# Rhythm Pharmaceuticals Presents First-ever Data Showing Improvements in Health-related Quality of Life for Patients Living with Bardet-Biedl Syndrome at ObesityWeek® 2021

November 1, 2021

*-- Additional oral presentation details safety and efficacy data from Phase 3 trial of setmelanotide in BBS --*
*-- Also presenting new hunger data from SRC1 and SH2B1 cohorts in Phase 2 Basket Trial and new data on utilization of URO® genetic testing program –*

BOSTON, Nov. 01, 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, this week presented the first-ever data on the health-related quality of life (HRQOL) and experience of patients with Bardet-Biedl syndrome (BBS) who were treated in its Phase 3 trial of setmelanotide at The Obesity Society's ObesityWeek ®, a virtual conference that runs from Nov. 1 to 5.

Also at ObesityWeek®, the company shared an oral presentation detailing efficacy and safety data from its Phase 3 trial of setmelanotide in BBS and Alström syndrome, as well as poster presentations with new hunger reduction data from the SRC1 and SH2B1 genetic deficiency cohorts in its exploratory Phase 2 Basket Trial. Additional presentations include new data on utilization of the Uncovering Rare Obesity® (URO) genetic testing program, an analysis of the frequency of melanocortin-4 receptor (MC4R) pathway variants in U.S. patients with severe obesity, and a review of single minded-1 (SIM1) missense variants associated with severe obesity.

"We are excited to share multiple presentations at ObesityWeek, which demonstrate continued progress toward our goal of transforming the care of people living with rare genetic diseases of obesity," said Linda Shapiro, M.D., Ph.D., Chief Medical Officer of Rhythm. "The new BBS HRQOL data build on the safety and efficacy results we first announced last year, further validating our belief in setmelanotide's potential as the first-ever therapy to address the hyperphagia and severe obesity that affect the lives of patients and families living with BBS. In addition, the new data from the cohorts of patients with SH2B1 and SRC1 genetic deficiencies in our Phase 2 Basket Trial demonstrated setmelanotide's ability to reduce hunger in people living with these rare genetic diseases of obesity in the trial, further reinforcing our confidence in the DAYBREAK and EMANATE trials we are launching soon to expand our clinical evaluation into a total of 36 genes with strong or very strong relevance to the MC4R pathway."

**Setmelanotide in BBS: HRQOL and Efficacy and Safety Data**
Elizabeth Forsythe, Ph.D., Great Ormond Street Institute of Child Health, Faculty of Population Health Sciences, University College London, presented a poster entitled, "Quality of Life in Patients with Bardet-Biedl Syndrome in a Setmelanotide Phase 3 Trial." This research was conducted as a post-hoc analysis of Rhythm's Phase 3 study, using the self-reported Pediatric Quality of Life Inventory (PedsQL) or the Impact of Weight on Quality of Life Questionnaire-Lite (IWQOL-Lite), both of which are 100-point scales, with zero being the worst and 100 being the best. Highlights include:

- 85% of patients reported clinically meaningful improvements in their HRQOL status after one year of setmelanotide therapy, or preserved their non-impaired HRQOL status;
- For adult patients, changes in their IWQOL score were clinically meaningful with a mean increase of 12 points after one year on setmelanotide therapy from 74.9 at baseline;
- In pediatric patients, changes in their PedsQL score were clinically meaningful with a mean increase of 11.2 after one year on setmelanotide therapy from 67.2 at baseline;
- For the subset of patients without cognitive impairment, clinically meaningful improvements in outcomes such as body mass index and hunger mirrored their improvements in HRQOL;
- HRQOL improvements were sustained over the 52-week trial period.

Robert Haws, M.D., Clinical Research Center at the Marshfield Clinic Research Institute, delivered an oral presentation entitled, "Efficacy and Safety of Open-Label Setmelanotide in Bardet-Biedl Syndrome: A Phase 3 Trial." Data from this trial showed that 52 weeks of setmelanotide treatment was associated with clinically significant reduction in BMI in patients with BBS:

- Patients 18 years old or older (n=15) achieved a mean reduction in BMI of 9.1% from baseline 46.4 kg/m$^2$; and
- Patients younger than 18 years (n=16) achieved a mean reduction in BMI of 9.5% from baseline 37.4 kg/m$^2$.

**Setmelanotide Therapy Achieved Hunger Reductions in SH2B1 and SRC1 Deficiency Obesities**
Rhythm also presented new hunger reduction data from its exploratory Phase 2 Basket Trial evaluating setmelanotide in patients with obesity due to variants of the SRC1 gene or the SH2B1 gene.

Jesús Argente, M.D., Ph.D., Professor in the Department of Pediatrics and Pediatric Endocrinology, Universidad Autónoma de Madrid in Spain, presented a poster entitled, "Effects of Setmelanotide on Obesity, Hunger, and Safety in SH2B1 Deficiency: A Phase 2 Trial;" and Sadaf Farooqi, M.D., Ph.D., Wellcome-MRC Institute of Metabolic Science and NIHR Cambridge Biomedical Research Centre, University of Cambridge, presented, "Effects of Setmelanotide on Obesity, Hunger, and Safety in SRC1 Insufficiency."

In addition to confirming that patients with SRC1 deficiency or SH2B1 deficiency experience severe obesity beginning at a young age, data from these cohorts demonstrated that three months of setmelanotide therapy resulted in reductions in most hunger scores in patients 12 years old and older, regardless of whether the patients met the study definition of weight responder.[1]

At the 59th Annual European Society for Paediatric Endocrinology (ESPE) Meeting in September 2021, Rhythm presented topline analyses from the Phase 2 Basket Trial that showed three months of setmelanotide therapy achieved clinically meaningful weight loss or BMI-Z reduction in 30% (9 of 30) of patients with SRC1 deficiency and in 43% (15 of 35) of patients with SH2B1 deficiency.

Additional Rhythm poster presentations at ObesityWeek include:

- Ida Moeller, ScD, ScM, MMSc, Director of Biomedical Informatics at Rhythm, presented, “Frequency of MC4R pathway variants in a large US cohort of patients with severe obesity;”
- Jill Garrison, Ph.D., Associate Director, Medical Affairs, at Rhythm, presented, “Uncovering Rare Obesity Genetic Testing Program: Overview and Health Care Provider Utilization;” and
- Megan Vogel, Ph.D., Scientist, Pre-Clinical Biology at Rhythm, presented, “Biochemical Characterization of Single Minded-1 Missense Variants Associated with Severe Obesity.”

All Rhythm’s presentations from ObesityWeek will be available on the Publication and Presentations section of its website: https://www.rhythmtx.com/publications/

[1]A responder was defined as having ≥5% weight loss in those ≥18 years old or ≥0.15 reduction in BMI Z score in those <18 years old.

**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. Rhythm’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 in July and September 2021, respectively, by the European Commission (EC) and Great Britain’s Medicines & Healthcare Products Regulatory Agency (MHRA) 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- and MHRA-authorized therapy for patients with these rare genetic diseases of obesity. The Company submitted a supplemental New Drug Application (sNDA) to the FDA in September 2021 and submitted a Type II variation application to the European Medicines Agency in October 2021 seeking regulatory approval and authorization for setmelanotide to treat obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS or Alström syndrome in both the United States and European Union. 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 37,500 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.

**IMCIVREE® (setmelanotide) Indication**
In the United States, 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).

In the EU and Great Britain, IMCIVREE is indicated 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 should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

**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 ≥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, EU SmPC and MHRA SmPC 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, our expectations surrounding potential regulatory submissions, approvals and timing thereof, our business strategy and plans, including regarding commercialization of setmelanotide, and our participation in upcoming events and presentations. 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 quarterly period ended June 30, 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

Source: Rhythm Pharmaceuticals, Inc.