



Rhythm Pharmaceuticals Announces First Patients Dosed in Phase 2 Trial Evaluating Oral MC4R Agonist LB54640 in Hypothalamic Obesity

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-- LB54640 has shown targeted effect on MC4R without hyperpigmentation --

BOSTON, July 23, 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 2 clinical trial evaluating LB54640, an investigational oral melanocortin-4 receptor (MC4R) agonist, in hypothalamic obesity.

"Based on LG Chem's significant preclinical work and encouraging results from a Phase 1 trial, we believe LB54640 has the potential to be an effective oral therapy for treating MC4R pathway diseases without hyperpigmentation," said David Meeker, M.D., Chair, Chief Executive Officer and President of Rhythm Pharmaceuticals. "We look forward to advancing this molecule 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."

The Phase 2 trial is a randomized, placebo-controlled, double-blind study to assess the effect of LB54640 on safety, weight reduction, hunger, and quality of life in patients 12 years of age and older (N=28) with hypothalamic obesity. Patients will take an oral daily dose of either LB54640 (low, middle, or high dose) or placebo for 14 weeks. The primary endpoint of the study is the change from baseline in body mass index after 14 weeks of treatment, and patients may continue on therapy for up to 52 weeks.

Rhythm entered into a global licensing agreement with LG Chem, Ltd. ("LG Chem") for LB54640 in January 2024. In a Phase 1 trial in healthy overweight adults, LB54640 demonstrated dose-dependent weight reduction and a favorable safety profile with no changes in blood pressure or heart rate observed and no hyperpigmentation observed.

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® (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 “gasping 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. 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 progress of LB54640, the potential timing, payments due, and benefits of the global licensing agreement for LB54640, expectations regarding the design, enrollment, or outcome of clinical trials of LB54640, the ability to reach any net sales or revenue milestones, and obtaining regulatory approvals in connection with the global licensing agreement; and the timing of any of the foregoing. Statements using words such as “expect”, “anticipate”, “believe”, “may”, “will”, “aim” and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including, but not limited to, risks relating to any of the following: 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, data analysis and reporting, failure to identify and develop additional product candidates, the impact of competition, product liability lawsuits, inability to maintain our collaborations, or the failure of these collaborations, our reliance on third parties, intellectual property, 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 general economic conditions on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and the other important factors discussed under the caption “Risk Factors” in Quarterly Report on Form 10-Q for the three months ended March 31, 2024 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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