Rhythm Pharmaceuticals Announces Presentation of Genetic Epidemiology of LEPR, POMC, And PCSK1 Variants at ENDO 2018

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- Late-breaking data suggest there are potentially more than 12,000 people in the U.S. living with rare genetic disorders of obesity -

BOSTON, March 19, 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 the presentation of results from analyses of genetic epidemiology data that provide potential estimates for the number of people living in the U.S. with variants in genes within the melanocortin-4 (MC4) receptor pathway, a key biological pathway that regulates weight by increasing energy expenditure and reducing appetite. The late-breaking data are being presented today at the Endocrine Society's Annual Meeting and Expo (ENDO 2018) in Chicago, Illinois.

Deficiencies within the MC4 pathway including the leptin receptor (LEPR) gene and two genes involved in pro-opiomelanocortin (POMC) deficiency obesity, POMC and proprotein convertase subtilisin/kexin type 1 (PCSK1), are all associated with hyperphagia and early onset, severe obesity. Researchers led by Kristin Ayers, Ph.D., senior scientist for the Department of Genetics and Genomic Sciences at the Icahn Institute for Genomics and Multiscale Biology, identified known loss of function (LoF) variants in LEPR, POMC, and PCSK1 genes through a comprehensive literature search and analysis of several genetic databases. Computationally-predicted LoF variants were also identified using a novel algorithm developed in partnership with WuXi NextCODE.

Results suggest an estimated combined prevalence of 12,800 people living in the U.S. who are homozygous or compound heterozygous for known and predicted LoF variants in LEPR (3,600 individuals), POMC (650 individuals), and PCSK1 (8,500 individuals). Additionally, researchers found that people with at least two LoF alleles in one or more of the LEPR, POMC, and PCSK1 genes had significantly increased body mass index (BMI) relative to non-carriers.

"These genetic epidemiology analyses suggest there may be more people living with rare genetic disorders of obesity in the U.S. than previously projected by clinical epidemiology, though this rare patient population remains relatively undiagnosed," said Keith Gottesdiener, M.D., chief executive officer of Rhythm. "As we work to develop setmelanotide as a first-in-class treatment for patients with MC4 pathway deficiencies, we are committed to expanding awareness and understanding of rare genetic disorders of obesity. We look forward to working closely with a specialized network of endocrinologists and other physicians to help improve the diagnosis of people living with these conditions."

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 POMC deficiency obesity and LEPR deficiency obesity. The Company also expects to initiate a Phase 3 study evaluating setmelanotide in Bardet-Biedl syndrome in 2018 and has enrolled the first patients in a Phase 2 proof-of-concept basket study evaluating setmelanotide in Alström Syndrome, POMC epigenetic disorders, and POMC heterozygous deficiency obesity. In addition, Rhythm has launched efforts to build a patient registry, Tracing the Effect of the MC4 Pathway in Obesity (TEMPO), and is supporting The Genetic Obesity Project and the GO-ID Genotyping 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 Rhythm's clinical research programs and its momentum in 2018, progress with ongoing and initiation of new pivotal trials, potential to address unmet needs in patients with certain forms of genetic obesity, anticipated timing for announcement of data, and the sufficiency of cash. 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, 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.

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