Rhythm Pharmaceuticals Announces Nature Medicine Publication of Longer-Term Data from Phase 2 Study of Setmelanotide for Treatment of LEPR Deficiency Obesity

May 9, 2018

Longer-term data from open label study show reductions in hyperphagia and body weight

In vitro analyses advance understanding of setmelanotide's activity at the MC4 receptor, a part of a key pathway regulating energy homeostasis and appetite

BOSTON, May 09, 2018 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (NASDAQ:RYTM), a biopharmaceutical company aimed at developing and commercializing therapies for the treatment of rare genetic disorders of obesity, today announced that *Nature Medicine* has published longer-term data from a Phase 2 study of setmelanotide, a first-in-class melanocortin-4 receptor (MC4R) agonist that is the company's lead investigational compound, in patients with leptin receptor (LEPR) deficiency obesity, an ultra-rare orphan disease that results in hyperphagia and severe, early-onset obesity for which the FDA previously granted Breakthrough Therapy Designation to setmelanotide.

The longer-term data from Rhythm's open label study show that once daily subcutaneous injection of setmelanotide resulted in reductions in hyperphagia and body-weight in three patients with LEPR deficiency obesity. The safety and tolerability of setmelanotide were consistent with previous findings and no serious adverse events were reported. Researchers also conducted a series of in vitro analyses of MC4R function with data suggesting that:

- setmelanotide's mechanism for MC4R activation may differentiate from the natural ligand and first-generation compounds;
- setmelanotide might overcome the presence of the naturally occurring neurotransmitter that inhibits the activation of MC4R; and,
- setmelanotide may rescue specific MC4R mutations where the natural ligand cannot.

Rhythm is currently enrolling patients in its pivotal Phase 3 clinical trial evaluating setmelanotide in LEPR deficiency obesity. Clinical trial sites are open across North America and Europe, and enrollment is expected to be complete by the end of 2018.

"We are pleased to recognize the publication of longer-term Phase 2 study results in the peer-reviewed journal *Nature Medicine*, which represents an important milestone for our clinical development program and for people living with rare genetic disorders of obesity who currently do not have approved treatment options," said Keith Gottesdiener, M.D., Chief Executive Officer of Rhythm. "We are also encouraged by ongoing efforts to improve our understanding of the cellular and molecular mechanisms along the MC4 pathway. The fact that in vitro data suggest setmelanotide may rescue specific MC4R mutations where the natural ligand cannot might identify a subset of patients who may benefit from treatment with setmelanotide, which warrants further study."

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 the potential efficacy of RM-853 in PWS, opportunities to develop a first-in-class therapy for PWS, timing of and Rhythm's plans to complete preclinical studies of RM-853 and file an investigational new drug application with the U.S. Food and Drug Administration, and opportunities to further evaluate setmelanotide in PWS and to explore opportunities to evaluate the two compounds in combination. Statements using word such as "expect", "anticipate", "believe", "may" 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, the impact of changes in the financial markets and global economic conditions, risks associated with data analysis and reporting, our use of cash 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:
Adam Daley
Berry & Company Public Relations

212-253-8881
adaley@berrypr.com

Rhythm Pharmaceuticals, Inc.