Rhythm Pharmaceuticals Announces Publication of Bardet-Biedl Syndrome Patient and Caregiver Perspectives of Hunger and Quality of Life with Setmelanotide

March 27, 2023

- Interview-based research published in Advances in Therapy *demonstrates setmelanotide improved hyperphagia and reduced body weight and obsessive focus on food –*

- Company also announces publication of health state utilities study in hyperphagia -

BOSTON, March 27, 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 the publication of interview-based patient and caregiver reported experiences of hunger and quality of life with setmelanotide treatment in Bardet-Biedl syndrome (BBS). The research is published in the peer-reviewed journal *Advances in Therapy*.

“Hyperphagia and early-onset, severe obesity are hallmark characteristics of BBS that place a considerable burden on patients and their families,” said Prof. Andrea M. Haqq, M.D., Department of Pediatrics, Faculty of Medicine & Dentistry, University of Alberta. “Our results show that hyperphagia – a pathological, all-consuming hunger leading to an obsessive focus on food – negatively affects the lives of patients and families, posing difficulties with concentration, emotional and physical manifestation, and impaired relationships. Our analyses also demonstrate that setmelanotide therapy resulted in meaningful improvements for these patients, such as weight loss and a decrease in obsessive focus on food and food-seeking behaviors. Further, these interviews exemplify the usefulness of patient experience data as recommended by the U.S. Food and Drug Administration for patient-centered drug development.”

The qualitative study publication, titled, “Interview-Based Patient- and Caregiver-Reported Experiences of Hunger and Improved Quality of Life With Setmelanotide Treatment in Bardet-Biedl Syndrome,” includes patients with BBS or their caregivers who participated in Phase 2 and 3 clinical trials of setmelanotide. A total of 19 interviews were conducted with patients (n=8) and caregivers (n=11) to explore patient experience and caregiver observations of hyperphagia before and during setmelanotide treatment. Before setmelanotide treatment, most patients (n=7; 87.5%) and caregivers (n=10; 90.9%) experienced negative effects directly related to hyperphagia. In addition, most participants (15 of 19 overall [78.9%]; 5 of 8 patients [62.5%] and 10 of 11 caregivers [90.9%]) described a lack of control with eating.

All participants reported substantial improvements in hyperphagia and satiety as well as weight loss after initiating setmelanotide treatment, including improved focus and concentration related to reductions in obsessive behaviors associated with food. All caregivers noted the ability to give their child greater autonomy around food choices and consumption and a reduced need to monitor their child’s food intake. Approximately half of patients and caregivers noted that improvements in hunger had benefited family dynamics.

“Until now, the impact of hyperphagia on the lives of these patients and their families has not been fully understood. This study confirms the substantial burden and provides additional insights into how treatment with setmelanotide facilitated improvements in hyperphagia and promoted beneficial changes in patient and caregiver experiences,” said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm.

Rhythm also announced the publication of a study, titled, “Health State Utilities Associated With Hyperphagia: Data for Use in Cost-Utility Models,” that evaluated the assessment of the substantial impact of severe hyperphagia on patients’ quality of life. This study is the first to estimate the impact of hyperphagia on health state utilities independently of any specific underlying indication. These data can be incorporated into cost-utility models conducted to assess the value of treatments for rare MC4R pathway diseases. Data published in the open-access journal *Obesity Science and Practice* show that increasing severity of hyperphagia is associated with profound impacts on quality of life that are comparable to other severe health states, such as stroke and progressive metastatic cancers, which similarly have a broad impact on many aspects of 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), an MC4R agonist designed to treat hyperphagia and severe obesity caused by rare MC4R pathway diseases, is approved by the U.S. Food and Drug Administration (FDA) for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency confirmed by genetic testing, or patients with a clinical diagnosis of Bardet-Biedl syndrome (BBS). Both the European Commission (EC) and the UK's Medicines & Healthcare Products Regulatory Agency (MHRA) have authorized setmelanotide for the treatment of obesity and the control of hunger associated with genetically confirmed BBS or genetically confirmed loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. 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 pro-opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 6 years of age and above.

Limitations of Use
In the United States and Europe, Setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

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.

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-foetal 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 U.S. 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, the potential benefits of setmelanotide for patients, including those with BBS, and our business strategy and plans, including regarding commercialization of setmelanotide. 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, 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 and general economic conditions on our business and operations, including our preclinical studies, clinical trials and commercialization prospects, and general economic conditions, and the other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the quarter ended December 31, 2022 and our other filings with the U.S. 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.

Corporate Contact:
David Connolly
Head of Investor Relations and Corporate Communications
Rhythm Pharmaceuticals, Inc.
857-264-4280
dconnolly@rhythmtx.com

Investor Contact:
Hannah Deresiewicz
Stern Investor Relations, Inc.
212-362-1200
hannah.deresiewicz@sternir.com

Media Contact:
Adam Daley
Berry & Company Public Relations
212-253-8881
adaley@berrypr.com

Source: Rhythm Pharmaceuticals, Inc.