Rhythm Pharmaceuticals Receives Positive Recommendation from NICE for ▼IMCIVREE® (setmelanotide) for Treatment of Obesity and Hyperphagia in Patients with Bardet-Biedl Syndrome

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IMCIVREE expected to be funded and available for use in England and Wales within three months through the National Health Service in specialist centres

BOSTON, May 22, 2024 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a global commercial-stage biopharmaceutical company focused on transforming the lives of patients and their families living with rare neuroendocrine diseases, today announced the National Institute for Health and Care Excellence (NICE) has issued guidance that recommends IMCIVREE® (setmelanotide) as an option for treating obesity and the control of hunger (hyperphagia) in genetically confirmed Bardet-Biedl syndrome (BBS) in people 6 years of age and over, if they are between 6 and 17 years of age when treatment starts. Patients may remain on reimbursed setmelanotide as adults whilst they continue to benefit from therapy.

“Access to IMCIVREE in England and Wales is an important milestone in our global efforts to bring this medicine to patients and families with BBS,” said Yann Mazabraud, Executive Vice President, Head of International at Rhythm Pharmaceuticals. “We are pleased with this positive recommendation from NICE, made possible by the collaboration and support of advocacy leaders at BBS U.K. and clinical experts, and engaging and productive discussions with NICE.”

BBS is a rare genetic disease with an estimated prevalence of approximately 900 patients in England and Wales. People living with BBS may experience insatiable hunger, also known as hyperphagia, and severe obesity beginning early in life. Results from clinical trials suggest that setmelanotide may reduce hyperphagia, weight and body mass index (BMI) in people aged 6 years and over. The most common adverse events are skin hyperpigmentation, injection site reactions, nausea and headache.

“BBS is a debilitating rare disease that severely affects quality of life of patients and their families,” said Philip Beales, M.D., UCL Great Ormond Street Institute of Child Health. “Hyperphagia – the feeling of extreme hunger that stays with patients all the time – leads to early-onset, life-long, severe obesity that affects many aspects of daily living. Until now there have been no licensed treatments for obesity and hyperphagia caused by BBS.”

The final NICE recommendation is aligned to the European Marketing Authorization (EMA) and U.K. Medicines and Healthcare Products Regulatory Agency (MHRA) approval. With this recommendation under the Highly Specialised Technologies (HST) pathway, IMCIVREE is expected to be funded and available for use within three months in the National Health Service covering England and Wales, and Northern Ireland is expected to adopt NICE guidance. Rhythm is moving ahead with submission to the Scottish Medicines Consortium with a decision expected in 2025.

About Rhythm Pharmaceuticals

Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients and their families living with rare neuroendocrine diseases. Rhythm’s lead asset, IMCIVREE ® (setmelanotide), an MC4R agonist designed to treat hyperphagia and severe obesity, 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 diseases, as well as investigational MC4R agonists LB54640 and RM-718, and a preclinical suite of small molecules 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 and United Kingdom, setmelanotide is indicated for the treatment of obesity and the control of hunger

associated with genetically confirmed BBS or loss-of-function biallelic POMC, including PCSK1, deficiency or biallelic LEPR deficiency in adults and children 6 years of age and above. In the European Union and United Kingdom, setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

Limitations of Use
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.

Contraindication
Prior serious hypersensitivity to setmelanotide or any of the excipients in IMCIVREE. Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported.

WARNINGS AND PRECAUTIONS

Skin Pigmentation and Darkening of Pre-Existing Nevi: Generalized increased skin pigmentation and darkening of pre-existing nevi have occurred because of its pharmacologic effect. Full body skin examinations prior to initiation and periodically during treatment should be conducted to monitor pre-existing and new pigmentary lesions.

Heart rate and blood pressure monitoring: In Europe, 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.

Disturbance in Sexual Arousal: Spontaneous penile erections in males and sexual adverse reactions in females have occurred. Patients who have an erection lasting longer than 4 hours should seek emergency medical attention.

Depression and Suicidal Ideation: Depression and suicidal ideation have occurred. Patients should be monitored for new onset or worsening depression or suicidal thoughts or behaviors. Consideration should be given to discontinuing setmelanotide if patients experience suicidal thoughts or behaviors, or clinically significant or persistent depression symptoms occur.

Hypersensitivity Reactions: Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported. If suspected, advise patients to promptly seek medical attention and discontinue setmelanotide.

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. In Europe, the prescribing physician should monitor growth (height and weight) using age- and sex-appropriate growth curves.

Risk of Serious Adverse Reactions Due to Benzyl Alcohol Preservative in Neonates and Low Birth Weight Infants: Setmelanotide 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

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

Lactation: Not recommended when breastfeeding.

REPORTING OF SIDE EFFECTS

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the package leaflet. You can also contact Rhythm Pharmaceuticals at +1 (833) 789-6337. To report directly via the Yellow Card Scheme please do so via: www.mhra.gov.uk/yellowcard. To report directly to the FDA contact 1-800-FDA-1088 or www.fda.gov/medwatch. [See section 4.8 of the Summary of Product Characteristics for information on reporting suspected adverse reactions in Europe.]

By reporting side effects, you can help provide more information on the safety of this medicine.

Please see the Summary of Product Characteristics and 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 our business strategy and plans, and the potential, safety, efficacy,

and regulatory and clinical progress of IMCIVREE, including regarding the impact of certain regulatory approvals of IMCIVREE for the treatment of BBS in England, Wales and Northern Ireland, expectations surrounding coverage and availability of IMCIVREE, the potential submission to the Scottish Medicines Consortium, and the timing of any of the foregoing. 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 ability to achieve necessary regulatory approvals, risks associated with data analysis and reporting, failure to identify and develop additional product candidates, unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, risks associated with the laws and regulations governing our international operations and the costs of any related compliance programs, the impact of competition, risks relating to product liability lawsuits, inability to maintain collaborations, or the failure of these collaborations, our reliance on third parties, risks relating to intellectual property, our ability to hire and retain necessary personnel, general economic conditions, and the other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the three months ended March 31, 2024 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.

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