Rhythm Pharmaceuticals Completes Rolling Submission of New Drug Application to U.S. Food and Drug Administration for Setmelanotide in POMC and LEPR Deficiency Obesities

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BOSTON, March 30, 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, today announced that it has completed its rolling submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for setmelanotide for the treatment of pro-opiomelanocortin (POMC) deficiency obesity and leptin receptor (LEPR) deficiency obesity.

“The completion of our first NDA submission marks an integral first step in our journey to transform the care of people living with not only POMC and LEPR deficiency obesities, but also many other rare genetic disorders of obesity,” said Murray Stewart, M.D., Chief Medical Officer of Rhythm Pharmaceuticals. “We look forward to further discussions with the FDA as we seek to obtain approval for setmelanotide, which we believe has the potential to address the insatiable hunger and early-onset, severe obesity that affects people living with POMC and LEPR deficiency obesities, who cannot be treated with lifestyle modifications alone and have no other treatment options.”

The FDA typically has a 60-day filing review period to determine whether the NDA is sufficiently complete and acceptable for filing. Rhythm has requested priority review for the application which, if granted, could provide a target FDA review period of six-months from the application filing date.

As first reported in August 2019, Rhythm’s Phase 3 clinical trials of setmelanotide in patients with POMC deficiency obesity and LEPR deficiency obesity met their primary endpoints and all key secondary endpoints, demonstrating a statistically significant and clinically meaningful reduction in weight loss and reduction in hunger after one year of treatment with setmelanotide. Over the course of the Phase 3 trials, for patients with POMC deficiency obesity, mean weight loss was 31.9 kilograms, or 70.2 pounds, and for patients with LEPR deficiency obesity mean weight loss was 16.7 kilograms, or 36.8 pounds.

About POMC and LEPR Deficiency Obesities
POMC and LEPR deficiency obesities are ultra-rare disorders. Rhythm estimates there are approximately 100 to 500 patients in the U.S. with POMC deficiency obesity and approximately 500 to 2,000 patients in the U.S. with LEPR deficiency obesity. POMC deficiency obesity is a disorder caused by variants in the *POMC* or *PCSK1* genes that can often lead to severe obesity beginning early in life and insatiable hunger, in addition to endocrine abnormalities, and sometimes red hair and light skin pigmentation. LEPR deficiency obesity is a disorder caused by variants in the *LEPR* gene that can often lead to severe obesity beginning early in life and insatiable hunger, in addition to endocrine abnormalities. Most patients with POMC and LEPR deficiency obesity experience exponential weight gain in the first months of life, which continues rapidly over the course of their lives. This weight gain cannot be mitigated by diet, exercise or other lifestyle changes, or by existing therapeutic interventions.

About Setmelanotide
Setmelanotide is an investigational, potent melanocortin-4 receptor (MC4R) agonist. The MC4R is part of the key biological pathway that independently regulates energy expenditure and appetite. Variants in genes may impair the function of the MC4R pathway, potentially leading to insatiable hunger and early-onset, severe obesity. Rhythm is currently developing setmelanotide as a targeted therapy to restore the function of an impaired MC4R pathway and, in so doing, 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 in the central melanocortin pathway, which includes POMC deficiency obesity, LEPR deficiency obesity, Bardet-Biedl syndrome (BBS) and Alström syndrome. The European Medicines Agency 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, BBS and Alström syndrome.

About Rhythm
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 and LEPR deficiency obesity and, in March 2020, completed its first rolling NDA submission to the FDA. 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, including the effectiveness of setmelanotide in patients with POMC and LEPR deficiency obesities, and the timing for approval of an NDA. 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 the COVID-19 outbreak and other global economic factors, 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, and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2019 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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