



Rhythm Pharmaceuticals Announces Collaborative Research Agreement with Clinical Registry Investigating Bardet-Biedl Syndrome

July 28, 2021

Population study to focus on natural history of weight gain, hyperphagia and quality of life in patients with Bardet-Biedl syndrome

BOSTON, July 28, 2021 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company committed to transforming the care of people living with rare genetic diseases of obesity, today announced a collaborative research agreement with the Clinical Registry Investigating Bardet-Biedl Syndrome (CRIBBS).

"This collaborative research agreement with Rhythm and CRIBBS paves the way for a comprehensive population study that we believe will deepen our understanding of the needs of patients and families living with Bardet-Biedl syndrome (BBS) and the real-world impact severe obesity and hyperphagia, or insatiable hunger, has on them," said Robert Haws, M.D., of the Marshfield Clinic Research Institute.

More than 600 individuals living with BBS are enrolled in CRIBBS, with more than 75 percent of them in the United States. The registry is designed to advance the understanding of BBS and its impact on patients and families, improve the care of people living with the disease, and augment scientific and clinical research. CRIBBS collects de-identified patient information through medical records, patient and caregiver interviews and annual surveys. It is supported by the BBS Foundation and Family Association, Bright Light to BBS, and Marshfield Clinic Research Institute.

Under the collaboration, health outcomes researchers will review data collected through registry questionnaires to quantify and describe unmet medical needs of adults and children with BBS and the impact severe obesity and hyperphagia has on them. Specifically, researchers will analyze natural history of treatment patterns and weight changes over time, as well as specific health outcomes and quality of life measures. The study also will examine the impact of hyperphagia on quality of life and developmental delays.

"With an improved understanding of the impacts of severe obesity and hyperphagia on long-term health and quality of life, we expect to be able to develop more tailored solutions to identify, properly diagnosis and treat people living with BBS and, we hope, improve our collective ability to address the needs and challenges facing this community," said Murray Stewart, M.D., Chief Medical Officer of Rhythm.

BBS is an ultra-rare genetic disease that affects multiple organ systems. Clinical features of BBS may include hyperphagia, early-onset, severe obesity, cognitive impairment, polydactyly, renal dysfunction, hypogonadism and visual impairment. There is great variability in presentation and severity of these symptoms across individuals with BBS. In the United States, Rhythm estimates that BBS affects approximately 1,500 to 2,500 people.

About Rhythm Pharmaceuticals

Rhythm is a commercial-stage biopharmaceutical company committed to transforming the treatment paradigm for people living with rare genetic diseases of obesity. The Company's precision medicine, IMCIVREE (setmelanotide), was approved in November 2020 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 obesity due to POMC, PCSK1 or LEPR deficiency confirmed by genetic testing and by the European Commission (EC) in July 2021 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. IMCIVREE is the first-ever FDA-approved and EC-authorized therapy for these rare genetic diseases of obesity. Rhythm is advancing a broad clinical development program for setmelanotide in other rare genetic diseases of obesity. The Company is leveraging the Rhythm Engine and the largest known obesity DNA database - now with approximately 37,500 sequencing samples - to improve the understanding, diagnosis and care of people living with severe obesity due to certain genetic deficiencies. The company is based in Boston, MA.

IMCIVREE™ (setmelanotide) Indication

IMCIVREE is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency. The condition must be confirmed by genetic testing demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

Limitations of Use

IMCIVREE is not indicated for the treatment of patients with the following conditions as IMCIVREE 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, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Important Safety Information

WARNINGS AND PRECAUTIONS

Disturbance in Sexual Arousal: Sexual adverse reactions may occur in patients treated with IMCIVREE. Spontaneous penile erections in males and sexual adverse reactions in females occurred in clinical studies with IMCIVREE. Instruct patients who have an erection lasting longer than 4 hours to seek emergency medical attention.

Depression and Suicidal Ideation: Some drugs that target the central nervous system, such as IMCIVREE, may cause depression or suicidal ideation. Monitor patients for new onset or worsening of depression. Consider discontinuing IMCIVREE if patients experience suicidal thoughts or behaviors.

Skin Pigmentation and Darkening of Pre-Existing Nevi: IMCIVREE may cause generalized increased skin pigmentation and darkening of pre-existing nevi due to its pharmacologic effect. This effect is reversible upon discontinuation of the drug. Perform a full body skin examination prior to initiation and periodically during treatment with IMCIVREE to monitor pre-existing and new skin pigmentary lesions.

Risk of Serious Adverse Reactions Due to Benzyl Alcohol Preservative in Neonates and Low Birth Weight Infants: IMCIVREE is not approved for use in neonates or infants.

ADVERSE REACTIONS

- The most common adverse reactions (incidence $\geq 23\%$) were injection site reactions, skin hyperpigmentation, nausea, headache, diarrhea, abdominal pain, back pain, fatigue, vomiting, depression, upper respiratory tract infection, and spontaneous penile erection.

USE IN SPECIFIC POPULATIONS

Discontinue IMCIVREE when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus.

Treatment with IMCIVREE is not recommended for use while breastfeeding.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See [Full Prescribing Information](#) for IMCIVREE.

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 benefits of and activities under our research collaboration with CRIBBS, and our business strategy and plans. 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, 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 the other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2021 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.

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

