Rhythm Pharmaceuticals and LG Chem Life Sciences Enter Agreement for Rhythm to Acquire Global Rights to Oral MC4R Agonist LB54640

January 4, 2024

-- LB54640 has shown targeted effect on MC4 receptor without hyperpigmentation --

-- Rhythm to advance LB54640 in two Phase 2 clinical trials --

BOSTON, Jan. 04, 2024 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a global commercial-stage biopharmaceutical company focused on transforming the lives of patients and their families living with rare neuroendocrine diseases, today announced it has 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 businesses, for LB54640, an investigational oral small molecule melanocortin-4 receptor (MC4R) agonist now in Phase 2 clinical trials.

“We are excited to build upon the strong chemistry and early translational work performed by LG Chem, a highly regarded company with deep and broad experience and expertise in the pharmaceutical business. 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 specific therapy for the MC4R without hyperpigmentation or cardiovascular side effects,” said David Meeker, MD, Chair, Chief Executive Officer and President of Rhythm Pharmaceuticals. “We believe Rhythm’s 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 a favorable safety profile in 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 the U.S. Food and Drug Administration for leptin receptor (LEPR) deficiency and proopiomelanocortin(POMC).

Dr. Jeewoong Son, President of LG Chem Life Sciences Company, said, “Rhythm has pioneered the development and global commercialization of the first and best-in-class therapy for patients with hyperphagia and severe obesity associated with diseases like Bardet-Biedl syndrome (BBS), hypothalamic obesity and certain genetically-defined pathway diseases. We believe Rhythm is the ideal partner because of its extensive genetic obesity database, global network of clinical trial sites and investigators, a track record of regulatory successes and - most importantly - because Rhythm values patients and addresses their urgent needs for care.”

Under the terms of the agreement, Rhythm will assume 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 proprotein convertase subtilisin/kexin type 1 (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.

Under the terms of the agreement, Rhythm has agreed to pay LG Chem $40 million in cash and $20 million in Rhythm equity at closing and an additional $40 million in cash 18 months after closing.

Also under the terms of the agreement, Rhythm has agreed to pay LG Chem up to $205 million upon achieving certain regulatory and sales milestones, as well as royalties.

About LG Chem
LG Chem is a leading global chemical company with a diversified business portfolio in the key areas of petrochemicals, advanced materials, and life sciences. The company manufactures a wide range of products from high-value added petrochemicals to renewable plastics, specializing in cutting-edge electronic and battery materials, as well as drugs and vaccines to deliver differentiated solutions for its customers. LG Chem Life Sciences develops, manufactures, and globally commercializes pharmaceutical products, with a focus on Oncology, Immunology, and Metabolic diseases. Our mission is to transform people’s lives through inspiring science and leading innovation. For more information, please visit www.lgchem.com.

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 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 Bardet-Biedl syndrome (BBS) or genetically confirmed loss-of-function biallelic proopiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 6 years of age and above.

Limitations of Use
In the United States and Europe, Setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

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.

WARNINGS AND PRECAUTIONS

Skin Monitoring: Setmelanotide may lead to generalized increased skin pigmentation and darkening of pre-existing naevi because of its pharmacologic effect. Full body skin examinations should be conducted annually to monitor pre-existing and new skin pigmentary lesions before and during treatment with setmelanotide.

Heart rate and blood pressure monitoring: 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.

Prolonged penile erection: Spontaneous penile erections have been reported in clinical trials with setmelanotide. Patients who have a penile erection lasting longer than 4 hours should be instructed to seek emergency medical attention for potential treatment of priapism.

Depression: In clinical trials, depression has been reported in patients treated with setmelanotide. Patients with depression should be monitored at each medical visit during treatment with setmelanotide. Consideration should be given to discontinuing setmelanotide if patients experience suicidal thoughts or behaviors.

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. The prescribing physician should monitor growth (height and weight) using age- and sex-appropriate growth curves.

Excipients: This medicinal product contains 10 mg benzyl alcohol in each ml. Benzyl alcohol may cause allergic reactions. Patients who are pregnant or breastfeeding should be advised of the potential risk from the excipient benzyl alcohol, which might accumulate over time and cause metabolic acidosis. This medicinal product should be used with caution in patients with hepatic or renal impairment, because of the potential risk from the excipient benzyl alcohol which might accumulate over time and cause metabolic acidosis.

Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free."

ADVERSE REACTIONS
The most frequent adverse reactions are hyperpigmentation (51%), injection site reaction (39%), nausea (33%), and headache (26%).

USE IN SPECIFIC POPULATIONS

Pregnancy
There are no data from the use of setmelanotide in pregnant women. Animal studies do not indicate direct harmful effects with respect to reproductive toxicity. However, administration of setmelanotide to pregnant rabbits resulted in decreased maternal food consumption leading to embryo-fetal effects. As a precautionary measure, setmelanotide should not be started during pregnancy or while attempting to get pregnant as weight loss during pregnancy may result in fetal harm. If a patient who is taking setmelanotide has reached a stable weight and becomes pregnant, consideration should be given to maintaining setmelanotide treatment as there was no proof of teratogenicity in the nonclinical data. If a patient who is taking setmelanotide and still losing weight gets pregnant, setmelanotide should either be discontinued, or the dose reduced while monitoring for the recommended weight gain during pregnancy. The treating physician should carefully monitor weight during pregnancy in a patient taking setmelanotide.

Breast-feeding
It is unknown whether setmelanotide is excreted in human milk. A nonclinical study showed that setmelanotide is excreted in the milk of nursing rats. No quantifiable setmelanotide concentrations were detected in plasma from nursing pups. A risk to the newborn/infant cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from setmelanotide therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the mother.

Fertility
No human data on the effect of setmelanotide on fertility are available. Animal studies did not indicate harmful effects with respect to fertility.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337. See Summary of Product Characteristics' APPENDIX V for a list of European national reporting systems to communicate adverse reactions.

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 setmelanotide and LB54640, the potential timing, payments due, and benefits of the global licensing agreement for LB54540, including with respect to the consummation of the transaction, expectations regarding the design, enrollment, or outcome of clinical trials of LB54640, the outcome of the Phase 2 trial of setmelanotide in hypothalamic obesity, the ability to reach any net sales or revenue milestones, and obtaining regulatory approvals in connection with the global licensing agreement. Statements using word 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 our liquidity and expenses, our ability to enroll patients in clinical trials, the design and outcome of clinical trials, the ability to achieve necessary regulatory approvals, risks associated with data analysis and reporting, failure to identify and develop additional product candidates, unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, risks associated with the laws and regulations governing our international operations and the costs of any related compliance programs, the impact of competition, risks relating to product liability lawsuits, inability to maintain our collaborations, or the failure of these collaborations, our reliance on third parties, risks relating to intellectual property, our ability to hire and retain necessary personnel, the impact of the COVID-19 pandemic and general economic conditions on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, failure to realize the anticipated benefits of our acquisition of Xinvento B.V. or significant integration difficulties related to the acquisition, and the other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarter ended September 30, 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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Source: Rhythm Pharmaceuticals, Inc.