Rhythm Pharmaceuticals Announces Publication of Results from Phase 2 Study of Setmelanotide in Bardet-Biedl Syndrome in Diabetes, Obesity and Metabolism

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-- Study demonstrated that treatment with setmelanotide reduced body weight and hunger in individuals living with Bardet-Biedl syndrome --

BOSTON, July 16, 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 its Phase 2 study evaluating setmelanotide for the treatment of obesity and insatiable hunger, known as hyperphagia, in patients living with Bardet-Biedl Syndrome (BBS) were published in the peer-reviewed journal *Diabetes, Obesity and Metabolism*. As previously reported, data from the study demonstrate that treatment with setmelanotide, the company's melanocortin-4 receptor (MC4R) agonist, reduced body weight and hunger in individuals with BBS.

"Treatment with setmelanotide demonstrated a substantial reduction in body weight and hunger, making this the first-ever Phase 2 study of any investigational pharmacologic agent to show positive results for the treatment of obesity and hunger in individuals living with BBS," said Robert M Haws, M.D., Director of the Clinical Research Center at the Marshfield Clinic Research Institute. "These findings also suggest that obesity and hyperphagia associated with BBS have ties to impaired signaling of the MC4R pathway and support further evaluation of MC4R activation as a potential treatment option."

Rhythm initially reported topline data from its Phase 2 Basket Study of setmelanotide in BBS in June 2018 and most recently, in September 2019, Rhythm announced updated data following approximately two years on therapy. The Phase 2 study participants received a daily subcutaneous injection of setmelanotide. The dose was titrated every two weeks for up to 12 weeks to establish the individual dose. The primary outcome was mean percent change from baseline in body weight at three months. Mean percent change in body weight was also assessed after six and 12 months of treatment as additional exploratory efficacy outcomes. Change in hunger scores, metabolic parameters, and safety were secondary outcomes.

"BBS is a complex disorder, and as the authors of this paper noted, there remains a crucial lack of clinical trials investigating obesity or hyperphagia treatment options in this population," said Murray Stewart, M.D., Chief Medical Officer of Rhythm. "There is a pressing need for a new therapy that may be able to reduce weight through hyperphagia management and potentially help manage or alleviate obesity related co-morbidities. We are encouraged by these Phase 2 study results and thank all the investigators for their efforts in conducting this important research."

As announced in December 2019, Rhythm completed enrollment of the pivotal cohort in its Phase 3 clinical trial evaluating setmelanotide for the treatment of hyperphagia and severe obesity in individuals living with BBS or Alström syndrome. This Phase 3 trial enrolled 32 individuals with BBS and six individuals with Alström syndrome in the pivotal cohort, and Rhythm has continued to enroll patients in a supplemental cohort to meet demand and provide further data on the use of setmelanotide in people living with BBS or Alström syndrome. The company expects to report topline data from the pivotal Phase 3 trial evaluating setmelanotide in BBS and Alström syndrome in the fourth quarter of 2020 or early in the first quarter of 2021.

The publication, *Effect of Setmelanotide, an MC4R Agonist, on Obesity in Bardet-Biedl Syndrome*, can be found online.

About Bardet-Biedl Syndrome
BBS is an ultra-rare genetic disorder that affects multiple organ systems. Clinical features of BBS may include Insatiable hunger, also known as hyperphagia, early-onset, severe obesity, cognitive impairment, polydactyly, renal dysfunction, hypogonadism and visual impairment. There is great variability in presentation and severity of these symptoms across individuals with BBS. In the United States, Rhythm estimates that BBS affects approximately 1,500 to 2,500 people. Currently, there are no approved therapies targeting the melanocortin-4 receptor (MC4R) pathway for reducing body weight and hunger in individuals living with BBS.

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 BBS, Alström syndrome, pro-opiomelanocortin (POMC) deficiency obesity and leptin receptor (LEPR) deficiency obesity. 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. The FDA has accepted Rhythm's NDA for setmelanotide for the treatment of POMC and LEPR deficiency obesities for filing, granted Priority Review of the NDA and assigned a Prescription Drug User Fee Act (PDUFA) goal date of November 27, 2020. Rhythm submitted an MAA for setmelanotide to treat individuals living with POMC deficiency obesity or LEPR deficiency obesity to the EMA in June 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. 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, anticipated trial enrollment and timing of data readouts, and our expectations surrounding the PDUFA goal date. 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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