticipated benefits of our CHI program or those benefits may take longer to realize than expected.** Since our inception, we have focused substantially all of our efforts and financial resources on the research and development of setmelanotide, which is approved by the FDA and Health Canada and authorized by the EC and the MHRA, as noted above, and is in development to address patients affected by several other indications. We have funded our operations to date primarily through the proceeds from the sales of common stock and preferred stock, asset sales, royalty interest financing, as well as capital contributions from

our former parent, Rhythm Holdings LLC, and have incurred losses in each year since our inception. Our net losses were $ **260. 6 million and $** 184. 7 ~~million and $ 181. 1~~ million for the years ended December 31, **2024 and** 2023 ~~and 2022~~, respectively. As of December 31, ~~2023~~ **2024**, we had an accumulated deficit of $ ~~894~~ **1, 155**. ~~7~~ **3** million. Substantially all ~~of~~ our operating losses have resulted from costs incurred in connection with our development programs and from commercial and general and administrative costs associated with our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with our additional clinical trials of setmelanotide, with clinical trials of our **product** ~~new investigational drug~~ candidates (RM- 718 **)**, which is designed to be a more selective MC4R agonist with weekly administration **(now in Phase 1 trials)**, and ~~LB54640~~ **bivamelagon**, an investigational oral small molecule **, which is also designed to be a more selective** MC4R agonist **, (** now in Phase 2 clinical trials), and with the development of any other product candidates we may choose to pursue, including a ~~therapeutic~~ **product candidate for CHI, yet to be identified. We also expect to devote substantial financial resources to the research and development and potential commercialization of a** product candidate for CHI. In addition, since we have market access for IMCIVREE for BBS or POMC and LEPR deficiencies, or both, in ~~14~~ **more than 15** countries **outside of the United States**, we expect to continue to incur significant sales, marketing and outsourced manufacturing expenses. Nevertheless, setmelanotide may not be a commercially successful drug. We have and will continue to incur additional costs associated with operating as a public company. As a result, we expect to continue ~~to~~ **54to** incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis. ~~51Our~~ -- **Our** ability to become profitable depends upon our ability to generate revenue. ~~To date~~ **As of December 31, 2024**, we have generated approximately $ ~~97~~ **227**. ~~0~~ **6** million of revenue from product sales. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to: ● continue to commercialize setmelanotide by building a commercial organization and / or entering into collaborations with third parties; ● ensure ~~setmelanotide~~ **IMCIVREE** is available to patients; ● continue to achieve market acceptance of setmelanotide in the medical community and with third- party payors; ● continue to initiate and successfully complete later- stage clinical trials for setmelanotide, RM- 718, ~~LB54640~~ **bivamelagon**, or other ~~drug~~ **product** candidates that meet their clinical endpoints; ● continue to initiate and successfully complete all ~~safety~~ studies required to obtain U. S. and foreign marketing approvals for setmelanotide as a treatment ~~for obesity caused by~~ **to address patients with** deficiencies affecting the MC4R pathway; and ● successfully manufacture or contract with others to manufacture setmelanotide, or RM- 718 and ~~LB54640~~ **bivamelagon** if approved ~~. As described above, absent our entering into collaboration or partnership agreements, we have and expect to continue to incur significant sales and marketing, commercialization, and research and development costs. Additionally, as a result of the acquisition of Xinvento B. V., we also expect to devote substantial financial resources to the research and development and potential commercialization of a therapeutic product candidate for CHI. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate significant product revenue, we will not become profitable and will be unable to continue operations without continued funding~~. We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations. We are currently in the early stages of commercializing IMCIVREE ~~for chronic weight management~~ in **its approved indications** ~~patients with obesity due to BBS, POMC, PCSK1 or LEPR deficiencies~~ in the **United States** ~~U. S.~~, Canada, the EU and ~~Great Britain~~ **the United Kingdom** and advancing setmelanotide through clinical development for additional indications in the United States and for potential **additional** approvals in other countries. Developing **pharmaceutical** ~~peptide therapeutic~~ products is expensive and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance setmelanotide in additional clinical trials, as well as in connection with research and development activities for setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon**, and in connection with **our CHI program and the potential identification and development of** a ~~therapeutic~~ product candidate for CHI ~~as a result of the acquisition of Xinvento B. V~~. We intend to use our available cash resources to advance the clinical development of setmelanotide, for disease- education and community- building activities, patient identification, and commercialization activities related to IMCIVREE. Depending on the status of additional regulatory approvals and commercialization of setmelanotide, as well as the progress we make in sales of IMCIVREE, we may still require significant additional capital to fund the continued development of setmelanotide and our operating needs thereafter, ~~,~~ as well as research and development activities for setmelanotide, RM- 718, ~~LB54640~~ **bivamelagon**, and a ~~therapeutic~~ product candidate for **our** CHI **program**. We may also need to raise additional funds if we choose to pursue additional indications and / or geographies for setmelanotide or otherwise expand more rapidly than we presently anticipate. From August 2015 through August 2017, we raised aggregate net proceeds of $ 80. 8 million through our issuance of series A preferred stock. In connection with our initial public offering, or IPO, in October 2017 and our underwritten follow- on offerings through December ~~2023~~ **2024**, we raised aggregate net proceeds of approximately $ ~~791~~ **832**. ~~5~~ **7** million through ~~52the~~ -- **the** issuance of our common stock after deducting underwriting discounts, commissions and offering related transaction costs. We received a further $ 100. 0 million from asset sales, specifically in connection with the sale of our Rare Pediatric Disease Priority Review Voucher, or PRV, to Alexion Pharmaceuticals, Inc. In June 2022, we entered into a Revenue Interest Financing Agreement, or RIFA, with HealthCare Royalty Partners for a total investment amount of up to $ 100. 0 ~~million~~ **55million**, conditioned upon our achievement of certain clinical development and sales milestones. As of December 31, ~~2023~~ **2024**, we have received $ 96. 7 million of aggregate proceeds, net of debt issuance costs, under the RIFA. **We also received $ 147. 8 million in net proceeds under the Investment Agreement, with certain affiliates of Perceptive Advisors LLC, or Perceptive, and certain other investors, relating to the issuance and sale of 150, 000 shares of a new series of the Company' s Series A Convertible**

**Preferred Stock, par value $ 0. 001 per share, titled the " Series A Convertible Preferred Stock ", or the Convertible Preferred Stock, for an aggregate purchase price of $ 150. 0 million, or $ 1, 000 per share.** As of December 31, ~~2023~~ **2024**, our cash and cash equivalents and short- term investments were approximately $ ~~275~~ **320** . ~~8~~ **6** million. We expect that our existing cash and cash equivalents and short- term investments will be sufficient to fund our operations into ~~the second half of 2025~~ **2027** . However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third- party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. We will also require additional capital to obtain additional regulatory approvals for, and to continue to commercialize, setmelanotide, as well as for research and development activities for setmelanotide, RM- 718, ~~LB54640~~ **bivamelagon** , and a ~~therapeutic~~ product candidate for **our** CHI **program** . Raising funds in the current economic and geopolitical environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations. We maintain the majority of our cash and cash equivalents in accounts with major U. S. and multi- national financial institutions, and our deposits at certain of these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position. Any additional fundraising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to **commercialize IMCIVREE and** develop ~~and, in the case of approved products, commercialize~~ setmelanotide **,** RM- 718, ~~LB54640~~ **bivamelagon** , and a ~~therapeutic~~ product candidate for **our** CHI **program** . In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or other third parties at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to setmelanotide or technologies or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of setmelanotide or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially adversely affect our business, financial condition and results of operations. Our Revenue Interest Financing Agreement with Healthcare Royalty Partners could restrict our ability to commercialize IMCIVREE, limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations. On June 16, 2022, we entered into the RIFA, with entities managed by HealthCare Royalty Management, collectively referred to as the **RIFA** Investors. Pursuant to the RIFA and subject to customary closing conditions, the **RIFA** Investors agreed to pay us an aggregate investment amount of up to $ 100. 0 million **(** ~~, or~~ the **" RIFA** Investment Amount **")** . Under the terms of the RIFA, we received $ 37. 5 million on June 29, 2022 upon FDA approval of IMCIVREE in BBS, and an additional $ 37. 5 million on September 29, 2022, following EC marketing authorization for BBS on September 6, 2022. On September 12, 2023, we received the remaining $ 24. 4 million of the **RIFA** Investment Amount, net of debt issuance ~~costs~~ **56costs** , following the achievement of a specified amount of cumulative net sales of IMCIVREE between July 1, 2022 and September 30, 2023. ~~53As~~ **As** consideration for the Investment Amount and pursuant to the RIFA, we agreed to pay the **RIFA** Investors a tiered royalty on our annual net revenues ~~, or~~ **(the "** Revenue Interest **")** , including worldwide net product sales and upfront payments and milestones. The applicable tiered percentage will initially be 11. 5 % on annual net revenues up to $ 125 million, 7. 5 % on annual net revenues of between $ 125 million and $ 300 million and 2. 5 % on annual net revenues exceeding $ 300 million. If the **RIFA** Investors have not received cumulative minimum payments equal to 60 % of the amount funded by the Investors to date by March 31, 2027 or 120 % of the amount funded by the **RIFA** Investors to date by March 31, 2029, we must make a cash payment immediately following each applicable date to the Investors sufficient to gross the Investors up to such minimum amounts after giving full consideration of the cumulative amounts paid by us to the **RIFA** Investors through each date, referred to as the Under Performance Payment. As the repayment of the funded amount is contingent upon worldwide net product sales and upfront payments, milestones, and royalties, the repayment term may be shortened or extended depending on actual worldwide net product sales and upfront payments, milestones, and royalties. **As of December 31, 2024 we have made $ 20. 4 million of payments, including $ 12. 9 million in the year ended December 31, 2024.** The **RIFA** Investors' rights to receive the Revenue Interests will terminate on the date on which the **RIFA** Investors have received payments equal to a certain percentage of the funded portion of the Investment Amount including the aggregate of all payments made to the **RIFA** Investors as of such date, each percentage tier referred to as the Hard Cap, unless the RIFA is earlier terminated. The total Revenue Interests payable by us to the **RIFA** Investors is capped between 185 % and 250 % of the **RIFA** Investment Amount paid to us, dependent on the aggregate royalty paid between 2028 and 2032. If a change of control ~~of~~ **event** occurs, the **RIFA** Investors may accelerate payments due under the RIFA **,** up to the Hard Cap plus any other obligations payable under the RIFA. Our obligations under the RIFA could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things: ~~•~~ ● increasing our vulnerability to adverse economic and industry conditions; ~~•~~ ● limiting our ability to obtain additional financing or enter into IMCIVREE

~~partnership~~ **collaboration or other business** agreements; ~~•~~ ● requiring the dedication of a portion of our cash flow from operations to service our indebtedness, which will reduce the amount of cash available for other purposes; ~~•~~ ● limiting our flexibility to plan for, or react to, changes in our business; ~~•~~ ● placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital; and ~~•~~ ● if we fail to comply with the terms of the RIFA, resulting in an event of default that is not cured or waived, Investors could seek to enforce their security interest in our cash and cash equivalents and all assets relating to IMCIVREE that secures such indebtedness. To the extent we incur additional debt (including without limitation additional amounts under the RIFA), the risks described above could increase. ~~Risks~~ **57Risks** Related to the Development of Setmelanotide and Other Product ~~CandidatesPositive~~ **Candidates and our CHI ProgramPositive** results from earlier clinical trials of setmelanotide may not be predictive of the results of later clinical trials of setmelanotide. If we cannot generate positive results in our later clinical trials of setmelanotide, we may be unable to successfully develop, obtain regulatory approval for, and commercialize additional indications for setmelanotide. Positive results from any of our Phase 1, Phase 2, or Phase 3 clinical trials of setmelanotide, or initial results from other clinical trials of setmelanotide, may not be predictive of the results of later clinical trials. The duration of effect of setmelanotide tested in our Phase 1 and Phase 2 clinical trials was often for shorter periods than in our pivotal Phase 3 clinical trials. The duration of effect of setmelanotide has only been studied in long- term durations for a small number of patients in our Phase 2 and Phase 3 clinical trials and safety or efficacy issues may arise when more patients are studied in longer trials and on commercial drug. It is possible that the effects seen in short- term clinical trials will not be replicated ~~54in~~ **in** long- term or larger clinical trials. In addition, not all of our trials demonstrated statistically significant weight loss **in all patient populations studied** and there can be no guarantee that future trials will ~~do so~~ **achieve their endpoints** . Positive results ~~for~~ **observed in** one ~~indication~~ **patient population** are not necessarily predictive of positive results for other ~~indications~~ **populations** . We have demonstrated statistically significant and clinically meaningful reductions in weight and hunger in Phase 3 clinical trials in obesity due to POMC, PCSK1 or LEPR deficiencies and BBS, and believe we have demonstrated proof of concept in Phase 2 clinical trials in impairments due to a variant in one of the two alleles in the POMC, PCSK1, or LEPR genes (HET obesity), as well as the SRC1 and SH2B1 genes, all genetic diseases of extreme and unrelenting appetite and obesity. We hypothesize that patients with other upstream genetic variants **in genes upstream of the MC4R** in the MC4R pathway may also respond with reductions in weight and hunger after treatment with setmelanotide. However, patients with other upstream genetic variants may not have a similar response to setmelanotide, and until we obtain more clinical data in other genetic variants, we will not be sure that we can achieve proof of concept **or magnitude of response sufficient to demonstrate statistical significance** in such ~~indications~~ **populations** . We are actively working to advance additional genetic variants related to **patient populations carrying such genetic variants in other MC4R pathway related genes in** the MC4R pathway through our clinical development ~~program~~ **programs** . Our continued development efforts are focused on obesity related to several single gene ~~related~~ , or monogenic, MC4R pathway impairments: BBS; obesity due to a genetic variant in one of the two alleles of the POMC, PCSK1 or LEPR gene, or HETs; obesity due to steroid receptor coactivator 1, or SRC1, variants; obesity due to SH2B adapter protein 1, or SH2B1; hypothalamic obesity; **Prader- Willi Syndrome (PWS)** and MC4R deficiency obesity. For example, in April 2022 we enrolled the first patient in our pivotal Phase 3 EMANATE clinical trial of setmelanotide. The trial is a randomized, double- blind, placebo- controlled study with four independent sub- studies evaluating setmelanotide in patients with: heterozygous POMC / PCSK1 obesity; heterozygous LEPR obesity; certain variants of the SRC1; or certain variants of SH2B1 genes. ~~After receiving feedback from the FDA in April 2022 that indicated that additional clinical trials to support potential registration for non- rare patient populations would likely be required, we eliminated a fifth sub- study intended to evaluate setmelanotide in patients with a PCSK1 N221D variant.~~ Each of the four sub- studies will be entirely independent of the others and, if successful, is designed to support separate regulatory submissions to the FDA and EMA in each studied ~~indication~~ **population** . However, the FDA and EMA may not view positive results in one sub- study, even if such results are statistically significant and clinically meaningful, as being sufficient for approval for any given indication. Success in a basket trial, or any trial in one ~~indication~~ **cohort** , may not predict success in another ~~indication~~ **cohort** . In contrast, in the event of an adverse safety issue, clinical hold, or other adverse finding in one or more ~~indications~~ **cohorts** being tested, such event could adversely affect our trials in the other ~~indications~~ **cohorts** and may delay or prevent completion of such clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials after achieving positive results in early- stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre- clinical findings made while clinical trials were underway. Additionally, setbacks may be caused by new safety or efficacy observations ~~made~~ in clinical trials **or in post- approval use in the real world** , including previously unreported adverse events, or AEs. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA approval or a marketing authorization from the EC or foreign regulatory authorities. If we fail to obtain positive results in our Phase 3 clinical trials ~~of~~ **58of** setmelanotide, the development timeline and regulatory approval and commercialization prospects for setmelanotide and, correspondingly, our business and financial prospects, would be materially adversely affected **, but even if we obtain results in our Phase 3 clinical trials that we believe are positive, there is no guarantee that the FDA or the EC or foreign regulatory authorities will agree that such results are sufficient to support submission or approval of an NDA or NDA supplement** . Interim, " topline " and preliminary data from our **preclinical and** clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is 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 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. As a result, the topline or preliminary results that we report ~~55may~~ -- **may** differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published or reported. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. **From time to time, we may also disclose real- world data from early access programs in particular patient cohorts, which are not controlled trials and may not be predictive of future results.** Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of ~~the~~ **a** particular program, the approvability or commercialization of the particular product candidate or product and our ~~company~~ **Company** in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and ~~you or~~ others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. The exclusive license agreement with LGC is important to our business. If we or LGC fail to adequately perform under the agreement, the development of ~~LB54640~~ **bivamelagon** could be delayed, or if we or LGC terminate the agreement, we would lose our rights to develop and commercialize ~~LB54640~~ **bivamelagon** . In January 2024, we entered into a license agreement and share issuance agreement with LGC. Pursuant to the terms of the license agreement, we obtained exclusive worldwide rights to ~~exploit~~ **develop** LGC' s proprietary compound ~~LB54640~~ **bivamelagon** and assumed sponsorship of two ongoing LGC Phase 2 studies designed to evaluate safety, tolerability, pharmacokinetics and weight loss efficacy of ~~LB54640~~ **bivamelagon, one of which remains ongoing** . ~~In addition and subject~~ **Subject** to the completion of Phase 2 development of ~~LB54640~~ **bivamelagon** , we ~~have~~ agreed to pay LGC royalties of between low- to- mid single digit percent of net revenues from our MC4R portfolio, including ~~LB54640~~ **bivamelagon** , commencing in 2029 and dependent upon achievement of various regulatory and indication approvals, and subject to customary deductions and anti- stacking. Royalties may further increase to a low double digit percent royalty, though such royalty would only be applicable on net sales of ~~LB54640~~ **bivamelagon** in a region if ~~LB54640~~ **bivamelagon** is covered by a composition of matter or method of use patent controlled by LGC in such region and the Company' s MC4R portfolio is not covered by any composition of matter or method of use patents controlled by ~~the~~ **59the** Company in such region. Such increased rate would only apply on net sales of ~~LB54640~~ **bivamelagon** for the limited remainder of the royalty term in the relevant region. The license agreement will continue until the expiration of the obligation to pay royalties in all countries or regions, unless terminated earlier. We or LGC can terminate the license agreement in certain circumstances, including for the other party' s material uncured breach. If the license agreement is terminated, we would lose our rights to develop and commercialize ~~LB54640~~ **bivamelagon** , and, under some circumstances, we could be subject to certain ongoing payments, penalties and fees, all of which in turn would have a material adverse effect on our business. The number of patients **with** ~~suffering from~~ each of the MC4R pathway variants we are targeting is small and has not been established with precision. If the actual number of patients is smaller than we estimate, our revenue and ability to achieve profitability may be materially adversely affected. Due to the rarity of our target indications, there is no comprehensive patient registry or other method of establishing with precision the actual number of patients with MC4R pathway deficiencies. As a result, we have had to rely on other available sources to derive clinical prevalence estimates for our target indications. In addition, we have internal genetic sequencing results from individuals with severe obesity that provide another approach to estimating prevalence. As of December 31, ~~2023~~ **2024** , our database had approximately ~~80~~ **100** , 000 sequencing samples. Since the published epidemiology studies for these genetic variants are based on relatively small population samples, and are not amenable to ~~56robust~~ -- **robust** statistical analyses, it is possible that these projections may significantly exceed the addressable population, particularly given the need to genotype patients to definitively confirm a diagnosis. Based on multiple epidemiological methods, we have estimated the potential addressable patient populations with these MC4R pathway deficiencies based on the following sources and assumptions **(which remain subject to change based on ongoing research and publications by us or any third party)** : ● POMC Deficiency Obesity. POMC Deficiency Obesity is defined by the presence of biallelic variants in the POMC or PCSK1 genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance. Our addressable patient population estimate for POMC deficiency obesity is approximately 100 to 500 patients in the United States, with a comparable addressable patient population in Europe. Our estimates are based on: ● approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we believe our addressable patient population for this deficiency may be approximately 100 to 500 patients in the United States, and a comparable addressable patient population in Europe, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency obesity is often unavailable and currently is rarely performed; ● our belief, based on discussions with experts in rare diseases, that the number of diagnosed cases could increase several- fold with increased awareness of this deficiency and the availability of new treatments; ● U. S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for adults with severe obesity (body mass index, or BMI, greater than 40 kg / m2) and for children with severe early-onset obesity (99th percentile at ages two to 17 years old); and ● our internal sequencing yield for POMC deficiency obesity

patients (including both POMC and PCSK1 gene diseases), defined as patients having biallelic variants in the POMC or PCSK1 genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, of approximately 0. 05 %. **60** ● LEPR Deficiency Obesity. LEPR Deficiency Obesity is defined by the presence of biallelic variants in the LEPR gene that are interpreted as pathogenic, likely pathogenic, or of uncertain significance. Our addressable patient population estimate for LEPR deficiency obesity is approximately 500 to 2, 000 patients in the United States, with a comparable addressable patient population in Europe. Our estimates are based on: ● epidemiology studies on LEPR deficiency obesity in small cohorts of patients comprised of children with severe obesity and adults with severe obesity who have a history of early onset obesity; ● U. S. Census Bureau figures for adults and children and CDC prevalence numbers for adults with severe obesity (BMI, greater than 40 kg / m2) and for children with severe early- onset obesity (99th percentile at ages two to 17 years old); ● with wider availability of genetic testing expected for LEPR deficiency obesity and increased awareness of new treatments, our belief that up to 40 % of patients with these diseases may eventually be diagnosed; and ● our internal sequencing yield for LEPR deficiency obesity patients, defined as patients having biallelic variants in the LEPR gene that are interpreted as pathogenic, likely pathogenic, or of uncertain significance, of approximately 0. 09 %. ~~57~~ ● Bardet- Biedl Syndrome. Our addressable patient population estimate for BBS is approximately 4, 000 to 5, 000 patients in the United States based on: ● published prevalence estimates of one in 100, 000 in North America, which projects to approximately 3, 250 people in the United States. We believe the majority of these patients are addressable patients; ● comparisons to our patient identification efforts in Europe where we believe there are approximately 1, 500 patients diagnosed and being cared for at academic centers in Europe; ● our patient identification efforts to date in the United States; ● our internal sequencing yield for biallelic pathogenic or likely pathogenic variants in BBS genes of approximately 0. 3 %; and ● our belief that with wider availability of genetic testing expected for BBS and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase. ● POMC, PCSK1, or LEPR Heterozygous Obesities; SRC1 and SH2B1 Obesities. Our potential setmelanotide- responsive patient population estimate for POMC, PCSK1, or LEPR heterozygous, SRC1 and SH2B1 obesity patients with at least one variant interpreted as pathogenic, likely pathogenic, or of uncertain significance suspected pathogenic is approximately 53, 000 patients in the United States. Our estimates are based on: ● U. S. Census Bureau population data and CDC prevalence numbers for early onset obesity ( **≥** 120 % the 95th percentile **with onset prior to 6** ~~between the ages of 2- 5~~ years **of age** ); ● our internal sequencing yield of patients with POMC, PCSK1, or LEPR heterozygous, SRC1 or SH2B1 variants interpreted as pathogenic, likely pathogenic, or of uncertain significance of approximately 10- 15 %; ~~and~~ **and61** ● a clinical response rate of 40 % for patients carrying pathogenic or likely pathogenic variants, and 20 % for patients carrying a variant of uncertain significance. The clinical response rate used in this calculation is based on the clinical data currently available to us from our trials and may change as more data become available. ● MC4R Deficiency Obesity. Our addressable patient population estimate for MC4R- rescuable deficiency obesity is approximately 10, 000 patients in the United States. This estimate is based on: ● U. S. Census Bureau population data and CDC prevalence numbers for early onset obesity ( **≥** 120 % the 95th percentile between the ages of 2- 5 years); ● a comprehensive ~~ongoing~~ biochemical screening study indicating there may be a defined subset of individuals who carry MC4R variants that may be rescued by an MC4R agonist; and ● our internal sequencing yield for MC4R deficiency obesity patients of approximately 2. 0 % prior to application of functional filters. ~~58~~ ● Hypothalamic obesity. Our addressable patient population estimate for hypothalamic obesity (HO) is 5, 000 to 10, 000 patients in the United States. This estimate is based on: ● diagnosis of an underlying HO etiology such as craniopharyngioma (CP), astrocytoma, or other brain tumors with CP accounting for approximately 50 % of HO etiologies; ● an annual incidence of CP of approximately 1. 3 to 2. 2 per million per year in the United States, which projects to approximately 600 cases of CP per year based on a United States population of approximately 329 million; ● approximately 50 % (based on a published range of 6 % to 91 %) of CP patients develop HO; ● published estimates of overall survival (OS) after CP diagnosis, with a 20- year OS of 84 %; ● allowing for patients that develop HO due to other factors besides CP, results in an estimated HO prevalence after CP diagnosis in the United States exceeding 2, 500- 7, 500 patients; and ● internal Company estimate is based on reported incidence of hypothalamic obesity following CP and long- term survival rates. ● Obesity due to a deficiency in the MC4R pathway caused by variants in the SEMA3 family, PHIP, TBX3 or PLXNA family. Our addressable patient population estimate for obesity patient with variants in these genes is approximately 63, 500 patients in the United States. This estimate is based on: ● ~~based on~~ results from our URO genetic testing program with samples from more than 36, 000 participants, classification of variants for pathogenic, likely pathogenic and 20 % of with a variant of uncertain significance and applied to established estimate of approximately 5 million people in the ~~US~~ **United States** with early- onset obesity. We believe that the patient populations in the EU are similar to those in the United States. However, we do not have comparable epidemiological data from the EU and these estimates are therefore based solely on applying relative population percentages to the Company- derived estimates described above. ~~Defining~~ **62Defining** the exact genetic variants that result in MC4R pathway diseases is complex, so if any approval that we obtain is based on a narrower definition of these patient populations than we had anticipated, then the potential market for setmelanotide for these indications will be smaller than we originally believed. In either case, a smaller patient population in our target indications would have a materially adverse effect on our ability to achieve commercialization and generate revenues. If we experience delays or difficulties in the enrollment and / or retention of patients in clinical trials, our regulatory submissions or receipt of additional marketing approvals could be delayed or prevented. We may not be able to initiate or continue our planned clinical trials on a timely basis or at all for our product candidates if we are unable to recruit and enroll a sufficient number of eligible patients to participate in these trials through completion of such trials as required by the FDA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. Our clinical trials will compete with other clinical trials that are in the same therapeutic areas as our product candidates, including general obesity, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our

competitors. Because the number of qualified clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who ~~59are~~ -- **are** available for our clinical trials at such clinical trial sites. In addition, there are limited patient pools from which to draw for clinical studies. In addition to the rarity of genetic diseases of obesity, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. Patient enrollment for our current or any future clinical trials may be affected by other factors, including: ● size and nature of the patient population; ● severity of the disease under investigation; ● availability and efficacy of approved drugs for the disease under investigation; ● patient eligibility criteria for the trial in question as defined in the protocol; ● perceived risks and benefits of the product candidate under study; ● clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or future product candidates being investigated for the indications we are investigating; ● clinicians' willingness to screen their patients for genetic markers to indicate which patients may be eligible for enrollment in our clinical trials; ● delays in or temporary suspension of the enrollment of patients in our planned clinical trial due to ~~the COVID- 19 pandemic or other~~ public health emergencies; ● ability to obtain and maintain patient consents; ● patient referral practices of physicians; ● the ability to monitor patients adequately during and after treatment; **63** ● proximity and availability of clinical trial sites for prospective patients; and ● the risk that patients enrolled in clinical trials will drop out of the trials before completion, including as a result of ~~contracting COVID- 19 or other~~ health conditions or being forced to quarantine, or, because they may be late- stage cancer patients or for other reasons, will not survive the full terms of the clinical trials. In addition, the pediatric population is an important patient population for setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** , and our addressable patient population estimates include pediatric populations. However, it may be more challenging to conduct studies in younger participants, and to locate and enroll pediatric patients. These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may also result in increased development costs for setmelanotide and any future product candidates and jeopardize our ability to obtain additional marketing approvals for the sale of setmelanotide. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods. ~~60Failures~~ -- **Failures** or delays in the commencement or completion of our planned clinical trials ~~of setmelanotide, RM- 718, or LB54640~~ could result in increased costs to us and could delay, prevent or limit our ability to generate revenue **, achieve profitability** and continue our business. Successful completion of our ongoing and planned clinical trials is a prerequisite to submitting an NDA or NDA supplement to the FDA, an MAA to the EMA, and other applications for marketing authorization to equivalent competent authorities in foreign jurisdictions, and consequently, successful completion of such trials, at a minimum, will be required for regulatory approvals and the commercial marketing of setmelanotide for additional indications as well as RM- 718 and ~~LB54640~~ **bivamelagon** . We do not know whether our planned clinical trials will begin or whether any of our clinical trials will be completed on schedule, if at all, as the commencement and successful completion of clinical trials can be delayed or prevented for a number of reasons, including but not limited to: ● inability to generate sufficient preclinical or other in vivo or in vitro data to support the initiation of clinical studies; ● delays in the completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA' s good laboratory practice requirements and other applicable regulations; ● the FDA or other equivalent competent authorities in foreign jurisdictions may deny permission to proceed with our ongoing or planned trials or any other clinical trials we may initiate, or may place a clinical trial on hold or **such trial may** be suspended; ● delays in filing or receiving authorization to proceed under an additional investigational new drug application, or IND, or similar foreign application if required; ● delays in reaching a consensus with the FDA and other regulatory agencies on study design and obtaining regulatory authorization to commence clinical trials; ● delays in reaching or failing to reach agreement on acceptable terms with prospective ~~contract research organizations, or~~ CROs ~~,~~ and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; ● difficulties in obtaining **or maintaining** Institutional Review Board, or IRB, and / or ethics committee approval or opinion to conduct a clinical trial at a prospective site or sites; **64** ● since many already diagnosed patients are at academic sites, delays in conducting clinical trials at academic sites due to the particular challenges and delays typically associated with those sites, as well as the lack of alternatives to these sites which have already diagnosed patients; ● inadequate quantity or quality of setmelanotide, RM- 718, ~~LB54640~~ **bivamelagon** or other materials necessary to conduct clinical trials, including delays in the manufacturing of sufficient supply of finished drug product; ● challenges in identifying, recruiting and training suitable clinical investigators; ● challenges in recruiting and enrolling suitable patients to participate in clinical trials; ● severe or unexpected drug related side effects experienced by patients in a clinical trial, including side effects previously identified in our completed clinical trials; ● difficulty collaborating with patient groups and investigators; ~~61~~ ● failure by our CROs, other third parties or us to perform in accordance with the FDA' s or any other regulatory authority' s ~~good clinical practice requirements, or~~ GCPs ~~,~~ or applicable regulatory guidelines in other countries; ● occurrence of adverse events associated with setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** that are viewed to outweigh their potential benefits, or occurrence of adverse events in trial of the same or similar class of agents conducted by other companies; ● changes to the clinical trial protocols; ● clinical sites deviating from trial protocol or dropping out of a trial; ● changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; ● changes in the standard of care on which a clinical development plan was based, which may require new or additional trials; ● selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data; ● the cost of clinical trials of our product candidates being greater than we anticipate; ● clinical trials **or related non-clinical trials** of our product candidates producing negative or inconclusive results, which may result in our deciding, or

regulators requiring us, to conduct additional clinical trials or **delay or** abandon development of such product candidates; and ● development of antibodies to the drug or adjuvants may result in loss of efficacy or safety events ~~. In addition, disruptions caused by the COVID- 19 pandemic and other public health emergencies may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results~~ . In addition, a clinical trial may be suspended or terminated by us, the FDA or other equivalent competent authorities in foreign jurisdictions, the IRB at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board, or DSMB, or Safety Monitoring Committee, or SMC, overseeing the clinical trial at issue or other equivalent competent authorities due to a number of factors, including, among others: ● failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols; **65** ● inspection of the clinical trial operations or trial sites by the FDA or other equivalent competent authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold; ● **inconclusive results,** unforeseen safety issues, adverse side effects or lack of effectiveness; ● changes in government regulations or administrative actions; ● problems with clinical trial supply materials; and ● lack of adequate funding to continue the clinical trial. Delays in the completion of any preclinical **or non- clinical** studies or clinical trials of setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** will increase our costs, slow down our product candidate development and **the regulatory** approval ~~process~~ **processes** and delay or potentially jeopardize our ability to commence product sales ~~and ,~~ generate product revenue **and achieve profitability** . In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of a regulatory approval ~~62for --~~ **for** setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** . Any delays to our preclinical studies or clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** , in each case if approved, and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, the FDA' s and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation (CTR) which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate clinical trial application (CTA) to be submitted in each member state **in which the clinical takes place** , to both the competent national health authority and an independent ethics committee, the ~~EU~~ CTR introduces a centralized process and only requires the submission of a single application ~~to all member states concerned~~ **for multi- center trials** . The ~~EU~~ CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The ~~EU~~ CTR ~~foresees a three- year~~ transition period **ended on** ~~. The extent to which ongoing and new clinical trials will be governed by the EU CTR varies. For clinical trials whose CTA was made under the EU Clinical Trials Directive before~~ January 31, ~~2022, the EU Clinical Trials Directive will continue to apply on a transitional basis until January 31,~~ 2025 ~~. Clinical trials for which an~~ **and** ~~application was submitted (i) prior to January 31, 2022 under the EU Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date,~~ all clinical trials ( ~~including those which~~ **and related applications)** are **now fully** ~~ongoing) will become~~ subject to the provisions of the ~~EU~~ CTR. Compliance with the ~~EU~~ CTR requirements by us and our third- party service providers, such as CROs, may impact our developments plans. It is currently unclear to what extent the United Kingdom ~~(UK)~~ will seek to align its regulations with the EU. On January 17, 2022, the MHRA launched an eight- week consultation on reframing the UK legislation for clinical trials and which aimed to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The UK Government published its response to the consultation on March 21, 2023 confirming that it would bring forward changes to the legislation. These resulting legislative amendments will determine how closely the UK regulations are aligned with the CTR. A decision by the UK not to closely align its regulations with the new approach adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries. **Under the terms of the Protocol on Ireland / Northern Ireland, provisions of the CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products apply in Northern Ireland. Once the changes brought by the Windsor Framework are implemented, this may have a further impact on the application of the CTR in Northern Ireland.** If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. **66Research and development in the pharmaceutical industry is costly, risky, time- intensive and complicated. In particular, our CHI program is a pre- clinical discovery- stage program and we may not succeed in identifying a CHI program candidate to translate to development and even if we do we may not succeed in developing a CHI program product candidate. Research and development in the pharmaceutical industry is an expensive, high- risk, lengthy, complicated, resource intensive process. In order to develop a product successfully, we must, among other things: ● conduct scientific discovery in areas that are uncertain, unproven and complex; ● identify potential product candidates; ● submit for and receive regulatory approvals or allowances to perform clinical trials; ● design and conduct appropriate preclinical studies and clinical trials according to good laboratory practices and good clinical practices and disease- specific expectations of the FDA and other regulatory bodies; ● Select and recruit suitable clinical investigators and subjects for our clinical trials; ● Obtain and correctly**

**interpret data establishing adequate safety of our product candidates and demonstrating that our product candidates are effective for their proposed indications; ● Submit for and receive regulatory approvals; and ● Manufacture the product candidates according to current Good Manufacturing Practices, or cGMPs, and other applicable standards and regulations. There is a high rate of failure inherent in this process, and potential products that appear promising at early stages of the research and development process may fail for a number of reasons. Importantly, positive results from preclinical studies of a product candidate may not be predictive of similar results in human clinical trials, promising results from earlier clinical trials of a product candidate may not be replicated in later clinical trials, and observations from ongoing trials, including observations based on interim, preliminary, or blinded data, may not be representative of results after the trials are completed and all data are collected and analyzed. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late- stage clinical trials even after achieving positive results in earlier stages of development and have abandoned development efforts or sought partnerships in order to continue development. In addition, there are many other difficulties and uncertainties inherent in pharmaceutical research and development that could significantly delay or otherwise materially impair our ability to develop future product candidates, including the following: ● Conditions imposed by regulators, ethics committees or institutional review boards for preclinical testing and clinical trials relating to the scope or design of our clinical trials, including selection of endpoints and number of required patients or clinical sites; ● Challenges in designing clinical trials that may support any potential claims of superiority over current standard of care or future competitive therapies; ● Restrictions placed upon, or other difficulties with respect to, clinical trials and clinical trial sites, including with respect to potential clinical holds or suspension or termination of clinical trials due to, among other things, potential safety or ethical concerns or noncompliance with regulatory requirements; 67 ● Delayed or reduced enrollment in clinical trials, high discontinuation rates or overly concentrated patient enrollment in specific geographic regions; ● Failure by third- party contractors, contract research organizations, or CROs, clinical investigators, clinical laboratories, or suppliers to comply with regulatory requirements or meet their contractual obligations in a timely manner; ● Greater than anticipated cost of our clinical trials; and ● Insufficient product supply or inadequate product quality. ● Evolving competitive landscape for our products and product candidates, which could cause us to modify our development programs, notwithstanding positive data or trial results in existing trials, in order to seek alternate indications or routes of administration or to substitute or otherwise modify our product candidates in light of the evolving competitive landscape and changing commercial prospects for our product and product candidates. In addition, we cannot state with certainty when or whether our CHI program will ever identify a product candidate to translate from research to the development stage or whether our other product candidates now under development will be approved or launched; whether, if initially granted, such approval will be maintained; whether we will be able to develop, license, or otherwise acquire additional products or product candidates; or whether our products, once launched, will be commercially successful. Failure to successfully develop setmelanotide for additional indications or to develop product candidates for any of the foregoing reasons may materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.** Setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** may cause undesirable side effects that could delay or prevent additional regulatory approvals, limit the commercial profile of approved labeling, or result in significant negative consequences following marketing approval. First generation MC4R agonists were predominantly small molecules that failed in clinical trials due to significant safety issues, particularly increases in blood pressure, and had limited efficacy. Undesirable side effects caused by setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive labeling or the delay or denial of additional regulatory approvals by the FDA or other equivalent competent authorities in foreign jurisdictions. Treatment- related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may adversely affect our business, financial condition and prospects significantly. ~~63Setmelanotide~~ **Setmelanotide**, RM- 718 and ~~LB54640~~ **bivamelagon** are MC4R agonists. Potential side effects of MC4R agonism, which have been noted either with setmelanotide or with other MC4R agonists in clinical trials and preclinical studies, may include: ● adverse effects on cardiovascular parameters, such as increases in heart rate and blood pressure; ● erections in males and similar effects in women, such as sexual arousal, clitoral swelling and hypersensitivity; ● nausea and vomiting; ● reduced appetite; **68** ● headache; ● effects on mood, depression, anxiety and other psychiatric manifestations; and ● other effects, for which most investigators reported as unrelated to setmelanotide and for which no increased incidence or pattern is currently evident. In addition, injection site reactions have been seen in subcutaneous, or SC, injections with setmelanotide. Also, setmelanotide has likely off target effects on the closely related MC1 receptor, which mediates ~~tanning~~ **skin pigmentation** in response to sun exposure. Other MC1 receptor mediated effects include darkening of skin blemishes, such as freckles and moles, and hair color change. ~~The~~ **These** ~~cosmetic~~ **MC1 receptor mediated skin** effects are not tolerated by all patients, as a small number of patients have withdrawn from treatment due to skin darkening. These effects have generally been reversible in clinical trials after discontinuation of setmelanotide, but it is still unknown if they will be reversible with long term exposure. The MC1 receptor mediated effects may also carry risks. The long term impact of MC1 receptor activation has not been tested in clinical trials, and could potentially include increases in skin cancer, excess biopsy procedures and cosmetic blemishes. These skin changes may also result in unblinding, which could make interpretation of clinical trial results more complex and possibly subject to bias. We have also initiated trials of setmelanotide in potential new indications that include patients who might have more serious underlying conditions. It is possible that the underlying conditions in these patients, such as congestive heart failure and potentially other conditions, may confound the understanding of the safety profile of setmelanotide. If these or other significant adverse events or other side effects are observed in any of our ongoing or planned clinical trials, we may have difficulty

recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, other comparable regulatory authorities or an IRB may also suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early- stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** from obtaining or maintaining marketing approval or obtaining additional approvals, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially adversely affect our business, financial condition and prospects. Further, if we or others identify undesirable side effects **associated with or** caused by the products, or any other similar product, before or after regulatory approvals, a number of potentially significant negative consequences could result, including: ● regulatory authorities may request that we withdraw the product from the market or may limit or vary their approval of the product through labeling or other means; ● regulatory authorities may require the addition of labeling statements, such as a " boxed " warning or a contraindication; ● the FDA, the EU competent authorities and other equivalent competent authorities in foreign jurisdictions may require the addition of a Risk Evaluation and Mitigation Strategy, or REMS, or other specific obligations ~~64as~~ **as** a condition for marketing authorization due to the need to limit treatment to rare patient populations, or to address safety concerns; ● we may be required to change the way the product is distributed or administered or change the labeling of the product; ● we may be required to conduct additional studies and clinical trials or comply with other post- market requirements to assess possible serious risks; **69** ● we may be required to conduct long term safety follow- up evaluations, including setting up disease and drug based registries; ● we may decide to remove the product from the marketplace; ● **our other MC4 agonist products or product candidates may be perceived by regulators or other third parties as unsafe, which could adversely affect our development efforts and product portfolio; ●** we could be sued and held liable for injury caused to individuals exposed to or taking the product; and ● our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** , and could substantially increase the costs of commercializing setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** and significantly impact our ability to successfully commercialize setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** and generate revenues. We may not be able to obtain or maintain orphan drug designations for setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** or to obtain or maintain **orphan** exclusivity ~~in any use~~ . Even with exclusivity, competitors may obtain approval for different drugs that treat the same indications as setmelanotide, RM- 718 and ~~LB54640~~ **bivamelagon** . The FDA may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is defined under the Federal Food, Drug and Cosmetic Act, or FDCA, as having a patient population of fewer than 200, 000 individuals in the United States, or a patient population greater than 200, 000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the disease or condition for which it has such designation, the product is entitled to a period of seven years of marketing exclusivity, which precludes the FDA from approving another marketing application for a product that constitutes the same drug treating the same disease or condition for that marketing exclusivity period, except in limited circumstances. The exclusivity period in the United States can be extended by six months if the NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. Orphan drug exclusivity may be revoked if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Other potential benefits of orphan drug designation and / or approval of a designated drug include eligibility for: exemption from certain prescription drug user fees, tax credits for certain qualified clinical testing expenses, and waivers from the pediatric assessment requirements of the Pediatric Research Equity Act. In the EU, orphan ~~drug~~ designation is granted by the EC based on a scientific opinion of the EMA' s Committee for Orphan Medicinal Products. A medicinal product may be designated as orphan if its sponsor can establish that (i) the product is intended for the diagnosis, prevention or treatment of a life- threatening or chronically debilitating condition; (ii) either (a) such condition affects no more than 5 in 10, 000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the medicinal product will be of significant benefit to those affected ~~65by~~ **by** the condition. The application for orphan designation must be submitted before the application for marketing authorization. Grant of orphan designation by the EC also entitles the holder of this designation to financial incentives such as reduction of fees or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. In ~~addition~~ **70addition** to a range of other benefits during the development and regulatory review, orphan medicinal products are, upon grant of marketing authorization **and assuming the requirement for orphan designation are also met at the time the marketing authorization is granted** , entitled to ten years of exclusivity in all EU member states for the approved therapeutic indication, which means that the competent authorities cannot accept another ~~marketing authorization application, or~~ MAA, grant a marketing authorization, or accept an application to extend a marketing authorization for a similar product for the same indication for a period of ten years. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed ~~Pediatric~~ **pediatric** ~~Investigation~~ **investigation** ~~Plan~~ **plan** , or PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process ~~. Marketing authorization may, however, be granted to a similar medicinal product with the same orphan indication during the ten- year period with the consent of the marketing authorization holder for the original orphan~~

~~medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities~~ . The ten- year market exclusivity in the EU may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan designation, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Additionally granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time: (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant cannot supply enough orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. In connection with IMCIVREE' s approval, the FDA granted us seven years of orphan drug exclusivity for setmelanotide for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1, or LEPR deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance. The FDA also granted us seven years of orphan drug exclusivity for setmelanotide for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to BBS. In the EU, we obtained ten years of market exclusivity for setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic ~~leptin receptor (~~ LEPR ~~)~~ deficiency in adults and children 6 years of age and above **. Following the FDA' s approval of the expanded indication for IMCIVREE to include patients as young as 2 years of age in December 2024, we believe the FDA will review the request we made to similarly expand the scope of the current orphan drug exclusivity for IMCIVREE, however, we cannot estimate when or if the scope of IMCIVREE' s orphan drug exclusivity will be expanded** . We have also been granted orphan designation for setmelanotide for the treatment of Alström syndrome in both the United States and the EU. Setmelanotide has also been granted orphan designation for setmelanotide in treating Prader- Willi syndrome and acquired hypothalamic obesity in the EU. There can be no assurance that we will be able to maintain the benefits **of** orphan drug exclusivity, or that the FDA or the EC will grant orphan designations for setmelanotide for other uses. In addition, orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. Even though we have obtained orphan drug exclusivity for certain uses of setmelanotide, such exclusivities may not effectively protect setmelanotide from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. As discussed above, similar rules apply in the EU. ~~66Although~~ **71Although** we have obtained ~~PRIME designation in the EU for setmelanotide for the treatment of obesity and the control of hunger associated with deficiency disorders of the MC4R receptor pathway and~~ Breakthrough Therapy designation for setmelanotide for the treatment of obesity associated with certain defects upstream of the MC4R in the leptin melanocortin pathway, which includes POMC deficiency obesity, LEPR deficiency obesity, Bardet- Biedl syndrome and Alström syndrome, as well as hypothalamic obesity in the United States **and PRIME designation in the EU for setmelanotide for the treatment of obesity and the control of hunger associated with deficiency disorders of the MC4R pathway** , the FDA may rescind the Breakthrough Therapy **designation and the EMA may withdraw the PRIME** designation and we may be unable to obtain Breakthrough Therapy designation **or the PRIME designation** for other uses. In addition, Breakthrough Therapy designation by the FDA or PRIME designation by the EMA may not lead to a faster development, regulatory review or approval process, and ~~it does not~~ **neither do they** increase the likelihood that setmelanotide will receive additional marketing approvals in the United States or additional marketing authorizations in the EU. The FDA is authorized under the FDCA to give certain product candidates " Breakthrough Therapy designation. " A Breakthrough Therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs **or biologics** , to treat a serious or life **-** threatening disease or condition ~~and~~ **, where** preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of Breakthrough Therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross disciplinary review. In addition, the FDA may consider reviewing portions of an NDA before the sponsor submits the complete application, ~~or~~ **a process also known as** rolling review. Product candidates designated as breakthrough therapies by the FDA may be eligible for other expedited programs, such as priority review, provided the relevant criteria are met. Designation as Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe ~~setmelanotide~~ **our product candidates** ~~meets~~ **meet** the criteria for designation as Breakthrough Therapy, the FDA may disagree. In any event, the receipt of Breakthrough Therapy designation for a product candidate, or acceptance for one or more of the FDA' s other expedited programs, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not guarantee ultimate approval by the FDA. Regulatory standards to demonstrate safety and efficacy must still be met. Additionally, the FDA may later decide that the product candidate no longer meets the conditions for designation and may withdraw designation at any time or decide that the time period for FDA review or approval will not be shortened. The PRIME **(PRIority MEdicines)** scheme was launched by the EMA in 2016. In the EU, innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the Breakthrough Therapy designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA' s support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. The benefits of a PRIME designation include the appointment of a rapporteur before submission of an MAA, early dialogue and

scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. In late June 2018, setmelanotide was granted eligibility to PRIME by the **Committee for Medicinal Products for Human Use, or** CHMP for the treatment of obesity and the control of hunger associated with deficiency disorders of the MC4R receptor pathway. Acknowledging that setmelanotide targets an unmet medical need, the EMA offers enhanced support in the development of the medicinal product through enhanced interaction and early dialogue to optimize our development plans and speed up regulatory evaluation in the EU. As part of this designation, the EMA has provided guidance to us concerning the development of setmelanotide. ~~The PRIME designation does~~ **However, the EMA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for review or approval will** not ~~, however, guarantee that the regulatory review process in the EU will~~ be ~~shorter~~ **shortened** ~~or less demanding~~. Neither does the PRIME designation guarantee that the EC will grant additional marketing authorizations for setmelanotide. ~~We~~ **Product developers that benefit from PRIME designation may be eligible for accelerated assessment (in 150 days instead of 210 days), which may be granted for medicinal products of major interest from a public health perspective or that target an unmet medical need, but this is not guaranteed. 72We** may not be able to translate the once-daily **, subcutaneous injection** formulations of setmelanotide ~~for~~ **into alternate formulations, including alternate** methods of delivery **for setmelanotide or alternative methods of delivery for or other product candidates** that would be acceptable to the FDA or other equivalent competent authorities in foreign jurisdictions or commercially successful. Setmelanotide is currently administered by once- daily **subcutaneous (** SC **)** injection using small insulin type needles and syringes. SC injection is generally less well received by patients than other methods of administration, such as oral administration. Considerable additional resources and efforts, including potential studies, may be necessary in order to translate the once- daily formulation of setmelanotide into a once- weekly formulation that may be well received by patients. ~~67We~~ **We** have entered into a license agreement with Camurus AB, or Camurus, for the use of Camurus' drug delivery technology, FluidCrystal, to formulate once-weekly setmelanotide. This formulation, if successfully developed for setmelanotide, and approved by the FDA and other regulatory authorities, will be delivered subcutaneously, similar to our once- daily formulation, except that we anticipate it ~~will~~ **would** be injected once weekly. In addition, we have initiated development of an auto- injector device designed to make administration of our once- weekly product candidate easier and more convenient for our patients. While we have started consultations with regulatory authorities about the potential path for approval of the once- weekly formulation, and have initiated clinical studies of the once- weekly formulation, we cannot yet estimate the requirements for non- clinical and clinical data, manufacturing program, time, cost, and probability of success for approval. Regulatory authorities have limited experience evaluating Camurus' formulations, which further complicates our understanding regarding the information that may be required to obtain approval of a once- weekly formulation. **While we believe that this** ~~We received FDA approval of the once- daily formulation in the initial NDA submission for setmelanotide, and plan to seek approval of the~~ once- weekly formulation ~~at~~ **may be more convenient and less burdensome than setmelanotide, which is currently approved as** a ~~later time. While~~ **once-daily administration,** we ~~plan to~~ **have paused** ~~develop~~ **development** ~~the~~ **of this** once- weekly formulation **in favor of advancing RM- 718. In the event RM- 718 shows sufficiently positive efficacy and safety results** , ~~or~~ **we plan** to **discontinue** ~~develop~~ **development of** ~~other~~ -- **the weekly** ~~new and useful formulations~~ - **formulation of** ~~and delivery technology for~~ setmelanotide **. Concurrently** , we **are engaging with applicable regulatory authorities to address the impact of our discontinuing development of the weekly formulation of setmelanotide, which was a component of our pediatric investigation plan, or PIP, in the EU (and the United Kingdom) and in January 2025 we submitted a request to modify the PIP to remove elements related to the weekly formulation and we expect to receive a decision sometine in Q2 2025. We** cannot estimate the probability of success **with respect to our development of additional formulations** , nor the resources and time needed to succeed. If we are unable to **develop and** gain approval **of** ~~and utilize the once- weekly formulation, or to develop~~ new formulations ~~,~~ **of** setmelanotide **or of our other product candidates, our products** may not achieve significant market acceptance and our business, financial condition and results of operations may be materially harmed. Our approach to treating patients with MC4R pathway deficiencies requires the identification of patients with unique genetic subtypes, for example, POMC genetic deficiency. The FDA or other equivalent competent authorities in foreign jurisdictions could require the clearance, approval or certification of an in vitro companion diagnostic device to ensure appropriate selection of patients as a condition of approving setmelanotide in additional indications. The requirement that we obtain clearance, approval or certification of an in vitro companion diagnostic device ~~will~~ **would** require substantial financial resources, and could delay or prevent the receipt of additional regulatory approvals for setmelanotide, or adversely affect those **approvals** we have already obtained. We have focused our development of setmelanotide as a treatment for obesity caused by certain genetic deficiencies affecting the MC4R pathway. To date, we have employed in vitro genetic diagnostic testing to select patients for enrollment in our clinical trials, including our clinical trials for IMCIVREE and for other potential indications for setmelanotide. If the safe and effective use of any of our product candidates depends on an in vitro diagnostic that is not otherwise commercially available, then the FDA may require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time as, or in connection with, the FDA approval of such product candidates. In the EU, until May 25, 2022, in vitro diagnostic medical devices were regulated by Directive 98 / 79 / EC, or the IVDD, which has been repealed and replaced by Regulation (EU) No 2017 / 746, or the IVDR. Unlike the IVDD, the IVDR is directly applicable in EU member states without the need for member states to implement into national law. The ~~regulation~~ **73regulation** of companion diagnostics is now subject to further requirements set forth in the IVDR. ~~However on October 14~~ **Following subsequent legislative changes** , **European institutions adopted** ~~2021, the EC proposed~~ a " progressive " roll- out of the IVDR to prevent disruption in the supply of in vitro diagnostic medical devices ~~. The European Parliament and Council adopted the proposed regulation on December 15, 2021~~ . The IVDR became applicable on May 26, 2022 but there is a tiered system extending the grace period for many devices (depending on their risk classification) before they have to be fully compliant with the regulation. For instance, **under these**

**provisions,** class C devices (including devices that are intended to be used as companion diagnostics) ~~have~~ **had** until May 26, 2026 to comply with the new requirements **. In June 2024, to address issues related to notified body capacity, the EC adopted an extension of the grace period, resulting in an extended transition period until December 31, 2028 for certain class C devices, subject to compliance with the transitional provisions** . The IVDR introduces a new classification system for companion diagnostics which are now specifically defined as diagnostic tests that support the safe and effective use of a specific medicinal product, by identifying patients that are suitable or unsuitable for treatment. Companion diagnostics will have to undergo a conformity assessment by a notified body. Before it can issue an EU certificate, the notified body must seek a scientific opinion from the EMA on the suitability of the companion diagnostic to the medicinal product concerned if the medicinal product falls exclusively within the scope of the centralized procedure for the authorization of medicines, or the medicinal product is already authorized through the centralized procedure, or MAA for the medicinal product has been submitted through the centralized procedure. For other substances, the notified body can seek the opinion from a national competent ~~authorities~~ **authority** or the EMA **. These modifications may make it more difficult and costly for us to obtain regulatory clearances or approvals or certification for our companion diagnostics or to manufacture, market or distribute our products after clearance, approval or certification is obtained** . Compliance with the new requirements may impact our development plans for setmelanotide. ~~68If~~ **If** the FDA or a comparable regulatory authority requires clearance, approval or certification of a companion diagnostic for setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** , any delay or failure by us or our current and future collaborators to develop or obtain regulatory clearance or approval of, or certification of, such tests, if necessary, could delay or prevent us from obtaining additional approvals for setmelanotide, or adversely affect the approvals we have already obtained. For example, in November 2020, the FDA approved IMCIVREE for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to POMC, PCSK1, or LEPR deficiencies confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance. Although the FDA did not require that we obtain approval of a companion diagnostic prior to approving the New Drug Application, or NDA, for IMCIVREE, in connection with the NDA approval we agreed as a post- marketing commitment to conduct adequate analytical and clinical validation testing to develop and establish an in vitro companion diagnostic device to accurately and reliably detect patients with variants in the POMC, PCSK1, and LEPR genes that may benefit from setmelanotide therapy. In September 2020, our collaboration partner, Prevention Genetics, submitted a de novo request seeking FDA authorization to market such an in vitro companion diagnostic device for IMCIVREE as a Class II medical device. In January 2022, the FDA granted the de novo request for classification for the POMC / PCSK1 / LEPR CDx Panel for market authorization as a Class II device. If the FDA or a comparable regulatory authority requires clearance, approval or certification of a companion diagnostic when we seek additional approvals for setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** , any delay or failure by us or our current and future collaborators to develop or obtain regulatory clearance or approval of, or certification of, such tests, if necessary, could delay or prevent us from obtaining such additional approvals for setmelanotide, or adversely affect the approvals we have already obtained. We rely, and expect that we will continue to rely, on third parties to conduct **research and discovery activities and in our** clinical trials ~~for setmelanotide, RM- 718 and LB54640~~ . If these third parties do not successfully carry out their contractual ~~duties~~ **obligations** or meet expected ~~deadlines~~ **timelines** , we may not be able to **advance our pre- clinical and clinical programs or** obtain **, on a timely basis or at all,** additional regulatory approvals for or commercialize ~~setmelanotide, RM- 718 or~~ **our** ~~LB54640~~ **product candidates** , and our business could be substantially harmed. We have agreements with third- party CROs to operationalize, provide monitors for and to manage data for our **research and discovery efforts (including in our CHI program) and our** ongoing clinical trials. We rely heavily on these parties for the execution of **research and discovery activities and** clinical trials and control only certain aspects of their activities. As a result, we have less direct control over the start- up, conduct, timing and completion of these **activities and** clinical trials, and the management of data developed through ~~the~~ **these activities and** clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. However, we remain responsible for the conduct of these **activities and these** trials and are subject to enforcement which may include civil and criminal liabilities for any ~~violations~~ **74violations** of FDA rules and regulations and the comparable foreign regulatory provisions during the conduct of our clinical trials. Outside parties may: ● have staffing difficulties; ● fail to comply with contractual obligations; ● devote inadequate resources to our clinical trials; ● experience regulatory compliance issues; ● undergo changes in priorities or become financially distressed; or ● form more favorable relationships with other entities, some of which may be our competitors. These factors, among others, may materially adversely affect the willingness or ability of third parties to conduct our **research and discovery activities and our** clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that **all of our activities and** each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on **third parties, including** CROs **,** does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCPs, which are **regulations and** guidelines enforced by the FDA, the competent authorities of the EU member states and equivalent competent authorities in foreign jurisdictions for any products in clinical development. The FDA and foreign regulatory authorities enforce ~~these regulations and GCP~~ **GCPs** ~~guidelines~~ through periodic inspections of clinical trial sponsors, principal investigators, and trial sites, and IRBs. If we or our CROs fail to comply with applicable GCPs, the ~~69clinical~~ -- **clinical** data generated in our clinical trials may be deemed unreliable and the FDA or other equivalent competent authorities in foreign jurisdictions may require us to perform additional clinical trials before approving our marketing applications **, if ever** . We cannot assure you that, upon inspection, the FDA or foreign regulatory authorities will determine that any of our clinical trials ~~comply~~ **have complied** with GCPs. In addition, our clinical trials must be conducted with products produced under ~~current Good Manufacturing Practices, or~~ cGMPs and similar foreign requirements. Our failure or the failure of our CROs to comply with these regulations may require us

to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties. If any of our relationships with these third- party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual ~~duties or~~ obligations or meet expected ~~deadlines~~ **timelines** , if they need to be replaced or if the quality or accuracy of the clinical **and other** data they obtain are compromised due to the failure to adhere to our ~~clinical~~ protocols, regulatory requirements or for other reasons, any ~~such~~ **related activities or** clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize **a CHI therapeutic product** , setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** . As a result, our financial results and the commercial prospects for setmelanotide, RM- 718 or ~~LB54640~~ **bivamelagon** , would be harmed, our costs could increase and our ability to generate revenue could be delayed. Risks Related to the Commercialization of IMCIVREE and, if Approved, our ~~Future ProductsThe~~ --- **Products CandidatesThe** successful commercialization of IMCIVREE and any other product candidates for which we obtain approval will depend in part on the extent to which governmental authorities, private health insurers, and other third- party payors provide coverage and adequate reimbursement ~~levels~~ . Failure to obtain or maintain coverage and adequate reimbursement for IMCIVREE or our other product candidates, if any and if approved, could limit our ability to market those products and decrease our ability to generate revenue. Our ability to successfully commercialize IMCIVREE or any other product candidates for which we obtain approval will depend in part on the extent to which coverage and reimbursement for these product candidates and related treatments will be available from government authorities, private health insurers and other organizations. Government ~~authorities~~ **75authorities** and third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and ~~establish~~ **provide** reimbursement ~~levels~~ . Increasing efforts by governmental and third- party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for recently approved products, such as IMCIVREE, and, as a result, they may not cover or provide adequate payment. Even if we show improved efficacy or improved convenience of administration, third- party payors may deny or revoke the reimbursement status of our product candidates, if approved, or establish prices for our product candidates at levels that are too low to enable us to realize an appropriate return on our investment. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize IMCIVREE or other product candidates, and may not be able to obtain a satisfactory financial return. Further, as we continue to grow as an organization, previously- established prices may no longer be sufficient and could create additional pricing pressure for us. No uniform policy for coverage and reimbursement for products exist among third- party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time- consuming and costly process that may require us to provide scientific and clinical support for the use of IMCIVREE to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance **or that step edits or other conditions on reimbursement will not be imposed** . Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. In some foreign countries, particularly in Canada, ~~Great Britain~~ **the United Kingdom** and in the EU member states, the pricing and reimbursement of prescription only medicinal products is subject to strict governmental control which varies widely between countries. In these countries, pricing negotiations with governmental authorities can take six to twelve months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of IMCIVREE with other available therapies. If reimbursement for IMCIVREE is unavailable in any country ~~70in~~ **in** which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected. In the EU, in particular, each EU member state can restrict the range of medicinal products for which its national health insurance system provides reimbursement and can control the prices of medicinal products for human use marketed in its territory. As a result, following receipt of marketing authorization in an EU member state, through any application route, an applicant is required to engage in pricing discussions and negotiations with the competent pricing authority in the individual EU member states. Some EU member states operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. Other EU member states approve a specific price for the medicinal product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. The downward pressure on healthcare costs in general, particularly prescription drugs, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, we may face competition for IMCIVREE from lower priced products in foreign countries that have placed price controls on pharmaceutical products. Health Technology Assessment, or HTA, of medicinal products, however, is becoming an increasingly common part of the pricing and reimbursement procedures in **Canada,** the United Kingdom and some EU member states, including France, Germany, Italy, Spain, the Netherlands, Belgium, Norway and Sweden. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities ~~of individual EU member states~~ . The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies ~~between EU member states~~ . In addition **, in the EU** , pursuant to Directive 2011 / 24 / EU on the application of patients' rights in cross border healthcare, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The ~~purpose~~ **76purpose** of the network is to

facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU member states and in pricing and reimbursement decisions and may negatively affect price in at least some EU member states. On December 13, 2021, Regulation No 2021 / 2282 on HTA, amending Directive 2011 / 24 / EU, was adopted. **The** ~~While the~~ Regulation entered into force in January 2022 **and has been applicable since** ~~, it will only begin to apply from~~ January 2025 ~~onwards~~, with ~~preparatory and implementation- related steps to take place in the interim. Once applicable, it will have a~~ phased implementation ~~depending~~ **based** on the ~~concerned~~ **type of product, i. e. oncology and advanced therapy medicinal** products **as of 2025, orphan medicinal products as of 2028, and all other medicinal products by 2030** . This Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non- clinical (e. g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement. If we are unable to establish **, maintain or expand our** sales ~~and ,~~ marketing **and distribution** capabilities or enter into agreements with third parties to market ~~and ,~~ sell **, and distribute** IMCIVREE, we may not be able to generate ~~any~~ revenue. In order to market IMCIVREE, we must continue to build our sales, marketing **, distribution** , managerial and other non- technical capabilities or make arrangements with third parties to perform these services. Although we have received FDA and Health Canada approval, and EC and MHRA marketing authorization for certain indications, we are early in our commercialization efforts ~~and have not yet established a full- scale commercial infrastructure~~ . Therefore, you should not compare us to commercial- stage biotechnology companies, and you should not expect that we will generate substantial revenues or become profitable in the near term. If we are unable to establish ~~adequate~~ **, maintain or expand our** sales, marketing **, market access, named patient sales, patient services, reimbursement** and distribution ~~71capabilities~~ -- **capabilities** , whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects would be materially adversely affected. We may never receive regulatory approval to market setmelanotide outside of the United States, Canada, the European Union and ~~Great Britain~~ **the United Kingdom** . We intend to seek marketing authorizations in various countries worldwide. In order to market any product outside of the United States, Canada, the EU or ~~Great Britain~~ **the United Kingdom** , we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Marketing authorization procedures vary among countries and can involve additional setmelanotide testing and additional administrative review periods. The time required to obtain marketing authorization in other countries might differ from that required to obtain FDA approval or marketing authorization from the EC or the MHRA. The marketing authorization processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States and Europe, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Grant of marketing authorization in one country does not ensure grant of marketing authorization in another country, but a failure or delay in obtaining marketing authorization in one country may have a negative effect on the regulatory process or commercial activities in others. Failure to obtain marketing authorization in other countries or any delay or other setback in obtaining such authorizations would impair our ability to market setmelanotide in such foreign markets. Any such impairment would reduce the size of our potential market share and could have a material adverse impact on our business, results of operations and prospects. We may not achieve **or maintain** market acceptance for IMCIVREE, which would limit the revenue that we generate from the sale of IMCIVREE. The commercial success of IMCIVREE will also depend upon the awareness and acceptance of IMCIVREE within the medical community, including physicians, patients and third- party payors. If IMCIVREE does not achieve **or 77maintain** an adequate level of acceptance by patients, physicians and third- party payors, we may not generate sufficient revenue to become or remain profitable. Before granting reimbursement approval, third- party payors may require us to demonstrate that, in addition to treating obesity caused by certain genetic deficiencies affecting the MC4R pathway, IMCIVREE also provides incremental health benefits to patients. Our efforts to educate the medical community and third- party payors about the benefits of IMCIVREE may require significant resources and may never be successful. All of these challenges may impact our ability to ever successfully market and sell IMCIVREE. Market acceptance of IMCIVREE will depend on a number of factors, including, among others: ● the ability of IMCIVREE to provide chronic weight management in patients with obesity caused by certain genetic deficiencies affecting the MC4R pathway and, if required by any competent authority in connection with the approval for these indications, to provide patients with incremental health benefits, as compared with other available treatments, therapies, devices or surgeries; ● the complexities of **clinical diagnosis and / or** genetic testing, **as needed, for certain of IMCIVREE' s indications,** including obtaining **and interpreting clinical or** genetic results that support patient treatment with IMCIVREE; ● the relative convenience and ease of SC injections as the necessary method of administration of IMCIVREE, including as compared with other treatments for patients with obesity; ● the prevalence and severity of any adverse side effects associated with IMCIVREE; ● limitations or warnings contained in the labeling approved for IMCIVREE by the FDA or the specific obligations imposed as a condition for marketing authorization imposed by other equivalent competent authorities in foreign jurisdictions, particularly by the EC; ~~72~~ ● availability of alternative treatments, including a number of obesity therapies already approved or expected to be commercially launched in the near future; ● our ability to increase awareness of these diseases among our target populations through marketing and other cross- functional efforts; ● the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these

therapies; ● the ability of IMCIVREE to treat the maximum range of pediatric patients, and any limitations on its indications for use; ● the strength of marketing and distribution support and timing of market introduction of competitive products; ● publicity concerning IMCIVREE or competing products and treatments; ● pricing and cost effectiveness; ● the effectiveness of our sales and marketing strategies **and** ~~; ●~~ our ability to increase awareness of IMCIVREE through marketing efforts; ● our ability to obtain sufficient third- party coverage or reimbursement; **78** ● the willingness of patients to pay out- of- pocket in the absence of third- party coverage **(including in the case of named patient sales, which can be a costly and uncertain source of revenues) and the willingness of healthcare providers to obtain reimbursement, which can be challenging and may factor into their decision to prescribe IMCIVREE** ; and ● the likelihood that competent authorities in foreign jurisdictions may require development of a REMS or other specific obligations as a condition of approval or post- approval, may not agree with our proposed REMS or other specific obligations, or may impose additional requirements that limit the promotion, advertising, distribution or sales of IMCIVREE. Our industry is intensely competitive. If we are not able to compete effectively against current and future competitors, we may not be able to generate revenue from the sale of IMCIVREE, our business will not grow and our financial condition and operations will suffer. The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop compounds **and generate data** that **could, even absent regulatory approvals, establish a perception of efficacy in our targeted patient population, which** could make IMCIVREE **appear** obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. In addition, payors may require that patients try other medications known as step therapy or a " step- edit, " including medications approved for treatment of general obesity, before receiving reimbursement for IMCIVREE. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to IMCIVREE and our other product candidates. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer. Currently, IMCIVREE is the only **treatment** approved ~~treatment for providing chronic~~ **to reduce excess body** weight ~~management~~ **and maintain weight reduction long term** in patients with obesity due to BBS or POMC, PCSK1 or LEPR deficiencies, and there are no **comparable treatments** approved ~~treatments~~ for ~~chronic weight management in~~ patients ~~with deficiencies~~ with deficiencies due to a variant in one of the two alleles in the POMC, PCSK1, or LEPR genes (HET obesity), SRC1 deficiency obesity, SH2B1 deficiency obesity, MC4R deficiency obesity, and hypothalamic obesity. Bariatric surgery is **often** not ~~a good~~ **considered an appropriate** treatment option for these genetic diseases of obesity because the severe obesity and hyperphagia associated with these diseases are considered to be risk factors for **poor outcomes with** bariatric surgery. Also, ~~73existing~~ -- **existing** therapies indicated for general obesity, including glucagon- like peptide- 1 (GLP- 1) receptor agonists, ~~such as Wegovy ®,~~ and glucose- dependent insulinotropic polypeptide (GIP) and glucagon- like peptide- 1 (GLP- 1) agonists, ~~such as tirzepatide which is being investigated as a treatment for obesity,~~ do not specifically restore function impaired by genetic deficiencies in the MC4R pathway, which we believe is the root cause of hyperphagia and obesity in patients with MC4R genetic variants. **At present** ~~Based on search results from ClinicalTrials. gov~~ , we are ~~unaware~~ -- **aware** of **multiple ongoing research and development programs** ~~any competitive products in therapeutic clinical studies~~ for ~~the~~ **general** obesity ~~and hyperphagia caused by upstream~~ **with various new mechanisms of action including some** MC4R **agonists** ~~pathway deficiencies~~ . New competitors may emerge which could limit our business opportunity in the future. We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability. The use of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** in clinical trials and the sale of IMCIVREE exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with IMCIVREE. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design or a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws and any equivalent laws in foreign countries. If we become subject to product liability claims and cannot successfully defend ~~ourselves~~ **79ourselves** against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things: ● withdrawal of patients from our clinical trials; ● substantial monetary awards to patients or other claimants; ● decreased demand for IMCIVREE or any future product candidates following marketing approval, if obtained; ● damage to our reputation and exposure to adverse publicity; ● litigation costs; ● distraction of management' s attention from our primary business; ● loss of revenue; and ● the inability to successfully commercialize IMCIVREE or any future product candidates, if approved. We maintain product liability insurance coverage for our clinical trials and commercial product with a $ ~~10~~ **20** . 0 million annual aggregate coverage limit. Our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected. ~~74We~~ **We** rely completely on third- party suppliers to manufacture our clinical and commercial drug supplies of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** , and we intend

to rely on third parties to produce preclinical, clinical and commercial supplies of any future product candidate. We do not currently have, nor do we plan to acquire, the infrastructure or capability to manufacture our clinical and commercial drug supply internally for setmelanotide, **RM- 718, bivamelagon,** or any future product candidates, for use in the conduct of our preclinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidate on a clinical or commercial scale. The facilities used by our contract manufacturing organizations, or CMOs, to manufacture the active pharmaceutical ingredient, or API, and final drug product must ~~pass~~ **successfully complete** inspection by the FDA and other equivalent competent authorities in foreign jurisdictions pursuant to inspections that have been and will be conducted following submission of ~~our~~ NDAs **, NDA supplements** or ~~relevant~~ **comparable** foreign regulatory ~~submission~~ **submissions** to the other equivalent competent authorities in foreign jurisdictions. Our failure or the failure of our CMOs to ~~pass~~ **successfully complete any potential** preapproval ~~inspection~~ **inspections** of the manufacturing facilities of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** could delay the regulatory approval process. In addition, our clinical trials must be conducted with products produced ~~under~~ **in accordance with** GMP and similar foreign regulations. Our failure or the failure of our CROs or CMOs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action, including civil and criminal penalties. When we import any drugs or drug substances, we would be subject to FDA, United States Department of Agriculture, and U. S. Bureau of Customs and Border Patrol import regulation requirements. Such enforcement for our failure or our CROs or CMOs' failure to comply with these regulations could result in import delays, detention of products, and, depending on criteria such as the history of violative activities, the FDA could place a foreign firm or certain drug substances or products on Import Alert and require that all such drug substances or products be subject to detention without physical examination ~~which~~ **80which** could significantly impact the global supply chain for setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** . With the exception of those on the FDA' s drug shortage list or properly imported by individuals, the FDCA prohibits the importation of prescription drug products for commercial use if they were manufactured in a foreign country, unless they have been approved or are otherwise authorized to be marketed in the United States and are labeled accordingly. We currently contract with third parties for the manufacture of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** and intend to continue to do so in the future. We have entered into process development and manufacturing service agreements with our CMOs, Corden Pharma Switzerland, LLC, or Corden, (formerly Peptisyntha SA prior to its acquisition by Corden), and Neuland Laboratories for certain process development and manufacturing services for regulatory starting materials and / or raw materials in connection with the manufacture of setmelanotide. We have entered into long- term commercial supply agreements with PolyPeptide Group and ~~Recipharm Monts~~ **Astrea MONTS** S. A. S. for manufacturing of drug substance and drug product for IMCIVREE. Under our agreements, we pay these third parties for services in accordance with the terms of mutually agreed upon work orders, which we may enter into from time to time. We may need to engage additional third- party suppliers to manufacture our clinical and / or commercial (subject to approval) drug supplies. We also have engaged other third parties to assist in, among other things, distribution, post- approval safety reporting and pharmacovigilance activities. We cannot be certain that we can engage third- party suppliers on terms as favorable as those that are currently in place. We do not perform the manufacturing of any drug products and are completely dependent on our CMOs to comply with GMPs and similar foreign requirements for manufacture of both drug substance, or API and finished drug product. We recognize that we are ultimately responsible for ensuring that our drug substances and finished drug product are manufactured in accordance with GMPs and similar foreign requirements, and, therefore, the company' s management practices and oversight, including routine auditing, are critical. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other equivalent competent authorities in foreign jurisdictions, they may be subject to administrative and judicial enforcement for non- compliance and the drug products would be deemed misbranded or adulterated and prohibited from distribution into interstate commerce. Furthermore, all of our CMOs are engaged with other companies to supply and / or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those other company materials and products may affect the regulatory clearance of our CMOs' facilities generally. In addition, satisfying the regulatory requirements for production of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** with multiple suppliers, while assuring more robust drug availability in the future, adds additional complexity and risk to regulatory approval. If the FDA or another equivalent competent foreign regulatory agency does not approve these facilities for the manufacture of setmelanotide, RM- 718, and ~~75LB54640~~ **bivamelagon** or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market setmelanotide, RM- 718, or ~~LB54640~~ **bivamelagon** . ~~We~~ **Our CMOs** are manufacturing finished drug product for use in our upcoming or ongoing clinical trials and for commercial supply. We believe we currently have a sufficient amount of finished setmelanotide, RM- 718, ~~LB54640~~ **bivamelagon** , and placebo to complete our ongoing and planned clinical trials, and for commercial IMCIVREE supply. However, these projections could change based on delays encountered with manufacturing activities, equipment scheduling and material lead times. Any such delays in the manufacturing of finished drug product could delay our planned clinical trials of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** , and our commercial IMCIVREE supply, which could delay, prevent or limit our ability to generate revenue and continue our business. We do not have long term supply agreements in place with all of our contractors involved with the manufacturing of our weekly formulation of setmelanotide ~~and~~ **,** RM- 718, and ~~LB54640~~ **bivamelagon** . We currently place individual batch or campaign orders with the CMOs / suppliers that are individually contracted under existing master services and quality agreements for the weekly formulation of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** . If we engage new contractors, such contractors must be approved by the FDA and other equivalent competent authorities in foreign jurisdictions. We will need to submit information to the FDA and other equivalent competent authorities in foreign jurisdictions describing the manufacturing changes. If manufacturing changes occur post- approval, the

FDA and foreign regulatory authorities may have to approve these changes. We plan to continue to rely upon CMOs and, potentially, collaboration partners to manufacture commercial quantities of setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon, if approved** . Our current scale of manufacturing appears adequate ~~to~~ **81to** support all of our current needs for clinical trial and initial commercial supplies for setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon, if approved** . Going forward, we may need to identify additional CMOs or partners to produce setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** on a larger scale. In light of our election to terminate the exclusive license agreement with RareStone Group Ltd., or RareStone, the development of setmelanotide in certain indications and commercialization of IMCIVREE in certain markets could be delayed or terminated and our business could be adversely affected. In December 2021, we entered into an Exclusive License Agreement with RareStone, or the RareStone License. Pursuant to the RareStone License, we granted to RareStone an exclusive, sublicensable, royalty- bearing license under certain patent rights and know- how to develop, manufacture, commercialize and otherwise exploit any pharmaceutical product that contains setmelanotide in the diagnosis, treatment or prevention of conditions and diseases in humans in China, including mainland China, Hong Kong and Macao. RareStone has a right of first negotiation in the event that **we** ~~the Company chooses~~ **choose** to grant a license to develop or commercialize the licensed product in Taiwan ~~. Under the RareStone License, we are dependent upon RareStone to successfully commercialize any applicable collaboration products in China, including mainland China, Hong Kong and Macao. We cannot directly control RareStone' s commercialization activities or the resources it allocates to setmelanotide. Our interests and RareStone' s interests may differ or conflict from time to time, or we may disagree with RareStone' s level of effort or resource allocation. RareStone may internally prioritize setmelanotide differently than we do or it may not allocate sufficient resources to effectively or optimally commercialize setmelanotide~~ . On October 28, 2022, we delivered a written notice to RareStone that we have terminated the RareStone License for cause **(the " October 2022 Notice ")** . In accordance with the **October 2022** ~~notice~~ **Notice** , we maintain that RareStone has materially breached its obligations under the RareStone License to fund, perform or seek certain key clinical studies and waivers, including with respect to **our** ~~the Company' s~~ global EMANATE trial, among other obligations. On December 21, 2022, RareStone provided **us** written notice ~~to the Company~~ that it objects to the claims in our October ~~28,~~ 2022 ~~notice~~ **Notice** , including **our** ~~the Company' s~~ termination of the RareStone License for cause. On March 16, 2023, we provided written notice to RareStone **(the " March 2023 Notice ")** reaffirming our position that RareStone has materially breached its obligations under the RareStone License and that we have terminated the RareStone License for cause, and also requested documentation supporting RareStone' s purported dispute notice objecting to the claims in the **October 2022** Notice. On May 10, 2023, RareStone provided **us** written notice ~~to the Company~~ reaffirming its objections to the claims in our October ~~28,~~ 2022 ~~notice~~ **Notice** and March ~~16~~ , 2023 ~~notice~~ **Notice** , including **our** ~~to the Company' s~~ termination of the RareStone License for cause. On November 29, 2023, RareStone wrote to us seeking to negotiate and execute a commercial ~~76supply~~ -- **supply** agreement as contemplated under the Exclusive License Agreement, and on January 19, 2024, we responded in writing again reaffirming our position that RareStone has materially breached its obligations under the RareStone License and that we have terminated the RareStone License for cause **. Since our last written response in January 2024, we have engaged in discussions with RareStone in an effort to reach a resolution, however, we cannot predict whether a resolution will ever be reached** . There can be no assurance that we will be able to negotiate an appropriate cure to the alleged material breaches, which we believe are incurable, and, if required, we expect to seek appropriate relief under the terms of the RareStone License. Termination of, or any possible litigation focused on, the RareStone License could cause significant delays in our product development and commercialization efforts for setmelanotide and could prevent us from commercializing IMCIVREE in the markets covered by the RareStone License without first expanding our internal capabilities or entering into another agreement with a third party. Any alternative collaboration or license could also be on less favorable terms to us. In addition, under the agreement, RareStone agreed to provide funding for certain clinical development activities. To date, no such funding has been provided. If the agreement were terminated, however, we may need to refund any such potential payments and seek additional funding to support the research and development of setmelanotide or discontinue any research and development activities for setmelanotide in China, including mainland China, Hong Kong and Macao, which could have a material adverse effect on our business. Risks Related to Our Intellectual Property RightsIf we are unable to adequately protect our proprietary technology or maintain issued patents **directed** ~~that are sufficient~~ to ~~protect~~ setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon** , others could compete against us **sooner** ~~more directly~~ , which ~~would~~ **could** have a material adverse impact on our business, results of operations, financial condition and prospects. Our commercial success will depend in part on our success in obtaining and maintaining issued patents and other intellectual property rights in the United States and elsewhere and protecting our proprietary technology. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our technologies ~~and~~ **82and** erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect setmelanotide, RM- 718, and ~~LB54640~~ **bivamelagon. In addition, our CHI program intellectual property may not have the scientific value and commercial potential which we envision** . Other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent ~~position~~ **positions** . The patent positions of biotechnology and pharmaceutical companies, including our patent ~~position~~ **positions** , involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Although an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and such patent may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Patents, if issued, may be challenged, deemed unenforceable, invalidated or circumvented. U. S. patents and patent applications or the

patents and patent application obtained or submitted pursuant to comparable foreign laws, may also be subject to interference proceedings, ex parte reexamination, inter partes review proceedings, post- grant review proceedings, supplemental examination and challenges in court. Patents may be subjected to opposition or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize setmelanotide **, RM- 718, or bivamelagon** . Competitors may also be able to design around our patents. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. The laws of some foreign countries ~~do~~ **may** not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our ~~77proprietary~~ -- **proprietary** rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales. In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering setmelanotide **, RM- 718, or bivamelagon** are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered setmelanotide, **RM- 718, or bivamelagon,** our financial position and results of operations would also be materially and adversely impacted. The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that: ● any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect setmelanotide **, RM- 718, or bivamelagon** ; ● any of our pending patent applications will issue as patents; ● we will be able to successfully commercialize IMCIVREE or our other product candidates before our relevant patents expire; ● we were the first to make the inventions covered by each of our patents and pending patent applications; ● we were the first to file patent applications for these inventions; **83** ● others will not develop similar or alternative technologies that do not infringe our patents; ● any of our patents will be found to ultimately be valid and enforceable; ● any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties; ● we will develop additional proprietary technologies or product candidates that are separately patentable; or ● our commercial activities or products will not infringe upon the patents of others. We rely upon unpatented trade secrets, unpatented know- how **,** and continuing technological innovation to develop and maintain our competitive ~~position~~ **positions** , which we seek to protect, in part, by confidentiality agreements with employees, consultants, collaborators and vendors. We also have agreements with employees and selected consultants that obligate them to assign their inventions to us. It is possible that technology relevant to our business will be independently developed by a person who is not a party to such an agreement. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, collaborators, vendors, former employees and current employees. Furthermore, if the parties to our confidentiality agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful. Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the attention of our management and key personnel from our business operations. Even if we prevail in any lawsuits that we initiate, the damages or other remedies awarded may not be commercially meaningful. In addition, in an infringement proceeding, ~~78a~~ **a** court may decide that a patent of ours or our licensors is not valid, is unenforceable and / or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. ~~We~~ **84We** may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing IMCIVREE or our other product candidates. Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties. For example, numerous third- party U. S. and non **-** U. S. patents and pending applications exist that cover melanocortin receptor analogs and methods of using these analogs. The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that

setmelanotide **, RM- 718, or bivamelagon** or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney' s fees if we are found to be willfully infringing another party' s patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced or choose to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing IMCIVREE or our other product candidates. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, in order to avoid infringing the intellectual property rights of third parties and any resulting intellectual property litigation or claims, we could be forced to do one or more of the following, which may not be possible and, even if possible, could be costly and time **-** consuming: ● cease development of setmelanotide and commercialization of IMCIVREE or our other product candidates; ● pay substantial damages for past use of the asserted intellectual property; ~~79~~ ● obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and ● in the case of trademark claims, rename setmelanotide and / or its trade name IMCIVREE. Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may also be subject to claims that former employees, collaborators or other third parties have an **inventorship or** ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. ~~Issued~~ **85Issued** patents covering setmelanotide or our other product candidates could be found invalid or unenforceable if challenged in court. If we or one of our licensing partners threatened or initiated legal proceedings against a third party to enforce a patent covering setmelanotide **or one of our other product candidates** , the defendant could claim that the patent covering setmelanotide or ~~our~~ **the** other product candidates are invalid and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any one of several statutory requirements, including novelty, non- obviousness and enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld material information from the U. S. PTO, or made a misleading statement, during patent prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, inter partes review, post grant review and equivalent proceedings in foreign jurisdictions, for example, opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover setmelanotide **, our other product candidates,** or competitive products. The outcome following legal assertions of invalidity and / or unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on setmelanotide **or our other product candidates** . Such a loss of patent protection would have a material adverse impact on our business. We do not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection. Filing, prosecuting and defending patents on setmelanotide **and our other product candidates** in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of ~~80our~~ -- **our** proprietary rights generally. For example, an April ~~2017~~ **2024** report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our

intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing setmelanotide or ~~LB54640~~ **bivamelagon** . We have licensed our rights to setmelanotide from Ipsen ~~Pharma SAS, or Ipsen~~ , and our rights to ~~LB54640~~ **bivamelagon** from ~~LG~~ **LGC** ~~Chem, Ltd, or LG Chem~~ . Our licenses with Ipsen and ~~LG~~ **LGC** ~~Chem~~ impose various obligations on us, and ~~provides~~ **provide** Ipsen and ~~LG~~ **LGC** ~~Chem~~ the right to terminate the license in the ~~event~~ **86event** of our material breach of the license agreement, our failure to initiate or complete certain development of a licensed product, or our commencement of an action seeking to have an Ipsen or ~~LG~~ **LGC** ~~Chem~~ licensed patent right declared invalid. Termination of our license from Ipsen or ~~LG~~ **LGC** ~~Chem~~ would result in our loss of the right to use the licensed intellectual property, which would materially adversely affect our ability to develop and commercialize setmelanotide and ~~LB54640~~ **bivamelagon** , respectively, as well as harm our competitive business position and our business prospects. Furthermore, if our license agreement with ~~LG~~ **LGC** ~~Chem~~ were terminated, we may be subject to certain refunds or be subject to certain payments to ~~LG~~ **LGC** ~~Chem~~ . We also have licensed from Camurus its drug delivery technology, FluidCrystal **®** , to formulate once- weekly setmelanotide. Our license with Camurus imposes various obligations on us, and provides Camurus the right to terminate the license in the event of our material breach of the license agreement. Termination of our license from Camurus would result in our inability to use the licensed intellectual property. We may enter into additional ~~licenses~~ **license agreements** to third- party intellectual property that are necessary or useful to our business. Future licensors may also allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensors may have the right to terminate our license at will. Any termination could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize setmelanotide, as well as harm our competitive business position and our business prospects. Any termination could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize setmelanotide or ~~LB54640~~ **bivamelagon** , as well as harm our competitive business position and our business prospects. While we have registered trademarks for the commercial trade name IMCIVREE (setmelanotide) in the United States, the ~~EU~~ **European Union** , and other ~~countries~~ **jurisdictions** , we have not yet obtained trademark protection for IMCIVREE in certain foreign jurisdictions and failure to secure such registrations could adversely affect our business. While we have received registered trademarks for the commercial trade name IMCIVREE (setmelanotide) and its logo in the United States, the EU, and other countries, we have not yet obtained trademark protection for IMCIVREE in certain foreign jurisdictions and are pursuing trademark registrations in other jurisdictions. Our trademark applications may be rejected during trademark registration proceedings. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome them. In addition, in the U. S. PTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive those proceedings. ~~81If~~ **If** we do not obtain additional protection under the Hatch- Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining product exclusivity for setmelanotide and our other product candidates, our business may be materially harmed. Depending upon the timing, duration and specifics of FDA marketing approval for setmelanotide and our other product candidates, one or more of the U. S. patents we **own or** license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch Waxman Amendments. The Hatch Waxman Amendments permit a patent term restoration of up to five years as compensation for patent term lost during product development and the FDA regulatory review process **. We** ~~, and we~~ have **received** ~~applied to the U. S. PTO for~~ patent term extension ~~.~~ **for IMCIVREE and will apply for patent term extension for our other product candidates at the appropriate time,** ~~However~~ **however** , we may not be granted an extension **for these other product candidates** because of, for example, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or otherwise failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected. ~~Because~~ **87Because** setmelanotide contains active ingredients that the FDA has determined to be a new chemical entity, it has been afforded five years of ~~marketing~~ **non- patent data** exclusivity by the FDA. Following the expiration of this ~~marketing~~ exclusivity **period** , the FDA may approve generic products **referencing the information included in our NDA for setmelanotide** . Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for setmelanotide. Recent legislation enacted by Congress created, among other things, new causes of action against innovator companies that refuse to offer samples of drugs for purposes of testing and developing generic or biosimilar products or to allow companies to participate in a shared Risk Evaluation and Mitigation Strategy (REMS). Competition that setmelanotide may face from generic versions could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in setmelanotide. ~~In the EU, the grant of orphan designation for setmelanotide means that this medicinal product would be entitled, upon grant of marketing authorization by the EC, to ten years of exclusivity in all EU member states. Marketing authorization may, however, be granted to a similar medicinal product with the same orphan indication during the ten year period if we are unable to supply sufficient quantities of setmelanotide. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the similar product is deemed safer, more effective or otherwise clinically superior to setmelanotide. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that setmelanotide is sufficiently profitable not to justify maintenance of market exclusivity.~~ If we fail to obtain an extension of patent protection under similar foreign legislation, where applicable, our

competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected in the foreign countries concerned. Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products. The United States ~~has~~ enacted ~~and is currently implementing~~ the America Invents Act of 2011, wide **is a wide-** ranging patent reform legislation. Further, the U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the federal courts and the U. S. PTO, 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 future patents. ~~82We~~ **We** may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers. Our employees have been previously employed at other biotechnology or pharmaceutical companies, including ~~our~~ competitors or potential competitors. We may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of the former employers of our employees. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize setmelanotide **or our other product candidates** , which would materially adversely affect our commercial development efforts. Risks Related to Regulatory Approval and Marketing of Setmelanotide and Other Legal **and** Compliance MattersEven if we complete the necessary clinical trials, the regulatory and marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining additional approvals for the commercialization of ~~setmelanotide. We depend primarily on the success of setmelanotide, and we cannot be certain that we will be able to obtain additional regulatory approvals for, or~~ **our product candidates** ~~successfully commercialize, setmelanotide~~ . If we are not able to obtain, or if there are delays in obtaining, required ~~additional~~ regulatory approvals **for our product candidates** , we will not be able to commercialize **such candidates** ~~setmelanotide in additional indications in the United States or in foreign jurisdictions,~~ and our ability to generate revenue will be materially impaired. **Our** ~~We currently have only one product candidate, setmelanotide, in clinical development, and our~~ business depends largely on its successful clinical development, regulatory approval and commercialization **of our product candidates** . In the United States, IMCIVREE is approved ~~for chronic~~ **to reduce excess body** weight ~~management~~ **and maintain weight reduction long term** in ~~adult~~ **adults** and pediatric patients ~~6~~ **2** years of age and older with **syndromic or** monogenic ~~or syndromic~~ obesity due to **BBS or** POMC, PCSK1 or LEPR deficiency as determined by a FDA- approved test demonstrating variants in POMC, PCSK1 or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance ~~, or BBS~~ . Health Canada has approved IMCIVREE for weight management in adult and pediatric patients 6 years of age and older with obesity due to BBS or genetically- confirmed POMC, PCSK1, or LEPR deficiency due to variants interpreted as pathogenic, likely pathogenic, or of VUS. The EC has authorized setmelanotide for the treatment of obesity and the control of hunger ~~associated~~ **88associated** with genetically confirmed BBS or genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children ~~6~~ **2** years of age and above. The UK' s MHRA authorized setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss- of- function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children ~~6~~ **2** years of age and above. Setmelanotide will require substantial additional clinical development, testing and regulatory approval before we are permitted to commence commercialization in indications beyond those currently approved for IMCIVREE in the United States, the EU and ~~Great Britain~~ **the United Kingdom, and our other product candidates will require similar efforts before we are permitted to commercialize them for any indication** . The clinical trials, manufacturing and marketing of ~~setmelanotide~~ **our product candidates** are subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market ~~setmelanotide~~ **such product candidates** . Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through nonclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and approval, if any, may be conditional on postmarketing studies and surveillance, and will require the expenditure of substantial resources beyond our existing cash resources. Of the large number of drugs in development in the United States and in other countries, only a small percentage will successfully complete the FDA regulatory approval process or the equivalent process in foreign jurisdictions and will be commercialized. In addition, we have not discussed all of our proposed development programs with the FDA or the competent authorities of foreign jurisdictions. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and clinical trials, we cannot assure you that setmelanotide will be successfully developed or commercialized. In addition, obtaining FDA **or EC** approval ~~of an NDA for additional indications and the approval of an MAA from the EC for additional indications~~ is a complex, lengthy, expensive and uncertain process, and the FDA, EMA or equivalent ~~83competent~~ -- **competent** authorities in foreign jurisdictions may delay, limit or deny approval of ~~setmelanotide~~ **our product candidates** for many reasons, including, among others: ● the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials; ● we may not be able to demonstrate to the satisfaction of the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions that ~~setmelanotide is~~ **our product candidates are** safe and effective **for** ~~in treating obesity caused by certain genetic deficiencies affecting the~~ **their** ~~MC4R pathway~~ **intended uses** ; ● the results of our clinical trials may not be interpretable or meet the level of statistical or clinical significance required by the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions for marketing approval. For example,

the potential unblinding of setmelanotide studies due to easily identifiable AEs may raise the concern that potential bias has affected the clinical trial results; ● the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with the number, size, conduct or implementation of our clinical trials; ● the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may require that we conduct additional clinical trials or pre- clinical studies; ● the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions or the applicable foreign regulatory agency may identify deficiencies in our chemistry, manufacturing or controls of ~~setmelanotide~~ **our product candidates** , or in the commercial production of ~~setmelanotide~~ **such product candidates that may be required** to support product approval; **89** ● the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials; ● the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may find the data from preclinical studies and clinical trials insufficient to demonstrate that clinical and other benefits of ~~setmelanotide~~ **a product candidate** outweigh its safety risks; ● the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from our preclinical studies and clinical trials; ● the FDA or other equivalent competent authorities in foreign jurisdictions may not approve the formulation, labeling or specifications of ~~setmelanotide~~ **our product candidates** ; ● the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not accept data generated at our clinical trial sites; ● the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions may require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions; ● ~~as part of our NDA approval,~~ we ~~were required~~ **may not be able** to ~~complete certain~~ **meet any** post- market requirements ~~and~~ **or** commitments **agreed** ~~, which we may not be able~~ to ~~meet;~~ **in connection with regulatory approvals** ● the FDA may require development of a REMS as a condition of additional approvals or may impose additional requirements that limit the promotion, advertising, distribution, or sales of ~~setmelanotide~~ **our product candidate** ; ~~84~~ ● the EC may grant only conditional ~~approval~~ marketing authorization or based on the EMA' s opinion impose specific obligations as a condition for marketing authorization, or may require us to conduct post authorization safety studies as a condition of grant of marketing authorization; ● the FDA or other equivalent competent foreign regulatory agencies may deem our manufacturing processes or our facilities or the facilities of our CMOs inadequate to preserve the identity, strength, quality, purity, or potency of our product; or ● the FDA or the equivalent competent authorities in foreign jurisdictions may change its approval policies or adopt new regulations and guidance. Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain additional regulatory approvals **,** ~~for~~ **or** ~~and~~ **to** successfully market IMCIVREE. Moreover, because our business is largely dependent upon setmelanotide, any such setback in our pursuit of regulatory approvals would have a material adverse effect on our business and prospects. Future regulatory legislation or regulation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates. The EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the EC in November 2020. The EC' s proposal for a revision of several legislative instruments related to medicinal products (potentially ~~revising~~ **reducing** the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be ~~substantially~~ **90substantially** revised before adoption, which is not anticipated before early 2026. The revisions, may **,** however **,** have a significant impact on the pharmaceutical industry and our business in the long term. **In the United States, the FDA oversees the rare pediatric disease priority review voucher program (the " PRV Program "), which aims to incentive drug development for rare pediatric diseases. Under the PRV Program, a company sponsor that receives a drug approval may qualify for a voucher that can be redeemed to receive priority review for a different product and these vouchers can be transferred or sold. Under the current provisions in the law enacting the PRV Program, the PRV Program began to sunset after December 20, 2024. These changes to the PRV Program could impact existing and future development programs and could negatively impact our business.** Disruptions at the FDA **, including those** ~~and other government agencies~~ caused by **changing presidential administrations and related priorities,** funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business. The ability of the FDA and foreign regulatory authorities to review and or approve new products can be affected by a variety of factors, including **reductions in force or hiring freezes,** government budget and funding levels, statutory, regulatory, and policy changes, the FDA' s and foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s and foreign regulatory authorities' ability to perform routine functions **, including uncertainty associated with the new presidential administration in the United States** . Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result **of some of these factors and could also fluctuate in the future** . In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies ~~, such as the EMA, following its relocation to Amsterdam and resulting staff changes,~~ may also slow the time necessary for new drugs and biologics to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Separately, in response to the COVID- 19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. ~~Even though the FDA has since resumed standard inspection operations, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID- 19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional or administrative delays.~~ If a prolonged government shutdown occurs, or if global health concerns ~~continue to~~ **or any other disruptions** prevent the FDA or other regulatory authorities from

conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. ~~85Our~~ -- **Our** failure to obtain marketing approval in foreign jurisdictions would prevent setmelanotide or our other product candidates from being marketed abroad, and any current or future approvals we have been or may be granted for setmelanotide or other products in the United States would not assure approval of setmelanotide or other products in foreign jurisdictions. In order to market and sell setmelanotide and any other product candidate that we may develop in the EU and many other jurisdictions, we or our third- party collaborators must obtain separate marketing authorizations and comply with numerous and varying regulatory requirements. The marketing authorization procedure varies among countries and can involve additional testing. The time required to obtain marketing authorization may differ substantially from that required to obtain FDA approval. The marketing authorization process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or these third parties may not obtain marketing authorization from competent authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure grant of marketing authorization by competent authorities in other countries or jurisdictions, and grant of marketing authorization by one competent authority outside the United States does not ensure grant of marketing authorization by competent authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing authorizations and may not receive necessary marketing authorization to commercialize setmelanotide in any market. Additionally, the UK' s withdrawal from the EU, commonly referred to as Brexit, has resulted in the relocation of the EMA from the UK to the Netherlands. This relocation has caused, and may continue to cause, disruption in the administrative and medical scientific links between the EMA and the MHRA, including delays in granting ~~clinical~~ **91clinical** trial authorization or marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of setmelanotide, or any other product candidates in the EU and / or the UK. Although we have obtained FDA approval and marketing authorization from the EC and the MHRA for setmelanotide, any delay in obtaining, or an inability to obtain, any marketing authorization, for any of our other product candidates, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the UK and / or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek marketing authorization in the UK and / or EU for any of our other product candidates, which could significantly and materially harm our business. The terms of our current and future potential marketing approvals for setmelanotide and other product candidates and ongoing regulation may limit how we manufacture and market setmelanotide and other products, and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue. Regulatory authorities may impose significant restrictions on setmelanotide' s indicated uses or marketing or impose ongoing requirements for potentially costly post approval studies, and the same may be true for our other product candidates ~~in the future~~ **, if approved** . We and setmelanotide will also be subject to ongoing requirements by the FDA and foreign regulatory authorities, governing labeling, packaging, storage, advertising, promotion, marketing, distribution, importation, exportation, post- approval changes, manufacturing, recordkeeping, and submission of safety and other post market information. Advertising and promotional materials must comply with the FDCA and implementing regulations and foreign regulations ~~,~~ and are subject to FDA and foreign regulatory authorities oversight and post- marketing reporting obligations, in addition to other potentially applicable federal and state laws. The FDA and the other competent foreign authorities have significant post market authority, including, for example, the authority to require labeling changes based on new safety information and to require post market studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA and foreign regulatory authorities also has the authority to require, as part of an NDA or similar foreign application or post approval, the submission of a REMS or other specific obligations, which may include Elements to Assure Safe Use. Any REMS or other specific obligations required by the FDA or foreign regulatory authorities may lead to increased costs to assure compliance with new post approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. The holder of an approved NDA also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process, or adding new manufacturers. Similar requirements apply in foreign jurisdictions. ~~86Manufacturers~~ -- **Manufacturers** of drug products and their facilities may be subject to payment of application and program fees and are subject to continual review and periodic inspections by the FDA and other equivalent competent authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with setmelanotide, such as AEs of unanticipated severity or frequency, or problems with the facility where setmelanotide is manufactured or disagrees with the promotion, marketing or labeling of the product, a regulatory agency may impose restrictions on setmelanotide, the manufacturer or us, including requiring withdrawal of setmelanotide from the market or suspension of manufacturing. If we or the manufacturing facilities for setmelanotide fail to comply with applicable regulatory requirements, a regulatory agency may, among other things: ● issue warning letters or untitled letters; ● seek an injunction or impose civil or criminal penalties or monetary fines; ● vary, suspend or withdraw marketing approval; ● suspend any ongoing clinical trials; ● refuse to approve pending applications or supplements to applications submitted by us; **92** ● suspend or impose restrictions on operations, including costly new manufacturing requirements; or ● seize or detain setmelanotide, refuse to permit the import or export of setmelanotide, or request that we initiate a product recall. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects. Accordingly, we and our CMOs will

continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post- approval regulatory requirements, we could have the marketing approvals for setmelanotide withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition. In addition, a sponsor' s responsibilities and obligations under the FDCA and FDA regulations, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability. Similar to the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states, both before and after grant of the manufacturing and marketing authorizations. This oversight includes control of compliance with GMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third- party manufacturers would be required to ensure that all of our processes, methods, and equipment are compliant with GMP. Failure by us or by any of our third- party partners, including suppliers, manufacturers, and distributors to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may ~~87result~~ -- **result** in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, revocation 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, EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that the EMA and the competent authorities of the EU member states have the authority to require companies to conduct additional post- approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, AE management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time consuming and expensive and could impact our profitability. Noncompliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures. ~~Current~~ **93Current** and future healthcare reform legislation or regulation may increase the difficulty and cost for us and any future collaborators to commercialize setmelanotide and may adversely affect the prices we, or they, may obtain and may have a negative impact on our business and results of operations. In the United States and some foreign jurisdictions there have been, and continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, restrict or regulate post- approval activities with respect to IMCIVREE and affect our ability, or the ability of any future collaborators, to profitably sell our products. Among policy makers and payors in the United States and elsewhere, **particularly under the new presidential administration,** there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and / or expanding access. In the United States and elsewhere, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative **and regulatory** initiatives. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, **including executive orders,** may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for IMCIVREE or any product candidates approved for sale. ~~In March 2010~~ **New and changing laws and regulations may also create uncertainty about how such laws and regulations will be interpreted and applied. If the Company is found to have violated laws and regulations** , **it could materially adversely affect the Company' s business, results of operations and financial condition. The** Patient Protection and Affordable Care Act **(** ~~, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the~~ ACA ~~,~~ **)** was signed into law **in 2010** . The ACA substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affects the U. S. pharmaceutical industry. Among the provisions of the ACA of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any product candidates that are approved for sale, are the following: ● an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications; ● expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133 % of the federal poverty level, thereby potentially increasing a manufacturer' s Medicaid rebate liability; ● expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs, revising the " average manufacturer price " definition, and extending rebate liability from fee- for- service Medicaid utilization to include the utilization of Medicaid managed care organizations as well ~~as Medicaid managed care~~ ; ● expansion of the list of entity types eligible for participation in the Public Health Service 340B drug pricing program, or the 340B program, to include certain free-standing cancer hospitals, critical access hospitals, ~~88rural~~ -- **rural** referral centers, and sole community hospitals, but exempting " orphan drugs, " such as IMCIVREE, from the 340B ceiling price requirements for these covered entities; ●

~~establishment of the Medicare Part D coverage gap discount program, which requires manufacturers to provide a 70 % point of sale discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; ●~~ a Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and ● establishment of the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, including prescription drug spending. Since its enactment, certain provisions of the ACA have been subject to judicial, executive, and legislative challenges ~~. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. In addition, other legislative changes have been proposed~~ and **may be subject** ~~adopted since the ACA was enacted. For example, beginning April 1, 2013, Medicare payments~~ to ~~providers were reduced under the sequestration required by the Budget Control Act of 2011, which will remain in effect through 2032, unless~~ additional **challenges in** ~~Congressional action is taken. Additionally, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other~~ -- **the future** ~~things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years~~ . ~~On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminated the statutory Medicaid drug rebate cap, beginning January 1, 2024. Previously, the Medicaid rebate was capped at 100 % of a drug' s average manufacturer price, or AMP. Additional~~ **94Additional** changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which was fully implemented in 2019. ~~At this time, it is unclear how the introduction of this Medicare quality payment program will impact overall physician reimbursement.~~ The cost of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States. There have been several Congressional inquiries, as well as legislative and regulatory initiatives and executive orders designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. ~~Moreover, the federal government and the individual states in the United States have become increasingly active in developing proposals, passing legislation and implementing regulations designed to control drug pricing, including price or patient reimbursement constraints, discounts, formulary flexibility, marketing cost disclosure, drug price increase reporting, and other transparency measures. These types of initiatives may result in additional reductions in Medicare, Medicaid, and other healthcare funding, and may otherwise affect the prices we may obtain for IMCIVREE or the frequency with which IMCIVREE is prescribed or used.~~ Most significantly, ~~on~~ **in** August ~~16,~~ 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) into law. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare ~~(beginning in 2026)~~ , with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); **redesigns the Medicare Part D benefit (beginning in 2024);** and replaces the Part D coverage gap discount program with a new **manufacturer** ~~discounting~~ --- **discount** program (beginning in 2025) **. CMS has published the negotiated prices for the initial ten drugs, which will first be effective in 2026, and has published the list of the subsequent 15 drugs that will be subject to negotiation** . The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented ~~. On August 29~~ , ~~2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, 89although~~ -- **although** the Medicare drug price negotiation program is currently subject to legal challenges. The impact of the IRA on **us and** the pharmaceutical industry cannot yet be fully determined, but is likely to be significant. **Under** ~~Further,~~ the ~~Biden administration~~ **IRA manufacturer discount program that** ~~released~~ - **replaced** ~~an additional executive order~~ **the coverage gap discount program as of January 1, 2025, manufacturers must give a 10 percent discount** on ~~October 14~~ **Part D drugs in the initial coverage phase** , **and** ~~2022, directing HHS to submit~~ a **20 percent discount** ~~report within 90 days~~ on ~~how~~ **Part D drugs in** the ~~Center~~ **so- called " catastrophic phase " (the phase after the patient incurs costs above the initial phase out- of- pocket threshold, which is $ 2, 000 beginning in 2025). The IRA allows the 10 and 20 percent discounts to be phased in over time** for **certain drugs for " specified manufacturers. " In April 2024, CMS informed us that we are deemed a specified manufacturer. We are still evaluating the potential impact of this status on our future revenues. IMCIVREE is not currently reimbursed under** Medicare ~~and Medicaid Innovation can~~ **Part D, but if we were to** be **reimbursed under** ~~further leveraged to test new models for lowering drug costs for~~ Medicare **Part D in** ~~and Medicaid beneficiaries. In response to the executive order, on February 14, 2023, HHS released a report outlining three~~ -- **the future,** ~~new models for testing by~~ the **reimbursement amount** ~~CMS Innovation Center which~~ will be ~~evaluated~~ **impacted by the 10 and 20 percent discounts under the IRA' s new discounting program. We anticipate that these increased discounts could impact IMCIVREE revenues, while also having an industry- wide impact on the cost of Part D drugs. The impact on IMCIVREE revenues could be offset because the IRA' s redesign of certain Part D components, some of which went into effect in 2024, resulted in an increase in the number of patients able to afford this therapy. The amount of the offset, if any, is inherently uncertain and difficult to predict. The IRA manufacturer discounting program also increases financial obligations of Part D prescription drug plans with respect to beneficiaries in the catastrophic coverage phase. This may incentivize Part D prescription drug plans to seek greater price concessions from us in order to include IMCIVREE** on their ~~ability to lower~~ **formularies. Moreover,** the **federal government and the individual states in the United States have become increasingly active in developing proposals, passing legislation and implementing regulations designed to control drug pricing, including price or patient**

**reimbursement constraints, discounts, formulary flexibility, marketing** cost ~~of~~ **disclosure, drug price increase reporting, and other transparency measures. Some states have enacted legislation creating so- called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain** drugs **in these states** ~~, promote accessibility and improve quality of care~~ . ~~It~~ **These types of initiatives may result in additional reductions in Medicare, Medicaid, and other healthcare funding, and may otherwise affect the prices we may obtain for IMCIVREE or the frequency with which IMCIVREE** is **prescribed or used** ~~unclear whether the models will be utilized in any health reform measures in the future~~ . We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage and payment criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our ~~drug~~ **product** ~~candidates~~ **95candidates** or additional pricing pressures. We cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of setmelanotide to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired. For more details concerning the risks related to pricing and reimbursement in the EU, please refer to the discussion in the risk factor " The successful commercialization of ~~setmelanotide~~ **IMCIVREE** and ~~our~~ **any** other product candidates **for which we obtain approval** will depend in part on the extent to which governmental authorities, private health insurers, and other third- party payors provide coverage and adequate reimbursement levels. Failure to obtain or maintain coverage and adequate reimbursement for ~~setmelanotide~~ **IMCIVREE** or our other product candidates, **if any and** if approved, could limit our ability to market those products and decrease our ability to generate revenue " in this Annual Report. If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in which we participate, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Medicaid is a joint federal and state program administered by the states for low income and disabled beneficiaries. We participate in and have certain price reporting obligations under the Medicaid Drug Rebate Program, or the MDRP, as a condition of having covered outpatient drugs payable under Medicaid and, if applicable, under Medicare Part B. The MDRP requires us to pay a rebate to state Medicaid programs every quarter for each unit of our covered outpatient drugs dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. The rebate is based on pricing data that we must report on a monthly and quarterly basis to the Centers for Medicare & Medicaid Services, or CMS, the federal agency that administers the MDRP and other governmental healthcare programs. These data include the average manufacturer price (AMP) for each drug and, in the case of innovator products, the best price, which in general represents the lowest price available from the manufacturer to certain entities in the **United States** ~~U. S.~~ in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. The Medicaid rebate consists of two components, the basic rebate and the additional rebate, which is triggered if the AMP for a drug increases faster than inflation. If we become aware that our MDRP government price reporting submission for a prior quarter was incorrect or has changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. If we fail to provide information timely or are found to have knowingly submitted false information to the government, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP. In the event that CMS terminates our rebate agreement pursuant to which we participate in the MDRP, no federal payments ~~90would~~ -- **would** be available under Medicaid or Medicare Part B for our covered outpatient drugs. Our failure to comply with our MDRP price reporting and rebate payment obligations could negatively impact our financial results ~~. The ACA made significant changes to the MDRP, as described under the risk factor " Current and future healthcare reform legislation or regulation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize setmelanotide and may adversely affect the prices we, or they, may obtain and may have a negative impact on our business and results of operations, " above. In addition, in March 2021, the American Rescue Plan Act of 2021 was signed into law, which, among other things, eliminated the statutory cap on drug manufacturers' MDRP rebate liability, effective January 1, 2024. Previously, under law enacted as part of the ACA, drug manufacturers' MDRP rebate liability was capped at 100 % of the AMP for a covered outpatient drug. Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the MDRP. Additional legislation or the issuance of regulations relating to the MDRP could have a material adverse effect on our results of operations~~ . The recently- enacted IRA imposes rebates under Medicare Part B and Medicare Part D that are triggered by price increases that outpace inflation (first due in 2023), as described under the risk factor " Current and future healthcare reform legislation or regulation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize setmelanotide and may adversely affect the prices we, or they, may obtain and may have a negative impact on our business and results of operations, " above. The Medicare Part D rebate will be calculated on the basis of the AMP figures we report pursuant to the MDRP. Federal law requires that any company that participates in the MDRP also participate in the Public Health Service' s 340B drug pricing program in order for federal funds to be available for the

manufacturer' s drugs under Medicaid and, if applicable, Medicare Part B. We participate in the 340B program, which is administered by the Health Resources and Services Administration, or HRSA, and requires us to charge statutorily defined covered entities no more than the 340B " ceiling price " for our covered outpatient drugs. These 340B covered entities include a variety of community health ~~clinics~~ **96clinics** and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low- income patients. The ACA expanded the list of covered entities to include certain free- standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts " orphan drugs, " such as IMCIVREE, from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes those prices to 340B covered entities. In addition, HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B- eligible drugs. HRSA has also finalized **a revised regulation implementing** an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B covered entities for engaging in unlawful diversion or duplicate discounting of 340B drugs. Our failure to comply 340B program requirements could negatively impact our financial results. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under ~~the ACA or other~~ legislation or regulation could affect our 340B ceiling price calculations and also negatively impact our financial results. In order for IMCIVREE or any product candidates, if approved, to be paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we also participate in the U. S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. As part of this program, we are required to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (VA, U. S. Department of Defense, or DOD, Public Health Service, and U. S. Coast Guard). The FCP is based on the Non- Federal Average Manufacturer Price, or Non- FAMP, which we must calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil monetary penalties for each item of false information. The FSS pricing and contracting obligations also contain extensive disclosure and certification requirements. ~~91We~~ **We** also participate in the Tricare Retail Pharmacy program, under which we are required to pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non- FAMP and FCP. We are required to list our innovator products on a Tricare Agreement in order for them to be eligible for DOD formulary inclusion. If we overcharge the government in connection with our FSS contract or Tricare Agreement, whether due to a misstated FCP or otherwise, we are required to refund the difference to the government. Failure to make necessary disclosures and / or to identify contract overcharges could result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time- consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation. Requirements of pharmaceutical manufacturers under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information. Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies, and the courts. CMS, the Department of Health & Human Services Office of Inspector General, and other governmental agencies have pursued manufacturers that were alleged to have failed to report these data to the government in a timely or accurate manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have ~~implications~~ **97implications** for amounts previously estimated or paid. We cannot assure you that any submissions we are required to make under the MDRP, the 340B program, the VA / FSS program, the Tricare Retail Pharmacy Program, and other governmental drug pricing programs will not be found to be incomplete or incorrect. The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. In the United States, the FDA strictly regulates marketing, labeling, advertising and promotion of prescription drugs. These regulations include standards and restrictions for direct- to- consumer advertising, industry- sponsored scientific and educational activities, promotional activities involving the internet and off- label promotion. Any regulatory approval that the FDA grants is limited to those specific diseases and indications for which a product is deemed to be safe and effective by the FDA. For example, the FDA- approved label for IMCIVREE is limited to ~~chronic~~ **the reduction of excess body** weight ~~management~~ **and maintenance of weight reduction long term** in adult and pediatric patients ~~6~~ **2** years of age and older with monogenic or syndromic obesity due **to BBS or** POMC, PCSK1, or LEPR, deficiency confirmed by FDA- approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance ~~, and due to BBS. In addition to the FDA approval required for new formulations, any new indication for an approved product also requires FDA approval. If we are not able to obtain FDA approval for any desired future indications for our drugs and drug candidates, our~~

~~ability to effectively market and sell our products may be reduced and our business may be adversely affected~~ . While physicians in the United States may choose, and are generally permitted, to prescribe drugs for uses that are not described in the product' s labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to promote the products is narrowly limited to those indications that are specifically approved by the FDA. These " off- label " uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. For example, we are actively evaluating **setmelanotide, the active ingredient in** IMCIVREE **,** in subjects with other forms of obesity caused by defects in the MCR4 pathway. We are not currently permitted to, and do not, market or promote setmelanotide for these uses. ~~92Regulatory --~~ **Regulatory** authorities in the United States generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies on the subject of off- label use. Although recent court decisions suggest that certain off- label promotional activities may be protected under the First Amendment, the scope of any such protection is unclear. If our promotional activities fail to comply with the FDA' s regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to issue warning letters or untitled letters, bring an enforcement action against us, suspend or withdraw an approved product from the market, require a recall or institute fines or civil fines, or could result in disgorgement of money, operating restrictions, injunctions or criminal prosecution, any of which could harm our reputation and our business. In the EU, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product' s Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off label promotion. The off label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU member states also prohibit the direct to consumer advertising of prescription only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals. ~~We~~ **98We** may be subject to federal, state and foreign healthcare laws and regulations, including fraud and abuse laws, health information privacy and security laws, and antitrust laws. If we are unable to comply or have not fully complied with such laws and regulations, we could face criminal sanctions, damages, substantial civil penalties, reputational harm and diminished profits and future earnings. Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of setmelanotide, and other product candidates, if approved. Our arrangements and interactions with healthcare professionals, third- party payors, patients and others will expose us to broadly applicable fraud and abuse, antikickback, false claims and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute setmelanotide, if we obtain marketing approval. The U. S. federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to: ● The United States federal healthcare Anti- Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, (anything of value), directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease order or arranging for or recommending the purchase, lease or order of any good or service for which payment may be made, in whole or in part, by federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers, formulary managers, and patients on the other. Liability under the Anti- Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. Although there are a number of statutory exceptions and regulatory safe harbors to the federal Anti- Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals or patients as consultants, advisors, or speakers, may be subject to scrutiny if they do not fit squarely within an exception or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti- kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product and patient support programs. ~~93~~ ● The federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Such private individuals may share in amounts paid by the entity to the government in recovery or settlement. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for unapproved and thus non- reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or

services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per false or fraudulent claim or statement for violations. Because of the potential for large monetary exposure, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of treble damages and per claim penalties that may be awarded ~~in~~ **99in** litigation proceedings. Settlements may require companies to enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non- government health benefit programs. ● The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, including private third- party payors, and also imposes obligations, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. Penalties for failure to comply with a requirement of HIPAA vary significantly and include civil monetary penalties as well as criminal penalties for knowingly obtaining or disclosing individually identifiable health information in violation of HIPAA. The criminal penalties increase if the wrongful conduct involves false pretenses or the intent to sell, transfer or use identifiable health information for commercial advantage, personal gain or malicious harm. HIPAA also prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal healthcare Anti- Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation. ● The federal Physician Payments Sunshine Act, implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics and medical supplies to report payments and other transfers of value to physicians for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services, Centers for Medicare and Medicaid Services, information related to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiology assistants and certified nurse- midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Manufacturers must submit reports on or before the 90th day of each calendar year disclosing reportable payments made in the previous calendar year. ~~94~~ ● Analogous state laws and regulations, such as state anti- kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, regardless of the payer, including private insurers. Some state laws require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing- related activities including the provision of gifts, meals, or other items to certain health care providers. Some states restrict the ability of manufacturers to offer co- pay support to patients for certain prescription drugs. Some states require the posting of information relating to clinical studies and their outcomes. Other states and cities require identification or licensing of sales representatives. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes of conduct. ● Analogous foreign laws and regulations, including restrictions imposed on the promotion and marketing of medicinal products in the EU member states and other countries, restrictions on interactions with healthcare professionals and requirements for public disclosure of payments made to physicians. Laws (including those governing promotion, marketing and anti- kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we may ~~decide~~ **100decide** not to directly promote or market our products, inappropriate activity by our international distribution partners could have implications for us. Ensuring that our business arrangements and interactions with healthcare professionals, third- party payors, patients and others comply with applicable healthcare laws and regulations will require substantial resources. Various state, federal and foreign regulatory and enforcement agencies continue actively to investigate violations of health care laws and regulations, and the United States Congress continues to strengthen the arsenal of enforcement tools. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable antitrust, fraud and abuse, privacy, or other healthcare laws and regulations. If our operations, including our engagements with healthcare professionals, researchers and patients, or our disease awareness and / or patient identification initiatives including genetic testing programs, or anticipated activities to be conducted by our field teams, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to costly investigations, significant civil, criminal and administrative monetary penalties, imprisonment, damages, fines, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could substantially disrupt our operations or financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and generate negative publicity, which could harm our financial condition and divert our management' s attention from the operation of our business. Our employees may engage in misconduct or other improper activities, **whether knowingly or unknowingly,** including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business. We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional **or unintentional** failures to comply with the regulations of the FDA and applicable non U. S. regulators, provide accurate

information to the FDA and applicable non U. S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and any precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or ~~95asserting~~ -- **asserting** our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. Some of these laws and related risks are described under the risk factor " We may be subject to federal and state healthcare laws and regulations. If we are unable to comply or have not fully complied with such laws and regulations, we could face criminal sanctions, damages, substantial civil penalties, reputational harm and diminished profits and future earnings " of this Annual Report. Actual or perceived failure to comply with data protection, privacy and security laws ~~,~~ **and** regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results. The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more ~~onerous~~ **101onerous** obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our financial performance, business and operating results. In the United States, numerous federal and state laws and regulations, including HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and regulations implemented thereunder, collectively HIPAA, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws, including Section 5 of the Federal Trade Commission Act, which govern the collection, use, disclosure and protection of health- related and other personal information, may apply to our operations and the operations of current and future collaborators. We may obtain health information from third parties, such as research institutions with which we collaborate, that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA, other than potentially with respect to providing certain employee benefits, we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA. In addition, state laws govern the privacy and security of health, research and genetic information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Further, we may also be subject to other state laws governing the privacy, processing and protection of personal information. For example, the California Consumer Privacy Act ~~of 2018, or CCPA, went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations,~~ as **amended by** ~~well as a private right of action for data breaches that has increased the likelihood, and risks associated with data breach litigation. Further,~~ the California Privacy Rights Act, **collectively or CPRA** ~~, generally went into effect on January 1, 2023, and significantly amends~~ the CCPA **, requires** ~~. It imposes additional data protection obligations on~~ covered businesses **that** ~~, including additional consumer rights processes~~ -- **process the personal information of California residents to** , ~~limitations~~ **among other things: (i) provide certain disclosures to California residents regarding the business' s collection, use, and disclosure of their personal information; (ii) receive and respond to requests from California residents to access, delete, and correct their personal information, or to opt out of certain disclosures of their personal information; and (iii) enter into specific contractual provisions with service providers that process California resident personal information** on **the business' s behalf** ~~data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement~~ . Additional compliance investment and potential business process changes may also be required. Similar laws have passed in ~~Virginia, Utah, Connecticut and Colorado, and have been proposed in~~ other states **,** and **are continuing to be proposed** at the **state and** federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In addition, some of our research activities involve minors, which may be subject to additional laws and can require specialized consent processes, privacy protections, and compliance procedures. In the event that we are subject to or affected by HIPAA, the CCPA, ~~the CPRA~~ or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. Furthermore, the Federal Trade Commission, or FTC, and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination and security ~~96practices~~ -- **practices** that appear to be unfair or deceptive. For example, according to the FTC, failing to take appropriate

steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5 (a) of the Federal Trade Commission Act. The FTC expects a company' s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. For example, in Europe, the collection and use of personal data, including health and genetic data, is governed by the provisions of the GDPR. The GDPR became effective on May 25, 2018, and imposes strict requirements for the processing of the personal data of individuals within the European Economic Area, or EEA, or in the context of our activities in the EEA, including health data from clinical trials and AE reporting. In particular, these requirements include certain obligations concerning the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EEA, security breach notifications, and security and confidentiality of the personal data, and violations of these requirements could result in substantial fines, up to the greater of 20 million Euros or 4 % of total global annual turnover. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease / change our processing of our data, enforcement notices, and / or assessment notices for a compulsory audit. We may also face civil claims including representative actions and other class action type litigation (where individuals have suffered harm), potentially amounting to significant compensation or damages liabilities, as well ~~as~~ **102as** associated costs, diversion of internal resources, and reputational harm. Data protection authorities from the different EU and EEA member states may also interpret the GDPR and national laws differently and impose additional requirements, which adds to the complexity of processing personal data in the EU and the EEA. Additionally, from January 1, 2021, we have had to comply with the GDPR and also the United Kingdom GDPR, or UK GDPR, which, together with the amended United Kingdom Data Protection Act 2018, retains the GDPR in United Kingdom national law following Brexit. The UK GDPR mirrors the fines under the GDPR, e. g. **,** fines up to the greater of € 20 million (£ 17. 5 million) or 4 % of global turnover. Among other requirements, the GDPR and UK GDPR also regulate transfers of personal data subject to the GDPR or UK GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States. Case law from the Court of Justice of the European Union, or the CJEU, states that reliance on the standard contractual clauses- a standard form of contract approved by the **EC** ~~European Commission~~ as an adequate personal data transfer mechanism- alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case- by- case basis. On ~~October 7~~ **July 10** , ~~2022~~ **2023** , ~~President Biden signed an Executive Order on ' Enhancing Safeguards for United States Intelligence Activities' which introduced new redress mechanisms and binding safeguards to address~~ the ~~concerns raised by the CJEU~~ **European Commission adopted its Adequacy Decision** in relation to ~~data transfers from the EEA to the United States and which formed the basis of~~ the new EU- US Data Privacy Framework ~~(" ~~**, or the** DPF ~~"), as released on December 13, 2022. The DPF also introduced a new redress mechanism for EU and UK citizens which addresses a key concern in the previous CJEU judgments and may mean transfers under standard contractual clauses are less likely to be challenged in the future. The European Commission adopted its Adequacy Decision in relation to the DPF on July 10, 2023~~ , rendering the DPF effective as a GDPR transfer mechanism to U. S. entities self- certified under the DPF. On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a ~~UK GDPR~~ data transfer mechanism **from the UK** to U. S. entities self- certified under ~~the UK Extension to the~~ DPF ~~. We currently rely on the EU standard contractual clauses and the UK Addendum to the EU standard contractual clauses as relevant to transfer personal data outside the EEA and the UK, including to the United States, with respect to both intragroup and third- party transfers~~ . Following a period of legal complexity and uncertainty regarding international personal data transfers, particularly to the United States, we expect the regulatory guidance and enforcement landscape to continue to develop, in relation to transfers to the United States and elsewhere. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result, we may have to make certain operational changes and implement revised standard contractual clauses and other relevant documentation for existing data transfers arrangements within required time frames. Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must ~~97comply~~ -- **comply** . Our failure to comply with our obligations under the GDPR or UK GDPR, including any failure to adopt measures to ensure that we can continue to conduct the data processing activities that we initiated in the EU before the GDPR entered into application, the UK GDPR, and other countries' privacy or data security- related laws could adversely impact our ability to use the data generated in our studies. And any actual or perceived failure to comply with these data protection laws or adequately address privacy and security concerns could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results. ~~Our~~ **In addition, we may use artificial intelligence, or AI, machine learning, and automated decision- making technologies, collectively, AI Technologies, in our business. The regulatory framework for AI Technologies is rapidly evolving as many federal, state, and foreign government bodies and agencies have introduced or are currently considering additional laws and regulations. Additionally, existing laws and regulations may be interpreted in ways that would affect the operation of AI Technologies. As a result, implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or market perception of their requirements may have on our business and may not always be able to anticipate how to respond to these laws or regulations. It is possible that new laws and regulations will be adopted in the United States and in other non- U. S. jurisdictions, or that existing laws and regulations, including competition and antitrust laws, may be interpreted in ways that would limit our ability to use AI Technologies for our business, or require us to change the way we use AI Technologies in a manner that negatively affects the performance of our**

**products, services, and business and the way in which we use AI Technologies. We may need to expend resources to adjust our products or services in certain jurisdictions if the laws, regulations, or decisions are not consistent across jurisdictions. Further, the cost to comply with such laws, regulations, or decisions and / or guidance interpreting existing laws, could be significant and would increase our operating expenses (such as by imposing additional reporting obligations regarding our use of AI Technologies). Such an increase in operating expenses, as well as any actual or perceived failure to comply with such laws and regulations, could adversely affect our business, financial condition and results of operations. 103Our** future growth depends, in part, on our ability to continue to penetrate foreign markets, where we will be subject to additional regulatory burdens and other risks and uncertainties. Our future profitability will depend, in part, on our ability to continue to commercialize setmelanotide and our other product candidates in foreign markets for which we intend to rely on collaborations with third parties. As we continue to commercialize setmelanotide in foreign markets, we will be subject to additional risks and uncertainties, including: ● our customers' ability to obtain reimbursement for setmelanotide in foreign markets; ● our inability to directly control commercial activities because we are relying on third parties; ● the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements; ● different medical practices and customs in foreign countries affecting acceptance in the marketplace; ● import or export licensing requirements; ● longer accounts receivable collection times; ● longer lead times for shipping; ● language barriers for technical training; ● reduced protection of intellectual property rights in some foreign countries; ● foreign currency exchange rate fluctuations; and ● the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute. Foreign sales of setmelanotide could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs. Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling setmelanotide or our other product candidates outside of the United States and require us to develop and implement costly compliance programs. If we continue to expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act of 1977, or the FCPA, prohibits any U. S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of such third party in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. ~~98Compliance~~ ~~-~~ **Compliance** with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions. ~~Various~~ **104Various** laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non- U. S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U. S. exchanges for violations of the FCPA' s accounting provisions. The results of the United Kingdom' s departure from the EU may have a negative effect on global economic conditions, financial markets and our business. Following a national referendum and enactment of legislation by the government of the UK, the UK formally withdrew from the EU on January 31, 2020. Since the end of the Brexit transition period on January 1, 2021, Great Britain (England, Scotland and Wales) has not been directly subject to EU law and has operated under a separate regulatory regime to the EU. It is currently unclear to what extent the UK Government will seek to align its regulations with the EU. EU law which has been transposed into UK law through secondary legislation still remains applicable in Great Britain ~~.~~ **,** ~~However~~ **however** , **new** ~~under the Retained~~ EU **legislation such as the CTR is not applicable in Great Britain post** ~~Law (Revocation and Reform) Bill 2022, a targeted number of EU~~ - **Brexit** ~~derived laws will be revoked in 2023~~ . While the UK has indicated a general intention that new laws regarding the development, manufacture and commercialization of medicinal products in the UK will align closely with EU law, there remain limited detailed proposals for the future regulation of medicinal products. Under the terms of the Ireland / Northern Ireland Protocol, EU law still generally applies to Northern Ireland. However, on February 27, 2023 **,** the UK Government and the **EC** ~~European Commission~~ reached a political agreement in the " Windsor Framework " to address discrepancies in the Protocol' s operation. This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA will be responsible for approving all medicinal products destined for the UK market (i. e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK- wide MA will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. The Windsor Framework was approved by the EU- UK Joint Committee on March 24, 2023, so the UK government and the EU will enact legislative measures to bring it into law. On June 9, 2023, the MHRA announced that the medicines aspects of the Windsor Framework will apply from January 1, 2025. ~~New EU legislation such as the (EU) CTR is not applicable in Great Britain post- Brexit.~~ Whilst the EU- UK Trade and Cooperation Agreement (TCA) includes the mutual recognition of ~~Good Manufacturing Practice (~~ GMP ~~)~~ inspections of

manufacturing facilities for medicinal products and GMP documents issued, it does not contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards. There may be divergent local requirements in Great Britain from the EU in the future, which may impact clinical and development activities that occur in the UK. Similarly, clinical trial submissions in the UK will not be able to be bundled with those of EU Member States within the EMA Clinical Trial Information System ~~(~~**, or** CTIS ~~)~~. Any divergences may increase the cost and complexity of running our business, including with respect to the conduct of clinical trials. ~~99Since~~ -- **Since** a significant proportion of the regulatory framework in the UK applicable to our business and our product candidates is derived from EU directives and regulations, the withdrawal could continue to impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK. Great Britain is no longer covered by the EU' s procedures for the grant of MA (Northern Ireland is **for now** covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). A separate MA is required to market ~~drugs~~ **medicinal products** in Great Britain. Such changes could increase our costs and otherwise adversely affect our business. Any delay in obtaining, or an inability to obtain regulatory approvals, as a result of Brexit or otherwise, may prevent us from commercializing our product candidates in Great Britain and restrict ~~our~~ **105our** ability to generate revenue and achieve or sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in Great Britain for our product candidates, which could significantly and materially harm our business. Any further changes in relation to international trade, tariff and import / export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non- tariff barriers on us. These developments, or the perception that any of them could occur, may reduce global trade and, in particular, trade between the impacted nations and the UK. It is unclear what financial, regulatory and legal implications the withdrawal of the UK from the EU will have in the long- term and how such withdrawal will affect us, and the full extent to which our business could be adversely affected. Risks Related to ~~the Acquisition of Xinvento B. V. We may fail to realize the anticipated benefits of our acquisition of Xinvento B. V., those benefits may take longer to realize than expected, and we may encounter significant integration difficulties. In February 2023, in order to expand our pipeline and build on our focus on rare endocrinology diseases, we acquired Xinvento B. V., a Netherlands- based biotech company focused on developing therapies for congenital hyperinsulinism (CHI). We expect that the integration process will be complex, costly and time- consuming. As a result, we are devoting, and will continue to be required to devote, significant management attention and resources to integrating Xinvento B. V. into our business. The integration process may be disruptive to our business and the expected benefits may not be achieved within the anticipated time frame, or at all. The Xinvento B. V. intellectual property may not have the scientific value and commercial potential which we envision. We may not be able to integrate the two businesses successfully, and we could assume unknown or contingent liabilities. It is possible that the integration process could result in the diversion of our management' s attention, the disruption or interruption of, or the loss of momentum in, our ongoing business or inconsistencies in standards, controls, procedures and policies, any of which could adversely affect our ability to maintain relationships with third parties or the ability to achieve the anticipated benefits of the acquisition of Xinvento B. V., or could otherwise adversely affect our business and financial results. We do not anticipate generating revenue from any Xinvento B. V. therapeutic candidate or technology sales for many years. We do not expect to derive revenue from the sale of any Xinvento B. V. therapeutic candidate or technology for many years, if at all, and there can be no assurance that regulatory approvals will be received or if received that they will be received when anticipated. Risks Related to~~ Employee Matters and Managing GrowthOur future success depends on our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel. We are highly dependent on our executive leadership team. We have employment agreements with these individuals **,** but any individual may terminate his or her employment with us at any time. The loss of their services might impede the achievement of our research, development and commercialization objectives. We also do not have any ~~100key~~ **key** - person life insurance on any of these key employees. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us and may not be subject to non- compete agreements. Recruiting and retaining qualified scientific ~~personnel~~ **, technical, clinical development, regulatory,** and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel. **In addition, we rely on existing employment- related visa programs to attract and retain qualified personnel. Immigration policy changes and uncertainty associated with the new presidential administration in the United States, including potential changes to the number of employment- related visas available as well as the process to obtain them, could make it more difficult to retain existing personnel and to recruit qualified candidates. If we and our impacted candidates or employees are unable to obtain work visas in sufficient quantities or at a sufficient rate for a significant period of time, our business could be adversely affected.** We will need to develop and expand our ~~company~~ **Company** , and we may encounter difficulties in managing this development and expansion, which could disrupt our operations. We expect to increase our number of employees and the scope of our operations. In particular, we will need to **continue our** transition from a research and development **focused** company to a commercial **- stage** company. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from their day- to- day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in

weaknesses in our infrastructure, and give rise to operational mistakes, loss of business and commercial opportunities, loss of employees and reduced productivity among remaining employees. **We may not be able to successfully recruit the personnel we require to operate and expand our business, including our expansion into new countries and markets due to a number of factors, including a lack of understanding of local employment practices, cultural barriers, low or no brand recognition as a desired employer or place to work, or the perceived risk of joining a company with a limited operating history.** If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. ~~The~~ **106The** physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of setmelanotide and our other product candidates. Many of our suppliers and collaborative and clinical trial relationships are located outside the United States, and we **have and** may **continue** ~~in the future seek~~ to hire employees located outside of the United States. Accordingly, our business **has and** may ~~become~~ **continue to be** subject to economic, political, regulatory and other risks associated with international operations, such as compliance with tax, employment, immigration and labor laws for employees living or traveling abroad, workforce uncertainty in countries where labor unrest is more common than in the United States, as well as difficulties associated with staffing and managing international operations, including differing labor relations. Any of these factors could materially affect our business, financial condition and results of operations. Our future financial performance and our ability to commercialize our approved products and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our ~~company~~ **Company** . Our information technology systems, or those of our third- party CROs, CMOs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of setmelanotide **and other product candidate** development programs, regulatory investigations, enforcement actions and lawsuits. In the ordinary course of our business, we **produce,** collect **, process** and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers, as well as personally identifiable information **, including** of **our** employees. Similarly, our third- party CROs, CMOs and other contractors and consultants possess certain **amounts** of our sensitive data. ~~The~~ **We have implemented and maintain an array of physical, administrative and technical controls to ensure the confidentiality, integrity and availability of such sensitive information, and the** secure maintenance of this information is material to our operations and business strategy. ~~Despite~~ **Even with** the implementation of **strong** security measures, our information technology systems and those of our third- party CROs, CMOs and other contractors and consultants are ~~vulnerable~~ **susceptible** to attack, damage, or interruption ~~by hacking,~~ **from computer security incidents and** cyberattacks **such as** ~~, computer viruses and~~ malware (e. g. **,** ransomware), ~~malicious code,~~ phishing ~~attacks~~ and other social engineering **attacks** ~~schemes, unauthorized access, natural disasters, terrorism, telecommunication and electrical failures,~~ employee **or contractor** theft ~~or~~ **,** misuse ~~,~~ **or** human error, ~~fraud,~~ denial or degradation of service attacks, ~~sophisticated~~ **supply chain attacks, advanced persistent threats from** nation- state ~~and nation- state- supported~~ actors ~~or~~ **and** unauthorized access or use by persons inside **or outside** our organization ~~,~~ **. As a result of** ~~or~~ **our** ~~persons with~~ **hybrid work environment, we also face increased cybersecurity risks due to employees** ~~access~~ **accessing** ~~to systems inside~~ **company resources from insecure networks, and using personal (i. e., " bring-** ~~our~~ **your** ~~organization~~ **- own- device ") or unmanaged devices which often lack enterprise-grade security controls and all of which creates additional opportunities for cybercriminals to exploit vulnerabilities and use social engineering techniques to carry out a cyberattack** . Any such attack, incident or breach could compromise our information technology systems ~~and the~~ **which may result in sensitive** information **being** ~~stored there could be~~ accessed, publicly disclosed, lost, corrupted or stolen. Further, **cyberattacks** ~~attacks upon information technology systems~~ are increasing in their frequency, ~~levels of~~ persistence, sophistication and intensity, **often** ~~and are being~~ conducted by ~~sophisticated and~~ organized **and well- funded criminal** groups ~~and individuals~~ with a wide range of motives and expertise. **Consequently** ~~As a result of the continued hybrid work enviornment , we may also face 101increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Because the techniques used to obtain unauthorized access to, or~~ **our security controls may** ~~to sabotage, systems change frequently and often are~~ not **always prevent** ~~recognized until launched against~~ a ~~target~~ **targeted cyberattack** , **and a** ~~we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that~~ **threat actor** may remain undetected **in our systems** for an extended period **of time** . **There can** ~~Even if identified, we may~~ be **no assurance that** ~~unable to adequately investigate or~~ **our** ~~remediate incidents~~ **cybersecurity risk management program and processes, including** ~~or~~ **our policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems and information. We maintain cyber liability insurance; however, it may not be sufficient to cover the financial, legal, business or reputational losses that may result from a service interruption or** ~~breaches~~ **breach** ~~due to attackers~~ **of our systems. The global healthcare industry is** increasingly ~~using~~ **integrating AI technologies and** tools ~~and techniques that~~ **. However, like any emerging technology, AI presents its own set of risks, many of which** are **not yet known or fully understood.** ~~designed to circumvent controls, to avoid detection, and to remove or~~ **For** ~~obfuscate forensic evidence~~ **example, AI algorithms may have inherent flaws, and data sets could be insufficient, low- quality, or biased. Additionally, inappropriate or controversial data practices by data scientists, engineers, and end- users could compromise results of AI processes. If AI applications generate flawed or inaccurate analyses or date, it could lead to competitive disadvantages, legal liabilities, and harm to our brand or reputation. Furthermore, the use of AI- based software might result in the inadvertent release of confidential information** . The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification, some also require implementation of reasonable security measures and provide a private right of action in the event of a breach. Costs of breach response, mitigation,

investigation, remediation, notice and ongoing assessments can be considerable. Thus, any access, disclosure, damage or other loss of information, including our data being breached at our partners or third- party providers, could result ~~in~~ **107in** legal claims or proceedings and liability under state, federal and international privacy laws, disruption of our operations, and damage to our reputation, which could adversely affect our business. We ~~and certain of our service providers~~ have ~~been~~ **put into place safeguards with technology, process** and **education** ~~from time~~ to ~~time will continue~~ **mitigate the risks inherent in our information technology systems and** to **defend against** ~~be subject to~~ cyberattacks and security incidents. ~~While~~ **Although** we do not believe that we have experienced any significant system failure, accident or security breach to date, **including any significant or material cyberattacks and / or other information technology security incidents,** if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs **and material harm to our business and reputation** . For example, the **breach or** loss of clinical trial data for setmelanotide or other product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of setmelanotide and our product candidates could be delayed **or prevented** . It could also expose us to risks, including an inability to provide our services and fulfill contractual demands, and could cause management distraction and the obligation to devote significant financial and other resources to mitigate such problems, which would increase our future information security costs, including through organizational changes, deploying additional personnel, reinforcing administrative, physical and technical safeguards, further training of employees, changing third- party vendor control practices and engaging third- party subject matter experts and consultants and reduce the demand for our product and services. ~~We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems. There can be no assurance that our cybersecurity risk management program and processes, including our policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems and information.~~ Risks Related to Our Common StockOur directors and executive officers and their affiliated entities own a significant percentage of our stock and, if they choose to act together, will be able to exert significant influence over matters subject to stockholder approval. Our executive officers and directors and their respective affiliates, in the aggregate, hold shares representing approximately 5. ~~5~~ **2** % of our outstanding voting stock as of December 31, ~~2023~~ **2024** . As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders could significantly influence elections of directors, any amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. ~~102Anti- takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. We are a Delaware corporation. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15 % of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively will provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. Any provision in our amended and restated certificate of incorporation and amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.~~ Market volatility may affect our stock price and the value of your investment. The market price for our common stock has been volatile and may continue to fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others: ● plans for, progress of, or results from preclinical studies and clinical trials of setmelanotide and our other product candidates; ● the failure of the FDA or EMA to approve IMCIVREE for additional indications **or to initially approve our other product candidates** ; ● announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors; ● the success or failure of other weight loss therapies and companies targeting **the** rare diseases ~~and orphan drug treatment~~ **we intend to address** ; ● regulatory or legal developments in the United States and other countries; ● failure of setmelanotide or our other product candidates, if approved, to achieve commercial success; **108** ● fluctuations in stock market prices and trading volumes of similar companies; ● general market conditions and overall fluctuations in U. S. equity markets; ● global macroeconomic conditions **or instability** , including with respect to inflation rates or interest rates, **curtailment of trade and other business restrictions such as tariffs, boycotts,** labor shortages, supply chain shortages, disruptions and instability in the banking industry and other parts of the financial services sector, **outbreak of disease or epidemics,** or other economic, political or legal **changes,** uncertainties or adverse developments; ● terrorism and / or political instability, unrest and wars, such as the conflicts involving Ukraine and Russia or Israel and Hamas, which could delay or disrupt our business, and if such political unrest escalates or spills over to or otherwise impacts additional regions it could heighten many of the other risk factors included in this sections; ~~103~~ ● natural disasters **and other extreme weather events** (including as a result of climate change), which could cause significant damage to the infrastructure upon which our business operations rely, and the timing, nature or severity of which we may be unable to prepare for; ● ~~economic instability~~ **global**

**political changes and uncertainty** , ~~outbreak of disease~~ **including in the United States with the changes arising from a new presidential administration and resulting changes and uncertainty in administrative agencies with authority over** ~~or~~ **our** ~~epidemics such as the COVID- 19 pandemic, boycotts, curtailment of trade and other~~ business ~~restrictions~~ ; ● variations in our quarterly operating results; ● changes in our financial guidance or securities analysts' estimates of our financial performance; ● changes in accounting principles; ● our ability to raise additional capital and the terms on which we can raise it; ● sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders; ● additions or departures of key personnel; ● discussion of us or our stock price by the press and by online investor communities; and ● other risks and uncertainties described in these risk factors. Our quarterly operating results may fluctuate significantly. We expect our operating results to be subject to quarterly fluctuations **, which may be significant and difficult to anticipate over time** . Our net loss and other operating results will be affected by numerous factors, including: ● variations in the level of expenses related to our development programs; ● addition or termination of clinical trials; ● any **lawsuit, including any** intellectual property infringement lawsuit in which we may become involved; **109** ● regulatory developments affecting setmelanotide and our other product candidates; ● our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements; ● the achievement and timing of milestone payments under our existing collaboration and license agreements; and ● the level of underlying demand for setmelanotide and **our** customers' buying patterns. If our quarterly operating results fall below the expectations of investors or securities analysts **for any given quarter** , the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. ~~104Our~~ **Our** ability to use certain net operating loss carryovers and other tax attributes may be limited. Under the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year, and can use such NOLs to offset future taxable income, if any, until such losses are used or, for NOLs arising in taxable years ending on or before December 31, 2017, until such NOLs expire. Other unused tax attributes, such as research tax credits may also be carried forward to offset future taxable income, if any, until such attributes are used or expire. As of December 31, ~~2023~~ **2024** , we had approximately $ ~~555~~ **610** . ~~6~~ **2** million and $ ~~598~~ **694** . 0 million of unused federal and state NOL carryforwards, respectively, and approximately $ 13. ~~1~~ **8** million and $ ~~3~~ **4** . 8 million of unused federal and state carryforwards of research tax credits, respectively. Of the federal NOL carryforwards at December 31, ~~2023~~ **2024** , $ ~~482~~ **537** . ~~4~~ **2** million can be carried forward indefinitely ~~, while $ 73. 2 million will begin to expire in 2033~~ . Additionally, as of December 31, ~~2023~~ **2024** , we had federal orphan drug credits related to qualifying research of $ ~~25~~ **34** . ~~5~~ **6** million. If a corporation undergoes an " ownership change, " very generally defined as a greater than 50 % change by value in its equity ownership by certain shareholders or groups of shareholders over a rolling three- year period, Sections 382 and 383 of the Code limit the corporation' s ability to use carryovers of its pre- change NOLs, credits and certain other tax attributes to reduce its tax liability for periods after the ownership change. Our issuance of common stock pursuant to prior public offerings may have resulted in a limitation under Code Sections 382 and 383, either separately or in combination with certain prior or subsequent shifts in the ownership of our common stock. Future changes in our stock ownership, some of which are outside of our control, could also result in an ownership change under Sections 382 and 383 of the Code. In addition, for taxable years beginning after December 31, 2020, utilization of federal NOLs generated in tax years beginning after December 31, 2017 are limited to a maximum of 80 % of the taxable income for such year, after taking into account utilization of NOLs generated in years beginning before January 1, 2018 and determined without regard to such NOL deduction. Further regulatory changes could also ~~limited~~ -- **limit** our ability to utilize our NOLs. As a result, our ability to use carryovers of NOLs and credits to reduce our future U. S. federal income tax liability may be subject to limitations. This could result in increased U. S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. Any such limitation could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 or 383 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study. The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods. We do not expect to generate positive taxable income in the near future and we may never achieve tax profitability. Substantial future sales or perceived potential sales of our common stock in the public market could cause the price of our common stock to decline significantly. Sales of our common stock in the public market, or the perception that these sales could occur, could cause the market price of our common stock to decline significantly. As of December 31, ~~2023~~ **2024** , we had ~~59~~ **62** , ~~426~~ **390** , ~~559~~ **654 shares of common 110stock outstanding. In addition, on July 10, 2023, we filed with the SEC a prospectus supplement to the prospectus included in the Company' s registration statement on Form S- 3ASR filed with the SEC on March 2, 2023, covering the resale from time to time by the holders of the Convertible Preferred Stock of up to an aggregate of 3, 124, 995** shares of common stock ~~outstanding~~ **, to satisfy registration rights that the Company granted to such holders in connection with the issuance of the Convertible Preferred Stock. To the extent the holders of the Convertible Preferred Stock convert their shares to common stock and sell such shares, the price of our common stock could be significantly impacted** . We may be at an increased risk of securities **litigation, including** class action litigation. Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years **and have an increased risk of securities litigation, including class action litigation** . If we were to be sued, it could result in substantial costs and a diversion of management' s attention and resources, which could harm our business. We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock. We have never declared or paid any cash dividends on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the

development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. **Additionally, our Convertible Preferred Stock ranks senior to the shares of the Company' s common stock, with respect to the payment of dividends and the distribution of assets upon a liquidation, dissolution or winding up of the Company. Holders of the Convertible Preferred Stock will be entitled to a regular dividend at a rate as specified in the Amended and Restated Certificate of Designations filed by the Company with the Secretary of State of the State of Delaware.** Therefore, ~~105the~~ **the** success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them. **Our common stock is subordinated to our Convertible Preferred Stock. In connection with the closing of our Investment Agreement, the Company issued 150, 000 shares of a new series of the Company' s Convertible Preferred Stock for an aggregate purchase price of $ 150. 0 million, or $ 1, 000 per share. The Convertible Preferred Stock ranks senior to the shares of the Company' s common stock, with respect to the payment of dividends and the distribution of assets upon a liquidation, dissolution or winding up of the Company. The Convertible Preferred Stock has an initial liquidation preference of $ 1, 000 per share; provided that the liquidation preference in dissolution or upon a change of control shall be increased to be 175 % of the then applicable liquidation preference, as described in the Amended and Restated Certificate of Designations. The Convertible Preferred Stock is convertible into shares of our common stock at the option of the holders thereof subject to the terms of the Amended and Restated Certificate of Designations. Additionally, holders of the Convertible Preferred Stock generally will be entitled to vote with the holders of the shares of our common stock, subject to certain restrictions pursuant to the terms of the Amended and Restated Certificate of Designations, on all matters submitted for a vote of holders of shares of our common stock (voting together with the holders of shares of our common stock as one class) on an as- converted basis, subject to certain ownership limitations. On May 7, 2024, the Company filed an Amended and Restated Certificate of Designations in respect of the Convertible Preferred Stock containing certain technical amendments to the terms of the Convertible Preferred Stock. The amendments contained in the Amended and Restated Certificate of Designations (x) limited the voting rights of the Convertible Preferred Stock to 24. 9438 shares of the Company' s common stock per $ 1, 000 liquidation preference of Convertible Preferred Stock and (y) eliminated a 1 % step up in the interest rate that otherwise would have applied in the unlikely event that the Company was required to obtain and failed to obtain stockholder approval for certain conversion shares underlying the Convertible Preferred Stock. Additionally, certain matters will require the approval of the holders of two- thirds of the outstanding Convertible Preferred Stock, voting as a separate class, including (1) the authorization, creation, increase in 111the authorized amount of, or issuance of any class or series of senior or pari passu equity securities or any security convertible into, or exchangeable or exercisable for, shares of senior or pari passu equity securities, (2) amendments, modifications or repeal of any provision of the Company' s charter or of the Amended and Restated Certificate of Designations that would adversely affect the rights, preferences or voting powers of the Convertible Preferred Stock, and (3) certain business combinations and binding or statutory share exchanges or involving the Convertible Preferred Stock unless such events do not adversely affect the rights, preferences or voting powers of the Convertible Preferred Stock. In the future, we may make additional offerings of debt or preferred equity securities, including convertible or non- convertible senior or subordinated notes, convertible or non- convertible preferred stock, medium- term notes and trust preferred securities, to raise cash or bolster our liquidity, to refinance indebtedness, for working capital, to finance strategic initiatives and future acquisitions or for other purposes. Upon liquidation, holders of our debt securities and shares of preferred stock and lenders with respect to other borrowings may receive distributions of our available assets prior to the holders of our common stock. In addition, any preferred stock we may issue could have a preference on liquidating distributions or a preference on distribution payments that could limit our ability to make a distribution to the holders of our common stock. Since our decision to issue securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing or nature of our future offerings. Thus, our stockholders bear the risk of our future offerings reducing the market price of our common stock.** Provisions in our certificate of incorporation and bylaws and Delaware law might discourage, delay or prevent a change in control of our ~~company~~ **Company** or changes in our management and, therefore, depress the market price of our common stock. Our certificate of incorporation and bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our ~~company~~ **Company** or changes in our management that the stockholders of our ~~company~~ **Company** may deem advantageous. These provisions, among other things: ● establish a classified board of directors so that not all members of our board are elected at one time; ● permit only the board of directors to establish the number of directors and fill vacancies on the board; ● provide that directors may only be removed " for cause " and only with the approval of two- thirds of our stockholders; ● authorize the issuance of " blank check " preferred stock that our board could use to implement a stockholder rights plan (also known as a " poison pill "); ● eliminate the ability of our stockholders to call special meetings of stockholders; ● prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders; ● prohibit cumulative voting; ● authorize our board of directors to amend the bylaws; ● establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and ● require a super- majority vote of stockholders to amend some provisions described above. In addition, Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, prohibits a publicly- held Delaware corporation from engaging in a business combination with an interested stockholder, generally a ~~person~~ **112person** which together with its affiliates owns, or within the last three years has owned, 15 % of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Any provision of our certificate of incorporation, bylaws or Delaware law that has the effect of delaying or

preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock. Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders and our bylaws designate the federal district courts of the United States as the exclusive forum for actions arising under the Securities Act, which could limit our stockholders' ability to obtain ~~a favorable~~ **an alternate preferred** judicial forum for disputes with us or our directors, officers or employees. Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of ~~106fiduciary~~ --- **fiduciary** duty; (iii) any action asserting a claim against us arising under the DGCL, our certificate of incorporation or our bylaws; and (iv) any action asserting a claim against us that is governed by the internal affairs doctrine. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to the provisions of our certificate of incorporation and bylaws described above. These exclusive- forum provisions may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find these provisions of our certificate of incorporation or bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business. General Risk FactorsWe **have in the past and** may **in the future** acquire businesses or products, form strategic alliances or create joint ventures in the future, and we may not realize their benefits. We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. ~~If~~ **For example, in February 2023, in order to expand our pipeline and build on our focus on rare endocrinology diseases, we acquired Xinvento B. V., a Netherlands- based biotech company focused on developing therapies for CHI. As** we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance, joint venture or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction. An active market for our common stock may not be maintained. Our stock began trading on the Nasdaq Global Market in October 2017 and we can provide no assurance that we will be able to continue to maintain an active trading market on the Nasdaq Global Market or any other exchange in the future. If an active market for our common stock is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration. ~~If~~ **113If** securities or industry analysts do not continue to publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline. The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not control these analysts. If we lose securities or industry analysts coverage of our ~~company~~ **Company** , the trading price for our stock would be negatively impacted. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts issues unfavorable commentary or ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline. Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights. We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. ~~To the extent that~~ **From time to time,** we **may** raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, **such as our sale of Convertible Preferred Stock under the Investment Agreement, which did cause in the case of the Investment Agreement and may cause in the future** a stockholder' s ownership interest in our ~~company~~ **Company** ~~will~~ **to** be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable ~~107rights~~ --- **rights** to setmelanotide, our intellectual property or future revenue streams, or grant licenses on terms that are not favorable to us. **See above, under the heading " Our common stock is subordinated to our Convertible Preferred Stock. "** Unfavorable global political or economic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global **political system,** economy and in the global financial markets. The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates ~~and~~ **,** uncertainty about economic stability **, and rising political uncertainty** . A severe or prolonged economic downturn or recession and a continued increase in inflation rates or interest rates could result in a variety of risks to our business, including weakened demand for setmelanotide and our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Increased inflation rates and related increases in interest rates can adversely affect us by increasing our costs, including labor and employee benefit costs. In

addition, geopolitical conflicts and war could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the **United States** ~~U. S.~~, the EU or Russia (e. g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and / or our supply chain, our CROs, CMOs and other third parties with which we conduct business. **The changes arising from a new presidential administration in the United States and the prospect of new leadership in key administrative agencies (such as the FDA and SEC) as well as volatile political conditions in other countries in which we do business could also create additional uncertainty for our industry and our business, including in ways that we cannot foresee.** Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. Business interruptions could adversely affect our operations. Our operations are vulnerable to interruption by fire, severe weather conditions, power loss, telecommunications failure, terrorist activity, public health crises and pandemic diseases, ~~such as COVID- 19,~~ and other natural and man- made disasters or events ~~beyond~~ **114beyond** our control. Our facilities **and employees** are located in regions that experience severe weather from time to time. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major tornado, flood, fire, earthquake, power loss, terrorist activity, public health crisis, pandemic diseases or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We have incurred and will continue to incur substantial costs as a result of operating as a public company, our management will continue to devote substantial time to **existing and** new compliance initiatives and corporation governance policies, and we will need to hire additional qualified accounting ~~and~~ **,** financial **, legal and compliance** personnel with appropriate public company experience. As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will continue to devote a substantial amount of time to these compliance initiatives and we will need to continue to hire **and retain** additional accounting ~~and~~ **,** financial **, legal and compliance** personnel with appropriate public company experience and technical accounting **and securities laws** knowledge. Even if we are able to hire appropriate personnel, our existing operating expenses and operations will be impacted by the direct costs of their employment and the indirect consequences related to the diversion of management resources from product development **and commercialization** efforts. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and make some activities more time consuming and costly. ~~108These~~ --- **These** rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in future uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. ~~If we~~ **We have in the past failed and may in the future** fail to maintain an effective system of internal control over financial reporting ~~, we~~ **. This** may **prevent us from** ~~not be able to~~ accurately ~~report~~ **reporting** our financial results or ~~prevent~~ **preventing** fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock. Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations ~~. As described further below below, we have identified a material weakness in our internal control over financial reporting. Any testing by us conducted in connection with Section 404, or any testing by our independent registered public accounting firm, may reveal additional deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement~~ . Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. To continue to achieve and maintain compliance with Section 404, we engage in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, from time to time we may not be able to conclude that our internal control over financial reporting is effective as required by Section 404, as ~~is~~ **was** the case **for the year ended December 31, 2023 and quarterly periods** in **2024** ~~this Annual Report on Form 10- K~~ , due to ~~the~~ **a** material weakness identified **in internal controls related to ineffective information technology general controls in the areas of user access** and ~~described below~~ **program change management over our key accounting and reporting information technology system** . Additionally, the material weakness in our internal control over financial reporting ~~has~~ resulted in our management being unable to conclude ~~, and any additional material weakness in our internal control over financial reporting may in the future result in our management being unable to conclude,~~ that our disclosure controls and procedures were effective for the applicable period. ~~In~~ **The material weakness has since been remediated; however, additional material weaknesses may arise in the future. 115In** addition ~~, as we no longer qualify as a non- accelerated filer~~ , we are required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. If we are unable to maintain effective internal control over financial reporting, we may not have adequate, accurate or timely financial information, our independent registered

public accounting firm may issue a report that is adverse, as it ~~has~~ **did** in ~~this~~ **our** Annual Report on Form 10- K **for the year ended December 31, 2023** . A material weakness could result in a restatement of our financial statements, failure to meet our reporting obligations in a timely manner, the imposition of sanctions, including the inability of registered broker dealers to make a market in our common stock, or investigation by regulatory authorities. Any such action or other negative results caused by our inability to meet our reporting requirements or comply with legal and regulatory requirements or by disclosure of an accounting, reporting or control issue could adversely affect the trading price of our securities and our business. Ineffective internal control over financial reporting could also reduce our ability to obtain financing or could increase the cost of any financing we obtain. Any of these could, in turn, result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. We have **previously** identified a material weakness in our internal controls over financial reporting and may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, which may result in material misstatements of our consolidated financial statements or cause us to fail to meet our periodic reporting obligations. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company' s annual or interim financial statements will not be prevented or detected on a timely basis. We **previously** identified a material weakness in internal control related to ineffective information technology general controls ~~(“~~ **, or** ITGCs **,** ~~”)~~ in the areas of user access and program change management over our key accounting and reporting information technology ~~(“~~ **, or** IT **,** ~~”)~~ system. As a result, the related ~~109business~~ **business** process controls (specifically, the IT application controls and IT- dependent manual controls) that are dependent on the ineffective ITGCs, or that use data produced from the system impacted by the ineffective ITGCs, were also ineffective. Although the material weakness identified above did not result in any material misstatements in our consolidated financial statements for the periods presented and there were no changes to previously released financial results, our management concluded that these control deficiencies constitute a material weakness and that our internal control over financial reporting was not effective as of December 31, 2023. Our management **designed** ~~, under the oversight of the Audit Committee of our Board of Directors~~ and ~~in consultation with outside advisors, has begun evaluating and implementing~~ **implemented new controls and** measures ~~designed to remediate the material weakness. In particular, we are taking steps~~ to remediate this material weakness ~~by (i) developing and implementing additional training and awareness programs addressing ITGCs and policies~~ , ~~including educating control owners concerning the principles~~ and ~~requirements of each control, with a focus on user access; (ii) increasing the extent of oversight and verification checks included in the operation of user access and program change management controls and processes; (iii) deploying additional tools to support administration of user access and program change management; and (iv) enhancing quarterly management reporting on the remediation measures to the Audit Committee of the Board of Directors. The above controls need to operate for a sufficient period of time so that management can conclude that our controls are operating effectively. As such, the material weakness will not be considered remediated until~~ management has concluded ~~through the implementation of these remediation measures and additional testing~~ that ~~these~~ **the controls are effective. Additionally, a** material ~~weakness~~ **weaknesses described** ~~in our internal control over financial reporting has resulted in our management being unable to conclude, and any additional material weakness in our internal control over financial reporting may in the future result in our management being unable to conclude, that our disclosure controls and procedures were effective for the applicable period. We are designing and implementing new controls and measures to remediate this material weakness as noted~~ above **have been remediated** . However, we cannot assure you that the measures we are taking will be sufficient to ~~remediate the material weakness or~~ avoid the identification of additional material weaknesses in the future. Our failure to implement and maintain effective internal control over financial reporting could result in errors in our consolidated financial statements that could result in a restatement of our financial statements and could cause us to fail to meet our periodic reporting obligations, any of which could diminish investor confidence in us and cause a decline in the price of our common stock. The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results. There has been increasing public focus by investors, customers, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. ~~In the future~~ **We have undertaken certain initiatives** , ~~we~~ **including disclosures, to improve the sustainability profile of our products and / or operations and respond to stakeholder expectations; however, such initiatives** may ~~engage in~~ **be costly and may not have the desired effect. For example,** sustainability- related initiatives **are often based on methodologies, standards, or data that are still evolving** and ~~voluntary~~ **subject to varying interpretations. We cannot guarantee that our approach, either now or in future, will align with the expectations of particular stakeholders or that certain** disclosures **will not** ~~or commitments, which may~~ be **considered erroneous** ~~costly and may not have the desired effect. We may experience increased costs in order to execute upon our~~ **or subject to misinterpretation** ~~sustainability goals and measure achievement of those goals, which could have a materially adverse impact on our business and financial condition~~ . In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. **Such** ~~If we fail to comply with new laws, regulations or reporting~~ requirements ~~, our reputation~~ and ~~business could~~ **other expectations are not uniform, and may** be **116** ~~adversely impacted. Moreover, our actions may subsequently be determined to be insufficient by various stakeholders, and we may be subject to investor or regulator engagement or activism. Additionally, many of our business partners and suppliers may be subject to similar reporting and stakeholder expectations, which may augment or create additional risks, including risks that may not be known to us. Short sellers of our stock may be manipulative and may drive down the market price of our common stock. Short selling is the practice of selling securities that~~

the seller does not own, but rather has borrowed or intends to borrow from a third party with the intention of buying identical securities at a later date to return to the lender. A short seller hopes to profit from a decline in the value of the securities between the sale of the borrowed securities and the purchase of the replacement shares, as the short seller expects to pay less in that purchase than it received in the sale. It is 110