



Rhythm Pharmaceuticals Presents New Disease Burden Findings and Analyses of Setmelanotide Data in Children and Adolescents with Rare MC4R Pathway Diseases at ESPE 2022

September 19, 2022

-- CARE-BBS multi-country survey of 242 caregivers of individuals with Bardet-Biedl syndrome (BBS) provides extensive details on impact of hyperphagia and obesity --

-- New analyses of Phase 3 data showed setmelanotide achieved substantial weight loss benefit in adolescent and pediatric patients (n=26) with severe obesity due to BBS or POMC or LEPR deficiency --

BOSTON, Sept. 19, 2022 (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, announced the presentation of new findings on the burden of hyperphagia and obesity on patients with Bardet-Biedl syndrome (BBS) and their caregivers during the 60th Annual Meeting of the European Society for Paediatric Endocrinology (ESPE 2022) held in Rome on Sept. 15 to 17.

Rhythm and its collaborators delivered one poster and three oral presentations during ESPE 2022, including data from new analyses that showed setmelanotide achieved substantial weight loss benefit in adolescent and pediatric patients with rare MC4R pathway diseases across three separate pivotal trials.

"The hyperphagia and severe obesity associated with BBS and other rare MC4R pathway diseases begin to affect individuals with these diseases, their caregivers and families well beyond the symptoms themselves beginning at an early age," said Elizabeth Forsythe, M.D., Ph.D., UCL Great Ormond Street Institute of Child Health, London. "In particular, the unrelenting food-seeking behaviors associated with BBS lead to substantial, negative impacts throughout the lives of patients, their caregivers and families, and these findings illustrate the need for a treatment or other intervention."

"We are pleased to share new data at ESPE, which further demonstrate the tremendous burden associated with MC4R pathway diseases, as well as the potential for our precision therapy to deliver meaningful relief to patients," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "We look forward to further executing our global launches in BBS, POMC and LEPR, as we work to deliver IMCIVREE as the first and only FDA-approved and EC-authorized therapy that targets a root cause of early-onset, severe obesity and hyperphagia."

CARE-BBS Findings Delivered in Two Presentations

Rhythm's CARE-BBS multi-country survey of adult caregivers of 242 individuals with hyperphagia and severe obesity due to BBS was designed to assess overall global impact and burden of disease on caregivers. CARE-BBS participants at the time of the survey were residents of the United States (n=60), Canada (n=62), United Kingdom (n=59) or Germany (n=61).

At ESPE 2022, Dr. Forsythe delivered an oral presentation entitled, "The Multifaceted Burden Experienced by Caregivers of Individuals with Bardet-Biedl Syndrome: Findings from the CARE-BBS Study," and a poster, "Caregiver Burden in Bardet-Biedl Syndrome: a Survey of Obesity and Hyperphagia Impacts." Together, these presentations highlighted that hyperphagia and obesity associated with BBS places a substantial burden on the lives of patients and their caregivers including their physical and mental health, productivity and social relationships. In addition, the findings illustrate how the negative impact of hyperphagia on caregivers affects family dynamics, emotional well-being, and caregiver employment.

New Analyses of Phase 3 Data in Adolescent and Pediatric Patients

Jesús Argente, MD, Professor in the Department of Pediatrics and Pediatric Endocrinology, Universidad Autónoma de Madrid, delivered an oral presentation entitled, "Effects of Setmelanotide Treatment in Children and Adolescents with Proopiomelanocortin (POMC) Deficiency, Leptin Receptor (LEPR) Deficiency, and Bardet-Biedl Syndrome (BBS)," on data from post-hoc analyses of Phase 3 data across three pivotal trials. Data in this presentation showed that setmelanotide achieved substantial weight loss benefit in adolescent and pediatric patients ages 6 to 17 years old (n=26) with severe obesity due to BBS, or POMC or LEPR deficiency. Highlights from the data include:

- mean reduction of -0.75 in BMI-Z score for patients (n=14) with BBS;
- mean reduction of -0.55 in BMI-Z score for patients (n=4) with LEPR deficiency; and
- mean reduction of -1.51 in BMI-Z score for patients (n=12) with POMC deficiency.

Dr. Argente also presented a poster entitled, “VENTURE: Design of a Phase 3 Multicenter, 1-Year, Open-label Trial of Setmelanotide in Pediatric Patients Aged 2 to <6 Years with Rare Genetic Diseases of Obesity.” In August 2022, Rhythm announced that it completed enrollment in this trial.

The presentations will be available on the [publications page](#) of Rhythm’s corporate website.

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) pathway diseases. Rhythm’s precision medicine, setmelanotide, 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). The European Commission (EC) has 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. The UK’s Medicines & Healthcare Products Regulatory Agency (MHRA) authorized setmelanotide for the treatment of obesity and the control of hunger associated with 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 genetic diseases of obesity and is leveraging the Rhythm Engine and the largest known obesity DNA database -- now with approximately 45,000 sequencing samples -- to improve the understanding, diagnosis and care of people living with severe obesity due to certain genetic deficiencies. Rhythm’s headquarters is in Boston, MA.

Setmelanotide Indication

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.

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.

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.

Paediatric 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 with severe obesity due to certain genetic deficiencies, and our expectations surrounding potential regulatory submissions, approvals and timing thereof, 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 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 Quarterly Report on Form 10-Q for the quarter ended June 30, 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



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