Rhythm Pharmaceuticals Announces Health Canada Approval of IMCIVREE® Setmelanotide Injection for Weight Management in Bardet-Biedl Syndrome or Genetically-confirmed Biallelic POMC, PCSK1, or LEPR Deficiency

May 8, 2023

-- First and only approved therapy in Canada that targets genetic impairment in the MC4R pathway - a root cause of early-onset, severe obesity in these patients –

-- Approval granted following a Priority Review by Health Canada –

BOSTON, May 08, 2023 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a commercial-stage biopharmaceutical company, today announced that Health Canada has approved IMCIVREE® (setmelanotide solution for subcutaneous injection) for weight management in adult and pediatric patients 6 years of age and older with obesity due to Bardet-Biedl syndrome (BBS) or genetically-confirmed biallelic pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency due to variants interpreted as pathogenic, likely pathogenic, or of uncertain significance. Please consult the IMCIVREE product monograph available at www.rhythmtx.ca.

"We are pleased to announce Health Canada's approval of IMCIVREE, marking a significant expansion of our footprint in North America and another important step forward in our efforts to deliver our precision medicine to people worldwide," said Jennifer Chien, Executive Vice President, Head of North America for Rhythm. "We will leverage insights from our experience with launches in the U.S. and Europe to support the strong team we have in Canada and look forward to making IMCIVREE commercially available in Canada in the months ahead."

The early-onset obesity in patients with BBS and POMC, PCSK1 and LEPR deficiencies are caused by genetic variants that result in impairments in the melanocortin-4 receptor (MC4R) pathway, a system in the hypothalamus that regulates hunger, satiety, and energy expenditure. IMCIVREE is the first and only therapy approved in Canada for weight management in these patients following a Priority Review, which shortened the review process and was granted based on the serious nature of these conditions and lack of treatment options in Canada.

IMCIVREE is not indicated for patients with obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign, or 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, as it would not be expected to be effective.

"Research has shown that the burden of severe obesity negatively affects the lives of patients and families," said Prof. Andrea M. Haqq, M.D., Department of Pediatrics, Faculty of Medicine & Dentistry, University of Alberta. "Access to a therapy that addresses an underlying cause of their obesity is a significant advancement for patients and their families living with BBS and POMC, PCSK1 and LEPR deficiencies."

Jill Hamilton, M.D., Pediatric Endocrinologist at The Hospital for Sick Children, added, "This approval will bring much-needed relief to patients and their families who need a therapeutic option that addresses an underlying cause of obesity associated with these rare MC4R pathway diseases. Setmelanotide has been shown to reduce the weight of patients living with BBS or POMC, PCSK1 or LEPR deficiency. The Health Canada approval will provide access to many patients in need, and I am excited to see the positive impact on these patients."

The Health Canada approval is based on the results of the largest studies conducted to date in patients with obesity due to BBS as well as POMC, PCSK1, and LEPR deficiencies. In Phase 3 trials in each of these diseases, setmelanotide achieved statistically significant, clinically meaningful and sustained reductions of body weight, represented by at least a 10% weight loss from baseline at week 52. The trials met all primary endpoints and key secondary endpoints among patients at 52 weeks on therapy. Results from these trials were featured in several publications, including the peer-reviewed journal *The Lancet Diabetes and Endocrinology*. In clinical trials, IMCIVREE was generally well-tolerated. Disturbance in sexual arousal, depression and suicidal ideation, increased skin pigmentation and darkening of pre-existing nevi, and benzyl alcohol toxicity in neonates and low birth-weight infants may occur. The most common adverse reactions were skin hyperpigmentation, injection site reactions and nausea.

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) is approved by the U.S. Food and Drug Administration (FDA), and authorized by the European Commission (EC) and the UK's Medicines & Healthcare Products Regulatory Agency (MHRA) for use in accordance with product labeling. 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.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337. You can report any suspected side effects associated with the use of health products to Health Canada by: Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or calling toll-free at 1-866-234-2345.

Please see the Product Monograph at https://rhythmtx.ca/wp-content/uploads/2023/05/IMCIVREE-Product-Monograph-EN.pdf for complete 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, the potential benefits of setmelanotide for patients with BBS or POMC, PCSK1 and LEPR deficiencies, potential regulatory submissions, approvals and timing thereof of setmelanotide, and our business strategy and plans, including regarding commercialization of IMCIVREE in Canada and 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, risks relating to our liquidity and expenses, our ability to enroll patients in clinical trials, the design and outcome of clinical trials, 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 our 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, 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, failure to realize the anticipated benefits of our acquisition of Xinvento B.V. or significant integration difficulties related to the acquisition, and the other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended December 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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