NICE Recommends Rhythm's ▼IMCIVREE® (setmelanotide) for Treating Obesity and Controlling Hunger Caused by POMC or LEPR Deficiency

July 18, 2022

- IMCIVREE will be funded and available for use within 90 days in the National Health Service -

BOSTON, July 18, 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 National Institute for Health and Care Excellence (NICE) has issued guidance that recommends IMCIVREE® (setmelanotide) as an option for treating obesity and controlling hunger caused by pro-opiomelanocortin (POMC) deficiency, including proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency in people six years of age and over. With this recommendation under the Highly Specialised Technologies (HST) pathway, IMCIVREE will be funded and available for use within 90 days in the National Health Service.

POMC and LEPR deficiencies are caused by genetic variants that disrupt signaling of the MC4R pathway, a system in the hypothalamus that regulates hunger, satiety and energy expenditure. Disrupted MC4R signaling causes hyperphagia and early-onset, severe obesity. People living with obesity due to POMC or LEPR deficiency struggle with insatiable hunger, also known as hyperphagia, and extreme obesity beginning at a young age.[1,2] These diseases severely affect the quality of life of people living with them, as well as that of their families and caregivers, with many reporting a significant psychological burden, which can manifest as poor mental health, low self-esteem or depression. NICE concluded that obesity caused by POMC or LEPR deficiency is a debilitating condition associated with multiple comorbidities.

Alex Potter, a resident of England who participated in the Rhythm clinical trial and served as a patient representative in the NICE deliberations, said, "LEPR deficiency casts a shadow over every aspect of life. Hunger permeates every thought, action, and conversation. The continuous search for food and severe weight gain has affected my engagement in normal daily activities, which in turn makes building meaningful relationships challenging. For me, participating in this trial has always been about giving other people the chance to live a more normal life - one I never had. This decision will affect the lives of so many families who, like me, continue to be physically and psychologically impacted by this disease."

"The effects of rare MC4R pathway diseases, including POMC and LEPR deficiency, go far beyond a patients' weight and hunger, severely affecting their ability to maintain a normal quality of life beginning in childhood," said Sadaf Farooqi, M.D., Ph.D., Professor at the Wellcome-MRC Institute of Metabolic Science and NIHR Cambridge Biomedical Research Centre. "In addition, caring for a person with one of these conditions can be physically and mentally draining for families who are often stigmatized in their communities. This NICE recommendation reflects the value of IMCIVREE and it is welcome news for clinicians and eligible patients who will soon have access to the first and only therapy to address the underlying cause of obesity and hunger in POMC and LEPR deficiencies."

The final NICE recommendation is aligned to the European Marketing Authorization (EMA) and UK Medicines and Healthcare Products Regulatory Agency (MHRA) approval as the only authorised treatment option for these rare genetic diseases of obesity. The most common adverse events were skin hyperpigmentation, injection site reactions, nausea and headache.

"We are delighted by this positive NICE recommendation, which makes available the first therapeutic option for patients with POMC or LEPR deficiency in England and Wales," said David Meeker, M.D., Chair, President and Chief Executive Officer of Rhythm. "We are grateful to NICE for their close partnership throughout this review process and look forward to continued collaboration with Health Technology Assessment bodies and payers across Europe as we execute on our country-by-country strategy to achieve market access for IMCIVREE."

The full text of the NICE recommendation can be found at: https://www.nice.org.uk/guidance/hst21/chapter/1-Recommendations.

Intended for UK healthcare professionals.

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 Great Britain and the European Union, IMCIVREE is indicated for the treatment of obesity and the control of hunger associated with 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, 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 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 Bardet-Biedl syndrome (BBS).

Limitations of Use
IMCIVREE should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

WARNINGS AND PRECAUTIONS

Skin Monitoring: Setmelanotide may lead to generalised 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 IMCIVREE. Consideration should be given to discontinuing IMCIVREE if patients experience suicidal thoughts or behaviours.

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.

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, IMCIVREE 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 IMCIVREE 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.

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 the United Kingdom, the United States and other international regions, including expectations surrounding funding and availability of IMCIVREE in the National Health Service and related timing. 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.

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[2] Krude H, Biebermann H, Luck W, Horn R, Brabant G, Grüters A. Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC variants in humans. Nat Genet. 1998;19(2):155-157.

Source: Rhythm Pharmaceuticals, Inc.