



## Rhythm Pharmaceuticals Announces First Patient Dosed in Phase 1 Trial Evaluating RM-718, a Weekly MC4R-specific Agonist

March 25, 2024

*-- Three-part study to evaluate safety, tolerability and pharmacokinetics now underway --*

*-- RM-718 showed potential to reduce body weight and hyperphagia, no hyperpigmentation observed in preclinical studies --*

BOSTON, March 25, 2024 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company focused on transforming the lives of patients and their families living with rare neuroendocrine diseases, today announced that the first patients have been dosed in the Company's Phase 1 clinical trial of RM-718, an investigational, weekly melanocortin-4 receptor (MC4R)-specific agonist designed to be MC1R-sparing and to potentially avoid hyperpigmentation.

"We are excited to begin clinical development of RM-718, our next-generation MC4R agonist," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "Based on encouraging preclinical data, we believe RM-718 has the potential to reduce hyperphagia – a pathological hunger that leads to abnormal food-seeking behavior – and treat severe obesity, which are the two hallmark symptoms of rare MC4R pathway diseases. In addition, RM-718 was designed to provide a weekly dosing regimen and to avoid hyperpigmentation."

This [Phase 1](#) trial is a three-part study to evaluate safety, tolerability and pharmacokinetics (PK). The study consists of Part A: single ascending doses (SAD) of RM-718 in healthy participants 18 to 55 years old with obesity; Part B: multiple ascending doses (MAD) of RM-718 in healthy participants 18 to 55 years old with obesity; and Part C: MAD of RM-718 in patients 12 to 65 years old with hypothalamic obesity. Cohorts in Parts A and B are double-blind, placebo-controlled, and randomized 2:1. Study participants will receive one weekly dose of either RM-718 or placebo in Part A, four weekly doses of either RM-718 or placebo in Part B, and four weekly doses of open-label RM-718 in Part C. RM-718 or placebo doses are administered weekly via subcutaneous injection. The anticipated enrollment for this study is 96 participants.

### **About RM-718**

RM-718 is an investigational, weekly, MC4R-specific agonist that has demonstrated the potential to reduce body weight and hunger in preclinical studies. RM-718 is designed to be highly selective and MC1R-sparing and thereby not cause hyperpigmentation.

### **About Rhythm Pharmaceuticals**

Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with rare neuroendocrine diseases. Rhythm's lead asset, IMCIVREE<sup>®</sup> (setmelanotide), an MC4R agonist designed to treat hyperphagia and severe obesity, is approved by the U.S. Food and Drug Administration (FDA) for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency confirmed by genetic testing, or patients with a clinical diagnosis of Bardet-Biedl syndrome (BBS). Both the European Commission (EC) and the UK's Medicines & Healthcare Products Regulatory Agency (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. Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare diseases, as well as investigational MC4R agonists LB54640 and RM-718, and a preclinical suite of small molecules for the treatment of congenital hyperinsulinism. Rhythm's headquarters is in Boston, MA.

### **Setmelanotide Indication**

In the United States, setmelanotide is indicated 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 (VUS) or BBS.

In the European Union, setmelanotide is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. In Europe, setmelanotide should be prescribed and supervised by a physician with

expertise in obesity with underlying genetic etiology.

### Limitations of Use

Setmelanotide is not indicated for the treatment of patients with the following conditions as setmelanotide would not be expected to be effective:

- Obesity due to suspected POMC, PCSK1 or LEPR deficiency with *POMC*, *PCSK1* or *LEPR* variants classified as benign or likely benign
- Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity.

### Contraindication

Prior serious hypersensitivity to setmelanotide or any of the excipients in IMCIVREE. Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported.

### WARNINGS AND PRECAUTIONS

**Skin Pigmentation and Darkening of Pre-Existing Nevi:** Generalized increased skin pigmentation and darkening of pre-existing nevi have occurred because of its pharmacologic effect. Full body skin examinations prior to initiation and periodically during treatment should be conducted to monitor pre-existing and new pigmentary lesions.

**Heart rate and blood pressure monitoring:** In Europe, heart rate and blood pressure should be monitored as part of standard clinical practice at each medical visit (at least every 6 months) for patients treated with setmelanotide.

**Disturbance in Sexual Arousal:** Spontaneous penile erections in males and sexual adverse reactions in females have occurred. Patients who have an erection lasting longer than 4 hours should seek emergency medical attention.

**Depression and Suicidal Ideation:** Depression and suicidal ideation have occurred. Patients should be monitored for new onset or worsening depression or suicidal thoughts or behaviors. Consideration should be given to discontinuing setmelanotide if patients experience suicidal thoughts or behaviors, or clinically significant or persistent depression symptoms occur.

**Hypersensitivity Reactions:** Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported. If suspected, advise patients to promptly seek medical attention and discontinue setmelanotide.

**Pediatric Population:** The prescribing physician should periodically assess response to setmelanotide therapy. In growing children, the impact of weight loss on growth and maturation should be evaluated. In Europe, the prescribing physician should monitor growth (height and weight) using age- and sex-appropriate growth curves.

**Risk of Serious Adverse Reactions Due to Benzyl Alcohol Preservative in Neonates and Low Birth Weight Infants:** Setmelanotide is not approved for use in neonates or infants. Serious and fatal adverse reactions including "gaspings syndrome" can occur in neonates and low birth weight infants treated with benzyl alcohol-preserved drugs.

### ADVERSE REACTIONS

Most common adverse reactions (incidence  $\geq 20\%$ ) included skin hyperpigmentation, injection site reactions, nausea, headache, diarrhea, abdominal pain, vomiting, depression, and spontaneous penile erection.

### USE IN SPECIFIC POPULATIONS

**Lactation:** Not recommended when breastfeeding.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch). See section 4.8 of the [Summary of Product Characteristics](#) for information on reporting suspected adverse reactions in Europe.

**Please see the full Prescribing Information for additional Important Safety Information.**

### Forward-looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the potential, safety, efficacy, and regulatory and clinical design or progress, trial enrollment, potential benefits and adverse effects, and potential regulatory submissions, approvals and timing thereof of RM-718. Statements using word such as "expect", "anticipate", "believe", "may", "will" and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including, but not limited to, our ability to enroll patients in clinical trials, the design and outcome of clinical trials, the impact of competition, the ability to achieve or obtain necessary regulatory approvals, risks associated with data analysis and reporting, our ability to successfully commercialize setmelanotide, our liquidity and expenses, our ability to retain our key employees and consultants, and to attract, retain and

motivate qualified personnel, and general economic conditions, and the other important factors discussed under the caption “Risk Factors” in our Annual Report on Form 10-K for the quarter ended December 31, 2023 and our other filings with the Securities and Exchange Commission. Except as required by law, we undertake no obligations to make any revisions to the forward-looking statements contained in this release or to update them to reflect events or circumstances occurring after the date of this release, whether as a result of new information, future developments or otherwise.

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