



Rhythm Pharmaceuticals Announces New Clinical Data on Setmelanotide at ObesityWeek® 2020

November 4, 2020

- Interim data from Phase 2 study showed that once-weekly formulation of setmelanotide achieved safety and efficacy results comparable to daily-dosing formulation --
- Additional data from long-term extension study in POMC deficiency obesity showed durable weight loss and reductions in hunger at up to three years on therapy --
- Setmelanotide was generally well tolerated --

BOSTON, Nov. 04, 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 new clinical data for setmelanotide, its investigational melanocortin-4 receptor (MC4R) agonist, being presented at The Obesity Society's ObesityWeek® 2020, held virtually from November 2-6, 2020.

"We are excited to share new data from across our setmelanotide development program that support its potential as a new medicine for people with rare genetic disorders of obesity," said Murray Stewart, M.D., Chief Medical Officer of Rhythm Pharmaceuticals. "As we prepare for a potential FDA approval in proopiomelanocortin (POMC) and leptin receptor (LEPR) deficiency obesities later this month, we are focused on ongoing efforts to fundamentally alter the treatment paradigm for rare genetic disorders of obesity and continue advancing weekly setmelanotide as a potential option that may be more convenient and less burdensome for patients and their families."

ObesityWeek Presentations

'A Randomized Trial of a Once-Weekly Formulation of Setmelanotide in Individuals with Obesity,' an oral presentation by Gregory Gordon, MD, JD, Vice President, Clinical at Rhythm

Rhythm is presenting interim results from its Phase 2 study evaluating a once-weekly formulation of setmelanotide in healthy obese volunteers, including new data from a larger number of individuals, which come in addition to data announced in [June 2020](#). The data show that healthy obese people treated with the weekly formulation of setmelanotide achieved comparable weight loss to those treated with the daily formulation and that both weekly and daily formulations of setmelanotide were observed to be generally well tolerated.

A total of 85 individuals were included in the full data analysis: 28 individuals were treated with weekly setmelanotide without titration for 12 weeks (10mg, 20mg or 30mg doses); 20 individuals were treated with weekly setmelanotide with titration (10mg for one week, followed by 20mg for 11 weeks or 20mg for one week, followed by 30mg for 11 weeks); 13 individuals were treated with daily setmelanotide (2mg daily for one week, followed by 3mg daily for 11 weeks); and 24 individuals were treated with placebo for 12 weeks.

As of the data cutoff of April 17, 2020, weekly setmelanotide administration was generally well tolerated, with no serious treatment-emergent adverse events (TEAE), and the safety results were similar to the daily administration and consistent with prior clinical experience. The most commonly reported TEAEs, rates of which were generally similar between individuals treated with the weekly and daily formulations, included injection site reaction, hyperpigmentation, nausea, headache and vomiting.

Healthy obese people treated with the weekly formulation of setmelanotide achieved comparable changes in weight and hunger scores as those treated with the daily formulation:

	10mg QW	20mg QW	30mg QW	10mg/20mg QW	20mg/30mg QW	2mg/3mg QD	Placebo
Weight Change from Baseline at Week 12 (kg)	-2.6	-3.3	-3.0	-1.1	-3.6	-2.1	0.5
Absolute Change in Most Hunger Score at Week 12¹	-2.1	-1.6	0.3	-1.9	-3.9	-2.3	-0.3

Data presented as of a cutoff of April 17, 2020

"These data demonstrate that the weight and hunger score changes with the weekly formulation were generally comparable to the daily formulation," said Dr. Gordon. "It is worth noting that the changes with both formulations in normal obese individuals were smaller relative to data we've reported separately in patients with rare genetic obesities associated with an impaired MC4R pathway. This reinforces the important role the MC4R pathway plays in regulating hunger, caloric intake, and energy expenditure and the potential for a precision medicine treatment approach in certain patients with severe obesity."

Additionally, as previously disclosed, pharmacokinetic (PK) analyses showed similar trough drug concentrations for the daily and weekly formulations over the duration of therapy. The weekly formulation of setmelanotide demonstrated a consistent 24-hour PK range and was detected steadily over one week, with a trough concentration consistent with the trough concentration of the efficacious daily formulation.

'Long-term Weight and Hunger Reduction With Setmelanotide in Individuals With POMC Deficiency Obesity,' a poster presentation by Karine Clément, MD, PhD, and Professor of Nutrition at Pitié-Salpêtrière Hospital and Sorbonne Université in Paris

Dr. Clément is presenting updated data from the long-term extension trial evaluating setmelanotide in POMC deficiency obesity. The long-term extension trial enrolled nine individuals, all of whom previously completed Rhythm's pivotal Phase 3 clinical trial evaluating setmelanotide for the treatment of severe obesity and insatiable hunger.

Efficacy and safety data from five individuals who reached 89 weeks on setmelanotide therapy during the long-term extension trial are being presented. As of a cutoff of April 16, 2020:

- The mean percent reduction in body weight from pivotal trial baseline at week 89 of the extension was -30.2%, a -0.1% change from the conclusion of the pivotal trial;
- The mean absolute reduction in body weight at week 89 of the extension was -40.2kg, a change of -0.5kg from the conclusion of the pivotal trial;
- The mean percent reduction in body mass index at week 89 of the extension was -32.5%, a change of -0.4% from the conclusion of the pivotal trial;
- The mean percent change in most hunger score from pivotal baseline was consistent through week 89 of the extension at -8.2%, a change of 10% from the conclusion of the pivotal trial.

[As previously reported](#), data showed that patients successfully maintained durable weight loss and stable hunger scores with long-term treatment with setmelanotide, for up to three years. Consistent with prior clinical experience, setmelanotide has been generally well-tolerated in the long-term extension trial and the safety results remained consistent across all patients treated for up to three years. The most common treatment-emergent adverse events included injection site reactions, nausea and vomiting, and hyperpigmentation.

'Suicidality and Depression in Individuals With Genetic Obesity Treated With Setmelanotide,' a poster presentation by Peter Kühnen, MD, Institute for Experimental Pediatric Endocrinology, Charité Universitätsmedizin in Berlin

Dr. Kühnen is presenting new data from Rhythm's pivotal Phase 3 clinical trials evaluating setmelanotide in POMC and LEPR deficiency obesities, which showed that treatment with setmelanotide was generally well-tolerated and did not induce a significant effect on depression or suicidality. Because of their severe obesity, individuals with POMC or LEPR deficiency may be at a higher risk for experiencing depression and/or suicidal ideation.

About Setmelanotide

Setmelanotide is an investigational MC4R agonist. The MC4R is part of the key biological pathway that independently regulates hunger, caloric intake, and energy expenditure. Variants in genes may impair the function of the MC4R pathway, potentially leading to hyperphagia and early-onset, severe obesity. Rhythm is currently developing setmelanotide as a targeted therapy to potentially restore the function of an impaired MC4R pathway and, in so doing, potentially reduce hunger and weight in patients with rare genetic disorders of obesity. Currently, no pharmacologic therapies exist to treat these conditions. The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to setmelanotide for the treatment of obesity associated with genetic defects upstream of the MC4R pathway, which includes POMC deficiency obesity, LEPR deficiency obesity, Bardet-Biedl Syndrome and Alström Syndrome. 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.

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. The FDA has accepted for filing an NDA for setmelanotide for the treatment of POMC deficiency obesity and LEPR deficiency obesity with Priority Review and assigned a Prescription Drug User Fee Act (PDUFA) goal date of November 27, 2020. Rhythm also submitted a Marketing Authorization Application (MAA) for setmelanotide to treat individuals living with POMC deficiency obesity or LEPR deficiency obesity to the European Medicines Agency (EMA) in June 2020. 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, expectations regarding regulatory approval, the anticipated timing for release of clinical trial data, our ongoing efforts related to patient identification and genetic sequencing and timing thereof, and our participation in upcoming events and presentations. 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, 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 the other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 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.

Corporate Contact:

David Connolly

Head of Investor Relations and Corporate Communications
Rhythm Pharmaceuticals, Inc.
857-264-4280
dconnolly@rhythmtx.com

Investor Contact:

Hannah Deresiewicz
Stern Investor Relations, Inc.
212-362-1200
hannah.deresiewicz@sternir.com

Media Contact:

Adam Daley
Berry & Company Public Relations
212-253-8881
adaley@berrypr.com

¹ Score is based on 0-10 Likert scale from question, "In the last 24 hours, how hungry did you feel when you were the most hungry?," with 0 being not hungry at all and 10 being the hungriest possible.



Source: Rhythm Pharmaceuticals, Inc.