Rhythm Pharmaceuticals Receives Rare Pediatric Disease Designation from U.S. Food and Drug Administration for Setmelanotide for Treatment of POMC and LEPR Deficiency Obesities

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BOSTON, July 01, 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 the U.S. Food and Drug Administration (FDA) has granted rare pediatric disease designations for setmelanotide, an investigational melanocortin-4 receptor (MC4R) agonist, for the treatment of pro-opiomelanocortin (POMC) deficiency obesity and leptin receptor (LEPR) deficiency obesity. As previously announced, the Company's New Drug Application (NDA) for setmelanotide was accepted for filing with priority review by the FDA and assigned a Prescription Drug User Fee Act (PDUFA) goal date of November 27, 2020.

Under the FDA's rare pediatric disease designation and voucher programs, the FDA may grant a priority review voucher to a sponsor who receives a product approval for a "rare pediatric disease," which is defined as a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and affects fewer than 200,000 people in the U.S. Subject to FDA approval of setmelanotide for the treatment of POMC and LEPR deficiency obesities, Rhythm would be eligible to receive one priority review voucher, which could then be redeemed to receive priority review for any subsequent marketing application, or sold or transferred to other companies for their programs.

"We believe that receipt of the rare pediatric disease designation for setmelanotide, for which we have previously received Breakthrough Therapy and orphan drug status, underscores the FDA's recognition of setmelanotide's potential to treat POMC and LEPR deficiency obesities; two serious, ultra-rare conditions for which existing treatment options are woefully inadequate," said Murray Stewart, M.D., Chief Medical Officer of Rhythm. "As a result of early-onset, severe obesity and insatiable hunger, many patients experience debilitating comorbidities beginning in childhood, which worsen over time and can greatly affect their quality of life. With setmelanotide, we believe we have the potential to modify this disease trajectory by delivering a therapy that can be dosed chronically beginning in childhood. We are grateful to the FDA for this designation and look forward to continuing to work toward our goal of delivering setmelanotide to people with rare genetic disorders of obesity."

In August 2019, Rhythm announced positive topline results from the pivotal cohorts in its two Phase 3 clinical trials evaluating setmelanotide for the treatment of POMC and LEPR deficiency obesities. Both trials met their primary endpoints and all key secondary endpoints, demonstrating a statistically significant and clinically meaningful reduction in weight loss and reductions in insatiable hunger, or hyperphagia, in patients with POMC and LEPR deficiency obesities.

In June 2020, Rhythm announced new data from eight supplemental patients, including four pediatric patients aged 6-12, who subsequently enrolled in its two pivotal Phase 3 clinical trials for POMC and LEPR deficiency obesities. All eight supplemental patients, four of whom had POMC deficiency obesity and four of whom had LEPR deficiency obesity, achieved the primary endpoint of 10 percent or greater weight loss at 52 weeks on setmelanotide therapy, as calculated under the statistical analysis plan.

About POMC and LEPR Deficiency Obesities
POMC and LEPR deficiency obesities are ultra-rare genetic disorders. Rhythm believes both disorders are underdiagnosed, and 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 in childhood 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 or 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, 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 potentially restore the function of an impaired MC4R pathway and, in so doing, potentially 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 pathway, which includes pro-opiomelanocortin (POMC) deficiency obesity and leptin receptor (LEPR) deficiency obesity. The 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. Both the FDA and EMA have granted orphan drug status to setmelanotide for POMC and LEPR deficiency obesities. The FDA has accepted Rhythm's NDA for setmelanotide for the treatment of POMC and LEPR deficiency obesities for filing, granted Priority Review of the NDA and assigned a Prescription Drug User Fee Act (PDUFA) goal date of November 27, 2020. Rhythm submitted a MAA for setmelanotide to treat individuals living with POMC deficiency obesity or LEPR deficiency obesity to the EMA in June 2020.

About Rhythm Pharmaceuticals
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 or LEPR deficiency obesity. 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, anticipated timing of data readouts, and our expectations surrounding the PDUFA goal date. 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 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, the impact of the COVID-19 pandemic on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and general economic conditions, and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2020 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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