Rhythm Pharmaceuticals Announces Presentation of Updated Clinical Data from Phase 2 Basket Studies Evaluating Setmelanotide in Bardet-Biedl Syndrome and Alström Syndrome at 57th Annual ESPE Meeting

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Updated data show continued reductions in body weight and decreased appetite in patients with rare genetic disorders of obesity

BOSTON, Sept. 28, 2018 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (NASDAQ:RYTM), a biopharmaceutical company focused on the development and commercialization of therapeutics for the treatment of rare genetic disorders of obesity, today announced that updated data from the company's ongoing Phase 2 basket studies evaluating setmelanotide in people with Bardet-Biedl Syndrome (BBS) and Alström Syndrome are being presented at the 57th Annual European Society for Paediatric Endocrinology (ESPE) Meeting held September 27-29, 2018 in Athens, Greece. Results from the studies demonstrate that treatment with setmelanotide led to marked reductions in body weight and decreased appetite as shown by lower hunger scores. Safety data were consistent with previous clinical studies.

"As we continue our mission to improve the understanding of rare genetic disorders of obesity and develop a potentially transformative therapy for people who currently have no treatment options, we are encouraged by our longer-term data with setmelanotide, which show that patients who have been on treatment for many months continue to experience sustained improvements in body weight and appetite," said Keith Gottesdiener, M.D., Chief Executive Officer of Rhythm. "These studies indicate that both BBS and Alström Syndrome are setmelanotide-responsive, and we look forward to initiating and enrolling the first patients in a combined Phase 3 clinical trial in these indications this year."

BBS and Alström Syndrome are life-threatening, ultra-rare orphan diseases that are closely related. Both cause severe obesity and insatiable hunger, also known as hyperphagia, that often present during childhood. BBS affects approximately one in 100,000 people in North America and is also associated with vision loss, polydactyly, and kidney abnormalities. Alström Syndrome has a prevalence of approximately one in one million in North America and can lead to progressive vision loss, deafness, cardiomegaly, and insulin resistance. Currently there are no approved therapies for regulating hunger in BBS or Alström Syndrome.

Setmelanotide is a potent, first-in-class melanocortin-4 receptor (MC4R) agonist that is being developed by Rhythm for the treatment of rare genetic disorders of obesity. The U.S. Food & Drug Administration (FDA) has included BBS and Alström Syndrome under a Breakthrough Therapy designation for setmelanotide for the treatment of obesity associated with genetic defects upstream of the MC4R in the leptin-melanocortin pathway. 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. In June 2018, Rhythm announced topline clinical data from the ongoing Phase 2 basket studies evaluating setmelanotide in BBS and Alström Syndrome.

Updated Data Presented at 57th Annual ESPE Meeting

In an oral presentation, Robert Haws, M.D., founder of the Marshfield Clinic Research Institute's BBS program, reported updated data on body weight, hunger scores, and the safety of treatment with setmelanotide in a total of nine patients with BBS as of August 2018:

- Four BBS patients previously categorized as long-term weight loss responders have now continued in the Phase 2 basket studies over a long-term treatment duration (range 59-71 weeks) and continue to demonstrate clinically important, marked average weight loss of 26.1 kg, and an average percent decrease in body weight of 22.3%. Hunger scores were reduced by an average of 78.3% in these four patients. As previously reported, a fifth BBS patient, a pediatric patient with Type 1 diabetes, experienced a 53% reduction in hunger score, a flattening of the weight curve relative to prior childhood weight gain, and an improvement in average blood sugar level from 10.1% to 7.6% before discontinuing the studies because of lack of weight response. Following discontinuation, this patient gained 5.9 kg, her appetite and hunger increased back to baseline levels, and her average blood sugar levels increased to 11.7%.
- Dr. Haws also presented updated data on an additional four BBS patients enrolled in the Phase 2 basket studies who have been on treatment for a shorter duration. Two adolescent BBS patients who have been on treatment for a short-term duration (range 15-18 weeks) demonstrated weight loss of 8.3 kg and 5.8 kg, respectively, and a percent decrease in body weight of 6.8% and 6.6%, respectively. Hunger scores were reduced by 66% and 21%, respectively, in these two patients. Two other BBS patients, one of whom was previously reported, discontinued the studies because of lack of weight response.

- Overall treatment with setmelanotide was well tolerated with no serious adverse events. Adverse events included mild injection site reactions and increased pigmentation of the skin. There were no discontinuations due to adverse events and no clinically significant detrimental changes in blood pressure or heart rate were reported.

A separate poster reported updated data on body weight, hunger scores, and the safety of treatment with setmelanotide in one patient with Alström Syndrome as of August 2018. The poster was presented by Joan Han, M.D., director of the Pediatric Obesity Program at Le Bonheur Children's Hospital and associate professor in the division of pediatric endocrinology at the University of Tennessee Health Science Center:

- After 50 weeks of treatment, the patient continued to demonstrate weight loss of 19.2 kg (decrease of 24%) and a 39% reduction in body fat.
- The patient's Body Mass Index was reduced from obese to normal weight.
- Baseline hunger scores decreased by 45%.
- Treatment with setmelanotide was well tolerated, with adverse events of increased pigmentation of the skin. Average ambulatory 24-hour blood pressure was prehypertensive at baseline and became normotensive after treatment with setmelanotide.
- Three additional Alström Syndrome patients have been enrolled in the studies. Two of these patients have been treated for a short duration and remain on therapy. As previously reported, one patient did not show improvements in either weight or hunger and was discontinued.

About Setmelanotide

Setmelanotide is a potent, first-in-class, melanocortin-4 receptor (MC4R) agonist in development for the treatment of rare genetic disorders of obesity. Setmelanotide activates MC4R, part of the key biological pathway that independently regulates energy expenditure and appetite. Variants in genes within the MC4R pathway are associated with unrelenting hunger and severe, early-onset obesity. Rhythm is currently developing setmelanotide as a replacement therapy for patients with monogenic defects upstream of MC4R, for whom there are no effective or approved therapies. The U.S. Food and Drug Administration has granted Breakthrough Therapy designation to setmelanotide for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes POMC deficiency obesity, LEPR deficiency obesity, Bardet-Biedl Syndrome and Alström Syndrome.

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 Rhythm's expectations regarding its anticipated timing for initiation and enrollment for clinical trials, and the development of a potentially transformative therapy. 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, 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, risks associated with data analysis and reporting, 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.

Investor Contact:
Hannah Deresiewicz
Stern Investor Relations, Inc.
212-362-1200
hannahd@sternir.com

Media Contact:
Lynn Granito
Berry & Company Public Relations
212-253-8881
lgranito@berrypr.com

Rhythm Pharmaceuticals, Inc.