Rhythm Pharmaceuticals Announces Positive Results from Phase 2 Study of Once-weekly Formulation of Setmelanotide in Healthy Obese Volunteers

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-- Once-weekly formulation of setmelanotide achieved weight loss efficacy comparable to daily-dosing formulation –

-- Both weekly and daily formulations of setmelanotide were observed to be safe and well-tolerated –

-- Pharmacokinetics analysis showed weekly formulation of setmelanotide trough drug concentration similar to daily formulation –

BOSTON, June 24, 2020 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq:RYTM), a late-stage biopharmaceutical company aimed at developing and commercializing therapies for the treatment of rare genetic disorders of obesity, today announced interim data from a Phase 2 study evaluating a once-weekly formulation of setmelanotide, the Company's investigational melanocortin-4 receptor (MC4R) agonist. Healthy obese people treated with the weekly formulation of setmelanotide achieved comparable weight loss to those treated with the daily formulation, and both weekly and daily formulations of setmelanotide were observed to be safe and well-tolerated. Pharmacokinetics (PK) analyses showed similar trough drug concentrations for the daily and weekly formulations over the duration of therapy.

"As a daily injection, setmelanotide has achieved statistically significant and clinically meaningful weight loss in patients with rare genetic disorders of obesity across multiple Phase 2 and Phase 3 clinical trials," said Murray Stewart, M.D., Chief Medical Officer of Rhythm. "These new data suggest that weekly setmelanotide may provide the same clinical benefit in a more convenient formulation, with the potential to reduce the burden on patients without compromising safety or efficacy. We look forward to evaluating these data further and continuing discussions with the U.S. Food and Drug Administration (FDA) about our path to registering weekly setmelanotide."

The Phase 2 study was designed to assess pharmacokinetics and the safety and tolerability of the weekly formulation of setmelanotide and its effect on reducing body weight in healthy individuals with a body mass index (BMI) of 40 kg/m^2 or greater. A total of 75 individuals were included in this interim analysis: 42 individuals were treated with weekly setmelanotide (10mg, 20mg, or 30mg doses) for 12 weeks, 23 individuals were treated with placebo for 12 weeks, and ten individuals were treated with daily setmelanotide (2mg daily for one week, followed by3 mg daily for 11 weeks).

The interim data analysis demonstrated that healthy obese people treated with weekly setmelanotide achieved similar weight loss to those treated with the daily formulation over 12 weeks of therapy. The mean difference in change from baseline on weight between each weekly dose of 10mg, 20mg or 30mg and daily dose of 2mg/3mg was -0.69kg (p=0.659), -0.02kg (p=0.990), and -1.71kg (p=0.296), respectively.

Weekly setmelanotide administration was well tolerated with no serious adverse events, and the safety profile was similar to the daily administration and consistent with prior clinical experience. Incidents of injection site reactions, hyperpigmentation and nausea or vomiting were classified as mild by investigators.

In addition, an analysis of pharmacokinetics data measuring mean trough drug concentrations in plasma samples taken weekly for the duration of treatment showed that 20mg and 30mg doses of weekly setmelanotide were very similar to the 3mg daily dose of setmelanotide with greater trough drug concentration seen in the 30mg weekly dose.

Rhythm is continuing to analyze these efficacy, safety and pharmacokinetics data for weekly setmelanotide, and it plans to share these data at an upcoming medical meeting. The Company also plans to discuss next steps towards registration with the FDA.

Rhythm is developing this weekly formulation of setmelanotide to treat early-onset, severe obesity and insatiable hunger, the hallmark characteristics of rare genetic disorders of obesity. The weekly formulation leverages the extended-release FluidCrystal® injection depot technology which Rhythm licensed to develop with setmelanotide form Camurus AB in 2016. This drug delivery technology has been approved in Europe and Australia and provisionally approved by the FDA for use in weekly and monthly formulations of buprenorphine for the treatment of opioid use disorder.

About Setmelanotide
Setmelanotide is an investigational, melanocortin-4 receptor (MC4R) agonist. The MC4R is part of the key biological pathway that independently regulates energy expenditure and appetite. Variants in genes may impair the function of the MC4R pathway, potentially leading to insatiable hunger and early-onset, severe obesity. Rhythm is currently developing setmelanotide as a targeted therapy to restore the function of an impaired MC4R pathway and, in so doing, reduce hunger and weight in patients with rare genetic disorders of obesity. Currently, no pharmacologic therapies exist to treat these conditions. The FDA has granted Breakthrough Therapy designation to setmelanotide for the treatment of obesity associated with genetic defects upstream of the MC4R in the central melanocortin pathway, which includes pro-opiomelanocortin (POMC) deficiency obesity and leptin receptor (LEPR) deficiency obesity. The European Medicines Agency (EMA) has also granted PRIority MEdicines (PRIME) designation for setmelanotide for the treatment of obesity and the control of hunger associated with deficiency disorders of the MC4R pathway. Both the FDA and EMA have granted orphan drug status to setmelanotide for POMC and LEPR deficiency obesities. The FDA has accepted Rhythm's New Drug Application (NDA) for setmelanotide for the treatment of POMC and LEPR deficiency obesities, granted Priority Review of the NDA and assigned a Prescription Drug User Fee Act (PDUFA) goal date of November 27, 2020. Rhythm expects to complete submission of a Marketing Authorization Application (MAA) for setmelanotide to treat individuals living with POMC deficiency obesity or LEPR deficiency obesity to the EMA in the second quarter of 2020.

About Rhythm Pharmaceuticals

Rhythm is a late-stage biopharmaceutical company focused on the development and commercialization of therapies for the treatment of rare genetic disorders of obesity. In August 2019, the company announced positive topline results from pivotal Phase 3 clinical trials of setmelanotide, its MC4R agonist, in people living with POMC deficiency obesity or LEPR deficiency obesity and, in March 2020, completed its first rolling NDA submission to the FDA. Rhythm is also evaluating setmelanotide for reduction in hunger and body weight in a pivotal Phase 3 trial in people living with Bardet-Biedl and Alström syndromes, with topline data from this trial expected in the fourth quarter of 2020 or early in the first quarter of 2021. Rhythm is leveraging the Rhythm Engine -- comprised of its Phase 2 basket study, TEMPO Registry, GO-ID genotyping study and Uncovering Rare Obesity program -- to improve the understanding, diagnosis and potentially the treatment of rare genetic disorders of obesity. For healthcare professionals, visit www.UNcommonObesity.com for more information. For patients and caregivers, visit www.LEADforRareObesity.com for more information. The company is based in Boston, MA.

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, including the weekly formulation of setmelanotide, anticipated discussions with the FDA regarding next steps towards registration, our expectations surrounding the PDUFA goal date and the timing for submission of an MAA. Statements using words such as "expect", "anticipate", "believe", "may", "will" and similar terms are also forward-looking statements. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the impact of our management transition, 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 liquidity and expenses, the impact of the COVID-19 pandemic on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and general economic conditions, and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2020 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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