



Rhythm Pharmaceuticals Announces Licensing Agreement with Takeda for the Development and Commercialization of Preclinical Treatment for Prader-Willi Syndrome

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*-- Oral Ghrelin O-Acyltransferase (GOAT) Inhibitor Complements and Expands Efforts in Prader-Willi Syndrome --
-- In Preclinical Models, Prevented Body Weight Gain and Reduced Fat Mass --
-- Rhythm Expects to File Investigational New Drug Application in First Quarter of 2020 --*

BOSTON, April 02, 2018 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (NASDAQ:RYTM), a biopharmaceutical company aimed at developing and commercializing therapies for the treatment of rare genetic disorders of obesity, today announced that it has acquired exclusive, worldwide rights from Takeda Pharmaceutical Company Limited (Takeda) to develop and commercialize T-3525770 (now RM-853). RM-853 is a potent, orally available ghrelin o-acyltransferase (GOAT) inhibitor currently in preclinical development for Prader-Willi Syndrome (PWS). PWS is a rare genetic disorder that results in hyperphagia and early-onset, life-threatening obesity, for which there are no approved therapeutic options.

Ghrelin is an orexigenic peptide, secreted by the stomach and proximal small intestine in response to a negative energy balance. Ghrelin plays a key physiological role in stimulating appetite and promoting food intake, thereby maintaining overall energy balance. In people living with PWS, levels of active ghrelin are elevated, contributing to an unrelenting hunger, known as hyperphagia, which leads to severe obesity. RM-853 is designed to block GOAT, the key enzyme involved in the production of the active form of ghrelin, with the expected effect of lowering active ghrelin levels. This blockage increases the levels of des-acyl-ghrelin (DAG), a ghrelin precursor. High levels of DAG are believed to have independent beneficial effects on the control of appetite and tissue homeostasis, which might add to the potential efficacy of RM-853 in PWS.

"The in-licensing of RM-853 represents an important milestone for Rhythm, as we execute on our mission of developing therapies for people living with rare genetic disorders of obesity," said Keith Gottesdiener, M.D., Chief Executive Officer of Rhythm. "While PWS is one of the most prevalent rare genetic disorders of obesity, there are no approved treatments available. With RM-853, we have the opportunity to develop a first-in-class therapy with a likely dual mechanism of action, which may more effectively mediate the hyperphagia and weight gain associated with PWS. We look forward to broadening our ongoing efforts in PWS and to advancing RM-853 through preclinical studies."

In preclinical research, RM-853 prevented body weight gain and reduced fat mass in high fat-fed mice, with a favorable pharmacokinetic, pharmacodynamic, and safety profile. Rhythm plans to complete preclinical studies of RM-853 and file an investigational new drug application with the U.S. Food and Drug Administration in the first quarter of 2020.

Under the terms of the agreement, Rhythm will assume sole responsibility for the global product development and commercialization of RM-853. Takeda will receive an upfront payment of \$5 million in Rhythm common stock, back-end development milestones, and single-digit royalties on future RM-853 sales.

"Rhythm aims to develop meaningful drug candidates for people living with metabolic disorders," said Lex H.T. Van der Ploeg, Ph.D., Chief Scientific Officer of Rhythm. "Our team has a deep understanding of the complex pathways involved in regulating bodyweight and appetite and is experienced in working with specialized endocrinologists and physicians to design and execute clinical trials that evaluate therapeutic options for people living with PWS. We believe this knowledge, coupled with our focus on rare genetic disorders of obesity, positions Rhythm well to seek to effectively develop RM-853. We are pleased to enter into this licensing agreement, which expands our efforts to develop treatments for PWS."

Rhythm's lead product candidate, setmelanotide, is an investigational, first-in-class melanocortin-4 receptor (MC4R) agonist. The Company is currently focusing setmelanotide clinical development on six rare genetic disorders of obesity: pro-opiomelanocortin (POMC) deficiency obesity, leptin receptor (LEPR) deficiency obesity, Bardet-Biedl syndrome (BBS), Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. The Company previously completed a Phase 2 trial of setmelanotide in PWS. In this trial, setmelanotide showed modest effects on reducing hyperphagia, but had no effect on weight across the study population, though there was some evidence of clinically-meaningful weight loss in the subset of patients treated at the highest dose level for the longest duration. Rhythm is currently assessing opportunities to further evaluate setmelanotide in PWS and plans to pursue these in parallel with the development of RM-853. Additionally, given setmelanotide and RM-853's distinct mechanisms of action, the Company will explore opportunities to evaluate the two compounds in combination, as there may be complementary effects.

About Prader-Willi Syndrome

Prader-Willi Syndrome (PWS) is the most common known genetic cause of life-threatening obesity in children. Prevalence estimates have ranges from one in 8,000 to one in 25,000, with at least 8,000 people in the U.S. diagnosed with PWS. A hallmark of PWS is severe hyperphagia, an overriding physiological drive to eat, leading to severe obesity and other complications. For PWS patients, hyperphagia and obesity are the greatest threats to their health. There is currently no approved treatment for the obesity and hyperphagia associated with PWS.

About Rhythm

Rhythm is a biopharmaceutical company focused on the development and commercialization of therapies for the treatment of rare genetic disorders of obesity. Rhythm is currently evaluating the efficacy and safety of setmelanotide, the Company's first-in-class melanocortin-4 receptor (MC4R) agonist, in Phase 3 studies in patients with pro-opiomelanocortin (POMC) deficiency obesity (which includes deficiencies in both the POMC and PCSK1 genes) and leptin receptor (LEPR) deficiency obesity. Rhythm also supports The Genetic Obesity Project (www.GeneticObesity.com), which is dedicated to improving the understanding of severe obesity that results from specific genetic disorders. The company is based in Boston, MA.

Forward-Looking Statements

This press release contains certain statements that are forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and that involve risks and uncertainties, including statements regarding the potential efficacy of RM-853 in PWS, opportunities to develop a first-in-class therapy for PWS, timing of and Rhythm's plans to complete preclinical studies of RM-853 and file an investigational new drug application with the U.S. Food and Drug Administration, and opportunities to further evaluate setmelanotide in PWS and to explore opportunities to evaluate the two compounds in combination. Statements using word such as "expect", "anticipate", "believe", "may" 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 outcome of clinical trials, the impact of competition, the ability to achieve or obtain necessary regulatory approvals, the impact of changes in the financial markets and global economic conditions, risks associated with data analysis and reporting, our use of cash and expenses, and other risks as may be detailed from time to time in our Annual Reports on Form 10-K and quarterly reports on Form 10-Q and other reports we file 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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