Rhythm Pharmaceuticals Announces Two Publications Detailing Burden of Hyperphagia and Obesity on Patients and Caregivers Living with Bardet-Biedl Syndrome

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Results of The CAREgiver Burden in BBS (CARE-BBS) study show multifaceted burden of hyperphagia

BOSTON, July 19, 2023 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company focused on transforming the lives of patients and their families living with hyperphagia and severe obesity caused by rare melanocortin-4 receptor (MC4R) pathway diseases, today announced two new publications detailing the burden of hyperphagia and obesity for adult caregivers, families and patients living with Bardet-Biedl Syndrome (BBS) based on results of The CAREgiver Burden in BBS (CARE-BBS) study. The research is published in the peer-reviewed journal, *The Orphanet Journal of Rare Diseases.*

“BBS is characterized by hyperphagia – an insatiable hunger that results in extreme food seeking behaviors – and early-onset, severe obesity, both of which have broad negative impacts on the lives of patients living with BBS and their caregivers,” said Prof. Andrea M. Haqq, M.D., Department of Pediatrics, Faculty of Medicine & Dentistry, University of Alberta. “These results demonstrate that hyperphagia and severe obesity associated with BBS negatively affect performance in school, work and social relationships. Importantly, the findings from the CARE-BBS study were similar across countries, demonstrating the universality of hyperphagia and underscoring the need for therapies that can effectively treat hyperphagia in order to alleviate the extensive clinical and nonclinical impacts of the disease.”

“Burden of Hyperphagia and Obesity in Bardet-Biedl Syndrome: a Multi-country Survey,” includes results from a cross-sectional survey of 242 adult caregivers of patients with BBS across the United States, the United Kingdom, Canada and Germany. Caregivers of patients with BBS reported that hyperphagia has broad impacts, well beyond contributing to obesity. Caregivers observed hyperphagic behaviors throughout the day, most frequently negotiating for food (90%) and waking up and asking or looking for food during the night (88%). Hyperphagia had at least a moderate negative impact on most patients’ mood/emotions (56%), sleep (54%), school (57%), leisure (62%), and familial relationships (51%).

“Caregiver Burden in Bardet-Biedl Syndrome: Findings from the CARE-BBS Study,” quantifies caregiver burden associated with obesity and hyperphagia. The findings show that patients’ hyperphagia had a moderate-to-severe impact on caregiver mood (56.6%), sleep (46.6%), and relationships (48.0%), contributing to a high level of personal strain and work productivity loss for caregivers in the workforce, as well as a meaningful family impact.

“We continue to learn more about the full extent of hyperphagia’s negative impact on BBS patients, their families and caregivers,” said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. “These results provide valuable insights into the physical, social and economic burdens of hyperphagia for both patients and their families and show the need for therapies designed to alleviate hyperphagia and, as a result, improve quality of life.”

About Bardet-Biedl Syndrome
Bardet-Biedl syndrome (BBS) is a heterogenous rare genetic syndromic disease that presents with a variety of symptoms that evolve over time including visual impairments, renal disease, polydactyly, genital abnormalities, cognitive impairment, and hyperphagia and early-onset, severe obesity arising from impairment of the hypothalamic MC4R pathway. In the United States, BBS affects approximately 4,000 to 5,000 individuals with similar prevalence in Europe.

About Rhythm Pharmaceuticals
Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with hyperphagia and severe obesity caused by rare melanocortin-4 receptor (MC4R) diseases. Rhythm’s lead asset, IMCIVREE (setmelanotide) is approved by the U.S. Food and Drug Administration (FDA) and authorized by the European Commission (EC) and the UK’s Medicines & Healthcare Products Regulatory Agency (MHRA) for use in accordance with product labeling. Additionally, Rhythm is advancing a broad clinical development program for setmelanotide in other rare MC4R pathway diseases, as well as a preclinical suite of investigational candidates for the treatment of congenital hyperinsulinism. Rhythm’s headquarters is in Boston, MA.

Setmelanotide Indication
In the United States, setmelanotide is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to POMC, PCSK1 or LEPR deficiency as determined by an FDA-approved test demonstrating variants in POMC, PCSK1 or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain

significance (VUS) or BBS.

In the European Union, setmelanotide is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS) or genetically confirmed loss-of-function biallelic proopiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 6 years of age and above.

In Canada, setmelanotide is indicated for the treatment of obesity due to Bardet-Biedl syndrome (BBS) or genetically-confirmed biallelic pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency due to variants interpreted as pathogenic, likely pathogenic, or of uncertain significance in adults and children 6 years of age and above.

Limitations of Use
Setmelanotide is not indicated for the treatment of patients with the following conditions as setmelanotide would not be expected to be effective:

- Obesity due to suspected POMC, PCSK1 or LEPR deficiency with *POMC*, *PCSK1* or *LEPR* variants classified as benign or likely benign
- Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity.

In Europe, Setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

WARNINGS AND PRECAUTIONS

Skin Monitoring: Setmelanotide may lead to generalized increased skin pigmentation and darkening of pre-existing naevi because of its pharmacologic effect. Full body skin examinations should be conducted annually to monitor pre-existing and new skin pigmentary lesions before and during treatment with setmelanotide.

Heart rate and blood pressure monitoring: Heart rate and blood pressure should be monitored as part of standard clinical practice at each medical visit (at least every 6 months) for patients treated with setmelanotide.

Prolonged penile erection: Spontaneous penile erections have been reported in clinical trials with setmelanotide. Patients who have a penile erection lasting longer than 4 hours should be instructed to seek emergency medical attention for potential treatment of priapism.

Depression: In clinical trials, depression has been reported in patients treated with setmelanotide. Patients with depression should be monitored at each medical visit during treatment with setmelanotide. Consideration should be given to discontinuing setmelanotide if patients experience suicidal thoughts or behaviors.

Pediatric Population: The prescribing physician should periodically assess response to setmelanotide therapy. In growing children, the impact of weight loss on growth and maturation should be evaluated. The prescribing physician should monitor growth (height and weight) using age- and sex-appropriate growth curves.

Excipients: This medicinal product contains 10 mg benzyl alcohol in each ml. Benzyl alcohol may cause allergic reactions. Patients who are pregnant or breastfeeding should be advised of the potential risk from the excipient benzyl alcohol, which might accumulate over time and cause metabolic acidosis. This medicinal product should be used with caution in patients with hepatic or renal impairment, because of the potential risk from the excipient benzyl alcohol which might accumulate over time and cause metabolic acidosis.

Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free.”

ADVERSE REACTIONS

The most frequent adverse reactions are hyperpigmentation (51%), injection site reaction (39%), nausea (33%), and headache (26%).

USE IN SPECIFIC POPULATIONS

Pregnancy
There are no data from the use of setmelanotide in pregnant women. Animal studies do not indicate direct harmful effects with respect to reproductive toxicity. However, administration of setmelanotide to pregnant rabbits resulted in decreased maternal food consumption leading to embryo-fetal effects. As a precautionary measure, setmelanotide should not be started during pregnancy or while attempting to get pregnant as weight loss during pregnancy may result in fetal harm. If a patient who is taking setmelanotide has reached a stable weight and becomes pregnant, consideration should be given to maintaining setmelanotide treatment as there was no proof of teratogenicity in the nonclinical data. If a patient who is taking setmelanotide and still losing weight gets pregnant, setmelanotide should either be discontinued, or the dose reduced while monitoring for the recommended weight gain during pregnancy. The treating physician should carefully monitor weight during pregnancy in a patient taking setmelanotide.

Breast-feeding
It is unknown whether setmelanotide is excreted in human milk. A nonclinical study showed that setmelanotide is excreted in the milk of nursing rats. No quantifiable setmelanotide concentrations were detected in plasma from nursing pups. A risk to the newborn/infant cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from setmelanotide therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the mother.

Fertility
No human data on the effect of setmelanotide on fertility are available. Animal studies did not indicate harmful effects with respect to fertility.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337. See Summary of Product Characteristics' APPENDIX V for a list of European national reporting systems to communicate adverse reactions.

Please see the full Prescribing Information for additional Important Safety Information.

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 for patients with BBS or POMC, PCSK1 and LEPR deficiencies, and the potential positive impacts of setmelanotide therapy for caregivers of patients with BBS. Statements using word such as "expect", "anticipate", "believe", "may", "will" and similar terms are also forward-looking statements. Such statements are subject to numerous risks and uncertainties, including, but not limited to, risks relating to our liquidity and expenses, our ability to enroll patients in clinical trials, the design and outcome of clinical trials, the ability to achieve necessary regulatory approvals, risks associated with data analysis and reporting, failure to identify and develop additional product candidates, unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, risks associated with the laws and regulations governing our international operations and the costs of any related compliance programs, the impact of competition, risks relating to product liability lawsuits, inability to maintain our collaborations, or the failure of these collaborations, our reliance on third parties, risks relating to intellectual property, our ability to hire and retain necessary personnel, the impact of the COVID-19 pandemic and general economic conditions on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and the other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the three months ended March 31, 2023 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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