Rhythm Pharmaceuticals Announces Progress in Clinical Development of Setmelanotide for Treatment of Rare Genetic Disorders of Obesity

January 4, 2018

- Final protocol confirmed for pivotal Phase 3 clinical trial in pro-opiomelanocortin (POMC) deficiency obesity -

- Setmelanotide granted Orphan Drug Designation for treatment of leptin receptor (LEPR) deficiency obesity; Opened enrollment in pivotal Phase 3 trial in LEPR -

- Enrolled patients with Alström Syndrome and POMC epigenetic disorder in a Phase 2 proof-of-concept study -

BOSTON, Jan. 04, 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 recent progress in the clinical development of the company's lead product candidate, setmelanotide, a first-in-class melanocortin-4 receptor (MC4R) agonist.

"We are pleased to announce important progress across our clinical development programs for setmelanotide, as we work to deliver a first-in-class therapy for the treatment of monogenic MC4 pathway defects that result in life-threatening obesity," said Keith Gottesdiener, M.D., Chief Executive Officer of Rhythm. "We continue to work closely with the U.S. Food and Drug Administration to advance our ongoing Phase 3 trial in POMC deficiency obesity, and recently opened enrollment in a second pivotal trial in LEPR deficiency obesity, while also enrolling patients to establish proof-of-concept in Alström Syndrome and POMC epigenetic disorder. We look forward to advancing these efforts in 2018, as we evaluate setmelanotide's ability to reestablish weight and appetite control in patients with genetic, MC4 pathway deficiencies."

Following recent discussions with the U.S. Food & Drug Administration (FDA), Rhythm has finalized the protocol for its ongoing, open-label, single-arm, multinational pivotal Phase 3 clinical trial evaluating setmelanotide in patients with POMC deficiency obesity, an ultra-rare orphan disease that results in hyperphagia and severe, early-onset obesity. The FDA previously granted Breakthrough Therapy Designation for setmelanotide in this indication.

The study originally positioned mean percentage change in weight from baseline as the primary endpoint, and a categorical analysis of responders for weight, defined as patients achieving a 10 percent change from baseline, as the first secondary endpoint. Following recent discussions with regulatory authorities, the study's primary endpoint will now be the responder analysis, with mean percentage change in weight as the first secondary endpoint, in a change that increases the power of the trial. Other key secondary endpoints on hunger remain unchanged.

Rhythm confirms plans to file a New Drug Application (NDA) with the FDA based on one-year data from a cohort of 10 patients. The company currently has eight patients enrolled in its pivotal Phase 3 clinical trial, and expects to complete enrollment of the 10 required patients in the first half of 2018. In addition, the company plans to continue enrolling supplemental patients who may not complete one year of treatment at the time of NDA filing, including patients between six and 11 years of age under the implementation of a pediatric amendment, to provide additional important data regarding the use of setmelanotide in people living with POMC deficiency obesity. The company continues to expect to report initial data from this trial in the first half of 2019.

"We are pleased with the final protocol for our ongoing, pivotal Phase 3 trial in patients with POMC deficiency obesity, which strengthens the trial's statistical power and further clarifies the expected regulatory threshold for approval," continued Dr. Gottesdiener. "We are also encouraged that we will be able to enroll additional patients in the trial, who may not complete one year of treatment at the time of filing, as this will enable us to better understand the benefits of setmelanotide treatment in a broader population, including younger patients."

Rhythm also recently initiated an open-label, single-arm, multinational pivotal Phase 3 clinical trial evaluating setmelanotide in patients with LEPR deficiency obesity, another ultra-rare orphan disease that results in hyperphagia and severe, early-onset obesity. The FDA previously granted Breakthrough Therapy Designation to setmelanotide for the treatment of LEPR deficiency obesity. In November 2017, the FDA also granted Orphan Drug Designation for setmelanotide in this indication. Rhythm plans for the study protocol to closely follow the design of the Phase 3 trial in patients with POMC deficiency obesity. The company has opened clinical trial sites in several countries, is scheduled to enroll the first patients in early 2018, and is targeting completion of enrollment by the end of 2018.

Rhythm continues to evaluate setmelanotide for the treatment of additional rare genetic disorders of obesity, including Bardet-Biedl Syndrome (BBS), Alström Syndrome, POMC heterozygous obesity and POMC epigenetic obesity. Following are highlights from the company's recent progress in additional development programs for setmelanotide:

- Rhythm expects to meet with regulatory authorities in early 2018 to discuss inclusion of BBS as a Breakthrough Designation Therapy, and to plan a pivotal Phase 3 clinical trial in BBS.
- Rhythm recently enrolled patients in a Phase 2 proof-of-concept study evaluating setmelanotide for the treatment of Alström Syndrome and POMC epigenetic disorder, and continues to expect to report initial results in both indications in the first half of 2018.
- Following the completion of a single-dose study, Rhythm recently completed a multi-dose study evaluating an extended-release, once-weekly formulation of setmelanotide. The formulation, which Rhythm is developing in collaboration with Camurus AB, demonstrated tolerability and pharmacokinetics that support further clinical development.

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's lead product candidate is setmelanotide, a first-in-class melanocortin-4 receptor (MC4R) agonist. 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 forward looking statements 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, including statements regarding our expectations about our progress across our clinical development program for setmelanotide, our anticipated timing for the initiation of clinical trials, the enrollment of patients and the report of data, our expectations regarding the impact of changes in our ongoing clinical trials, our advancement of our clinical programs, our goals to develop and commercialize setmelanotide, and other statements identified by words such as "anticipates," "believes," "could," "estimates," "expects," "intends," "may," "might," "likely," "plans," "potential," "predicts," "projects," "seeks," "should," "target," "will," "would," or similar expressions and the negatives of those terms. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include our limited operating history, our ability to obtain necessary funding, our ability to generate positive clinical trial results for setmelanotide, risks associated with the small population of patients we are targeting, and our ability to establish that population and identify patients, changes in laws and regulations to which we are subject, our ability to identify additional product candidates, and other risks set forth under the heading "Risk Factors" of our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017. Our actual results could differ materially from the results described in or implied by such forward-looking statements. Forward-looking statements speak only as of the date hereof, and, except as required by law, we undertake no obligation to update or revise these forward-looking statements.

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.