



## Rhythm Pharmaceuticals Announces Publication of Results from Phase 3 Clinical Trials of Setmelanotide in The Lancet Diabetes & Endocrinology

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### Largest studies in POMC and LEPR deficiency obesities demonstrate that treatment with setmelanotide reduced body weight and hunger

BOSTON, Oct. 30, 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, announced today that results from two pivotal Phase 3 studies evaluating setmelanotide in proopiomelanocortin (POMC) deficiency obesity and leptin receptor (LEPR) deficiency obesity were published in *The Lancet Diabetes & Endocrinology*. As previously reported, data from the studies demonstrate that treatment with setmelanotide, the company's melanocortin-4 receptor (MC4R) agonist, led to statistically significant and clinically meaningful reductions of weight and hunger.

"Results from Rhythm's pivotal Phase 3 studies, which are the largest studies to date in POMC and LEPR deficiency obesities, provide evidence regarding the safety and efficacy of setmelanotide and we believe they validate its potential long-term use as a novel treatment for severe obesity and hyperphagia," said co-author Peter Kühnen, M.D., Institute for Experimental Pediatric Endocrinology, Charité Universitätsmedizin Berlin, Germany. "It is important to recognize the signs of these rare genetic disorders because we may soon have a targeted treatment option available for the first time for obesity disorders caused by impairments of the MC4R pathway."

Rhythm initially [reported positive topline data](#) from the Phase 3 studies in August 2019 and subsequently [presented updated data](#) in a late-breaking research forum during the 37<sup>th</sup> Annual Meeting of The Obesity Society at ObesityWeek<sup>®</sup> 2019.

Eight of 10 participants with POMC deficiency obesity (80%;  $P < 0.0001$  compared with historical data) and five of 11 participants with LEPR deficiency obesity (45%;  $P = 0.0001$  compared with historical data) achieved at least 10 percent weight loss at approximately one year. The mean percent change in "most hunger" score in participants aged 12 years and older was -27.1 percent ( $n = 7$ ;  $P = 0.0005$ ) in POMC deficiency obesity and -43.7 percent ( $n = 7$ ;  $P < 0.0001$ ) in LEPR deficiency obesity. Consistent with prior clinical experience, setmelanotide was generally well-tolerated in both trials. The most common adverse events were injection site reaction, skin hyperpigmentation, and nausea.

"These results are significant because, as we know from natural history data, individuals living with POMC or LEPR deficiency obesity consistently experience substantial weight gain each year beginning in early childhood, and we would not expect any of these patients to be able to achieve 10 percent weight loss over the course of a year without continued treatment," said co-author Karine Clément, professor of nutrition at Pitié-Salpêtrière hospital and Sorbonne University in Paris. "These data and the significant unmet need to address the obesity and hyperphagia caused by rare genetic disorders of obesity underscore the importance of testing for genetic variants that may impair MC4R activation and lead to severe obesity."

In May 2020, Rhythm announced that the U.S. Food and Drug Administration (FDA) accepted the company's New Drug Application (NDA) for setmelanotide for the treatment of POMC deficiency obesity and LEPR deficiency obesity, granted Priority Review of the NDA and assigned a Prescription Drug User Fee Act (PDUFA) goal date of November 27, 2020. In July 2020, the Company announced the submission of its Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for the treatment of POMC deficiency obesity and LEPR deficiency obesity.

"We are grateful to the authors and the investigators involved in our pivotal Phase 3 clinical trials for their continued partnership in advancing setmelanotide to address significant unmet needs facing people with rare genetic disorders of obesity," Murray Stewart, M.D., Chief Medical Officer of Rhythm, said.

The article is available online here: [http://www.thelancet.com/journals/landia/article/PIIS2213-8587\(20\)30364-8/fulltext](http://www.thelancet.com/journals/landia/article/PIIS2213-8587(20)30364-8/fulltext). To request a copy of the article, email [medinfo@rhythmtx.com](mailto:medinfo@rhythmtx.com).

#### About Setmelanotide

Setmelanotide is an investigational, melanocortin-4 receptor (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 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 (BBS) and Alström syndrome. The 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. Rhythm is also evaluating setmelanotide for reduction in hunger and body weight in a pivotal Phase 3 trial in people living with BBS and Alström syndromes, with topline data from this trial expected in the fourth quarter of 2020 or early in the first quarter of 2021.

#### 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. 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](http://www.UNcommonObesity.com) for more information. For patients and caregivers, visit [www.LEADforRareObesity.com](http://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 our business strategy and plans, including regarding commercialization of setmelanotide; the potential, safety, efficacy, and regulatory and clinical progress of setmelanotide, including anticipated timing of data readouts and our expectations surrounding potential regulatory approvals and timing thereof. 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 June 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.*

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