



Rhythm Pharmaceuticals Announces Commercial Launch of IMCIVREE® (setmelanotide) in Germany for the Treatment of Obesity and Control of Hunger in Bardet-Biedl Syndrome

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IMCIVREE is eligible for federal reimbursement by Statutory Health Insurances in Germany

BOSTON, April 24, 2023 (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 the commercial launch of IMCIVREE® (setmelanotide) in Germany for the treatment of obesity and control of hunger associated with Bardet-Biedl syndrome (BBS).

The German Federal Joint Committee (G-BA) ruled that IMCIVREE is eligible for reimbursement by Statutory Health Insurances for BBS. The G-BA unanimously voted to exclude IMCIVREE from its lifestyle exemption list for patients with BBS, as done previously for biallelic pro-opiomelanocortin (POMC), including proprotein convertase subtilisin/kexin type 1 (PCSK1), deficiency or biallelic leptin receptor (LEPR) deficiency.

"We are excited and well prepared to bring IMCIVREE to patients in Germany, which is an important market with many identified patients in need of a therapy for hyperphagia and severe obesity that significantly burden people living with BBS and their families," said Yann Mazabraud, Executive Vice President, Head of International at Rhythm. "Receiving exemption status from the G-BA to provide access to IMCIVREE is an important recognition of the severity of BBS and further reinforces the critical distinction between rare MC4R pathway diseases and general obesity. IMCIVREE is the first and only precision medicine for patients with monogenic and syndromic obesity."

BBS is a rare genetic disease that affects between 4,000-5,000 people in the European Union (EU) and United Kingdom (UK), with an estimated prevalence of 1,200 people in Germany. People living with BBS may experience insatiable hunger, also known as hyperphagia, and severe obesity beginning early in life. BBS may also be associated with cognitive impairment, polydactyly, renal dysfunction, hypogonadism, and visual impairment. IMCIVREE is the first and only U.S. Food and Drug Administration (FDA)-approved and European Commission (EC)-authorized therapy that targets a root cause of hyperphagia and early-onset, severe obesity, and is the only approved therapy for BBS in Germany.

"Until now, the insatiable hunger leading to significant obesity has been a serious and unresolved medical issue for patients with BBS, also leading to comorbidities and psychological stress. The targeted therapy with setmelanotide could represent a turning point for many patients and demonstrate the considerable potential of precision medicine for patients with rare genetic forms of obesity," said Dr. Annette Grüters-Kieslich, emeritus professor and scientist at the Institute for Experimental Pediatric Endocrinology and Diabetology, Charité - Universitätsmedizin Berlin.

With this launch, IMCIVREE is now available to patients in nine global markets, including the United States, for treatment of POMC, PCSK1, or LEPR deficiency obesity and/or BBS. In 2022, Rhythm was granted marketing authorization for IMCIVREE by the EC for BBS and early-access authorization for setmelanotide in France. Rhythm expects to launch IMCIVREE for the treatment of patients with BBS in the Netherlands later this year and in Italy, Spain, and the UK in 2024.

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) diseases. Rhythm's lead asset, IMCIVREE (setmelanotide), an MC4R agonist designed to treat hyperphagia and severe obesity caused by rare MC4R pathway diseases, 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 MC4R pathway diseases, as well as a preclinical suite of investigational candidates 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, setmelanotide is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS) or 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.

Limitations of Use

In the United States and Europe, Setmelanotide should be prescribed and supervised by a physician with expertise in obesity with underlying genetic etiology.

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.

WARNINGS AND PRECAUTIONS

Skin Monitoring: Setmelanotide may lead to generalized 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 setmelanotide. Consideration should be given to discontinuing setmelanotide if patients experience suicidal thoughts or behaviors.

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. 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.

Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free.”

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, setmelanotide 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 setmelanotide 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. See [Summary of Product Characteristics' APPENDIX V](#) for a list of European national reporting systems to communicate adverse reactions.

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 U.S. 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, the potential benefits of setmelanotide for patients with BBS, and our expectations surrounding potential regulatory submissions, approvals and timing thereof, and our business strategy and plans, including regarding commercialization of setmelanotide in Germany other international regions. 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 and general economic conditions 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 Annual Report on Form 10-K for the quarter ended December 31, 2022 and our other filings with the U.S. 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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