Rhythm Pharmaceuticals Announces Early Access Authorization for Setmelanotide for Use in Patients with Bardet-Biedl Syndrome in France

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-- Reimbursed early access program allows for patients in France to receive setmelanotide for treatment of obesity and control of hunger associated with BBS --

BOSTON, July 20, 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, today announced that the French National Agency for Medicines and Health Products Safety (ANSM) and Haute Autorité de santé (HAS) have granted pre-marketing authorization AP1 (autorisation d'accès précoce - early access authorization), for IMCIVREE ® (setmelanotide), an MC4R agonist, for patients with genetically-confirmed Bardet-Biedl syndrome (BBS) for the treatment of obesity and the control of hunger.

AP1 allows for early access to innovative therapies in France prior to regulatory approval when a positive benefit/risk ratio is recognized and when no other therapeutic alternatives are available. The AP1 for setmelanotide was granted following review of efficacy and safety data from clinical studies by the ANSM and HAS. Products included in the AP1 programs are fully covered by France's National Health System and Rhythm can expect to be reimbursed for any patients receiving treatments through this program.

"We are delighted to announce that the French regulatory authorities granted AP1 status to setmelanotide, making it available for patients with BBS living with hyperphagia and severe obesity," said Yann Mazabraud, Executive Vice President and Head of International at Rhythm. "We look forward to collaborating with the broad and established network of French BBS experts to deliver setmelanotide to patients living with BBS in France, as we work to transform the care of patients with BBS globally."

BBS is a rare genetic disease that affects approximately 1,500-2,500 people in the United States and approximately 2,500 patients in Europe. In France, Rhythm estimates that there are approximately 700 patients diagnosed with BBS. In addition to insatiable hunger, known as hyperphagia, and severe obesity, BBS is also associated with cognitive impairment, polydactyly, renal dysfunction, hypogonadism, and visual impairment. Impairments in the MC4R pathway are a root cause of the early-onset obesity and hyperphagia associated with BBS.

"It is important to understand that efforts to control weight and appetite with traditional lifestyle changes are not effective for people who are suffering from the extreme hunger and weight gain associated with rare MC4R pathway diseases," said Hélène Dolffus, M.D., Ph.D., Professor of Genetics at Hôpitaux Universaires de Strasbourg, Head of the 1112 INSERM Research Unit and Head of the European Rare Diseases Network - EYE. "This AP1 addresses a significant unmet need for patients with severe obesity and hyperphagia, two hallmark symptoms of BBS."

Rhythm's Type II variation application to the European Medicines Agency (EMA) for the treatment of obesity and control of hunger in adult and pediatric patients 6 years of age and older with BBS is under review. Rhythm anticipates that the EMA's Committee for Medicinal Products for Human Use (CHMP) will make its recommendation on this application in the third quarter of 2022, with a final decision from the European Commission expected to follow.

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, IMCIVREE (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 POMC, PCSK1 or LEPR deficiency confirmed by genetic testing, or patients with a clinical diagnosis of Bardet-Biedl syndrome (BBS).
The European Commission (EC) and Great Britain's Medicines & Healthcare Products Regulatory Agency (MHRA) have authorized IMCIVREE 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 living with these rare genetic diseases of obesity. The Company submitted a Type II variation application to the European Medicines Agency 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 in the 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 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.

IMCIVREE® (setmelanotide) Indication
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.

In the United States, IMCIVREE is indicated 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 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)
- Bardet-Biedl syndrome (BBS)

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, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity

WARNINGS AND PRECAUTIONS

Disturbance in Sexual Arousal: Spontaneous penile erections in males and sexual adverse reactions in females have occurred. Inform patients that these events may occur and instruct patients who have an erection lasting longer than 4 hours to seek emergency medical attention.

Depression and Suicidal Ideation: Depression and suicidal ideation have occurred. Monitor patients for new onset or worsening depression or suicidal thoughts or behaviors. Consider discontinuing IMCIVREE if patients experience suicidal thoughts or behaviors, or clinically significant or persistent depression symptoms occur.

Skin Pigmentation and Darkening of Pre-existing Nevi: Generalized increased skin pigmentation and darkening of pre-existing nevi have occurred. Perform a full body skin examination prior to initiation and periodically during treatment to monitor pre-existing and new 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. Serious and fatal adverse reactions including "gasping syndrome" can occur in neonates and low birth weight infants treated with benzyl alcohol-preserved drugs.

ADVERSE REACTIONS

- The most common adverse reactions (incidence ≥20%) included skin hyperpigmentation, injection site reactions, nausea, headache, diarrhea, abdominal pain, vomiting, depression, and spontaneous penile erection.

USE IN SPECIFIC POPULATIONS
Treatment with IMCIVREE is not recommended when breastfeeding. Discontinue IMCIVREE when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus.

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

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, and our expectations surrounding potential regulatory submissions, approvals and timing thereof, and our business strategy and plans, including regarding commercialization of IMCIVREE in France, the United States and other international regions, including expectations surrounding coverage and availability of IMCIVREE in France and related revenues. 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, the ability to obtain or maintain coverage and adequate reimbursement for IMCIVREE or our other product candidates, 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 March 31, 2022 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

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