Rhythm Pharmaceuticals Announces Publication of New Bardet-Biedl Syndrome Diagnostic Algorithm in the American Journal of Medical Genetics

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BOSTON, May 28, 2026 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM), a global commercial-stage biopharmaceutical company focused on transforming the lives of patients living with rare neuroendocrine diseases, today announced the publication of a new, evidence-based consensus-driven diagnostic algorithm for Bardet-Biedl syndrome (BBS). "Streamlining Diagnosis of Bardet-Biedl Syndrome: New Diagnostic Algorithm with Updated Criteria," was published in the peer-reviewed *American Journal of Medical Genetics*.

This simplified and practical diagnostic algorithm for healthcare practitioners is designed to reduce time to an informed diagnosis of BBS. A multidisciplinary group of international experts and patient advocacy organizations came together for this effort, reaffirming that BBS diagnosis can be made clinically, and providing guidance on how genetic testing can help with earlier diagnosis when all clinical criteria are not yet met. Building on the original Beales' Criteria published in 1999, these updates integrate advances in understanding BBS, including its multisystem manifestations and broader clinical presentation, as well as progress in genetic testing.

"The original diagnostic criteria were pivotal in defining Bardet-Biedl syndrome over two decades ago; however, advances in our understanding of this disease now support a more practical and integrated approach," said Professor Philip Beales, Emeritus Professor of Molecular Genetics and Genomic Medicine at University College London, primary author on the original Beales' Criteria and senior author on this new publication. "This algorithm offers clearer guidance to support earlier diagnosis, which is essential for timely management and care."

BBS is often difficult to recognize due to its variable and progressive presentation, as well as its multi-organ involvement. These factors may contribute to significant delays in diagnosis. The new algorithm provides diagnostic pathways applicable across all age groups and across a range of clinical presentations. It also outlines organ-specific manifestations based on prevalence data from multiple sources, enabling multidisciplinary specialists to more easily diagnose BBS.

"Early and accurate BBS diagnosis can make an enormous difference for affected families," said Tim Ogden, Executive Director of the Bardet Biedl Syndrome Foundation and author on this publication. "I know from personal experience that diagnosis opens the door to appropriate clinical care and support services, and better outcomes are possible the earlier that happens. Even in 2026, too many families spend years searching for answers before they get an accurate diagnosis."

Next month, Brooke Sweeney, MD, Professor of Internal Medicine/Pediatrics and Medical Director of Weight Management at Children's Mercy Kansas City and an author on this new publication, will present the updated BBS diagnostic algorithm during Rhythm's inaugural MOMENTUM MC4R Pathway Summit on Friday, June 12 in Chicago, ahead of The Endocrine Society's Annual Meeting (ENDO). For more information on MOMENTUM, please email: MC4Rsummit@rhythmtx.com.

Writing and editorial assistance for "Streamlining Diagnosis of Bardet-Biedl Syndrome: New Diagnostic Algorithm with Updated Criteria," was provided under the direction of the authors and funded by Rhythm Pharmaceuticals, Inc.

About Bardet-Biedl Syndrome

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive ciliopathy that presents with a variety of symptoms that may evolve over time. At least 28 genes have been associated with BBS to date, and some of these genes play a critical role in MC4R signaling. Variants in genes encoding the BBSome (a complex of 8 BBS proteins), or those that support BBSome function, can result in dysfunction of primary cilium, leading to impaired leptin receptor trafficking. This impairs MC4R pathway signaling, thereby causing hyperphagia and early-onset, severe obesity. BBS is estimated to affect approximately 4,000-5,000 people in the United States and 4,000-5,000 people in Europe.

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) to reduce excess body weight and maintain weight reduction long term in adult and pediatric patients aged 4 years and older with acquired hypothalamic obesity, adult and pediatric patients 2 years of age and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS) or genetically confirmed pro-opiomelanocortin (POMC), including proprotein convertase subtilisin/kexin type 1 (PCSK1), deficiency or

leptin receptor (LEPR) deficiency. The European Commission (EC) has authorized setmelanotide for the treatment of obesity and control of hunger in patients 4 years of age and above with acquired hypothalamic obesity; and both the 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 2 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 bivamelagon 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 to reduce excess body weight and maintain weight reduction long term in adults and pediatric patients aged 4 years and older with acquired hypothalamic obesity, in adult and pediatric patients aged 2 years and older with syndromic or monogenic obesity due to Bardet-Biedl syndrome (BBS) or Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

In the European Union and the 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 2 years of age and above. In the European Union and the 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 acquired HO, BBS, or POMC, PCSK1 or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Important Safety Information

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Disturbance in Sexual Arousal: Spontaneous penile erections and increased frequency of penile erections in males 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.

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

Skin Hyperpigmentation, Darkening of Pre-existing Nevi, and Development of New Melanocytic Nevi: Generalized or focal increases in skin pigmentation occurred in the majority of IMCIVREE-treated patients. IMCIVREE may also cause development of new melanocytic nevi or darkening of pre-existing nevi. Perform a full body skin examination prior to initiation and periodically during treatment to monitor pre-existing and new pigmented lesions.

Acute Adrenal Insufficiency with Acquired HO: Patients with acquired HO and secondary adrenal insufficiency reported serious adverse reactions related to acute adrenal insufficiency in 5% of IMCIVREE-treated patients and no placebo-treated patients. In patients with secondary adrenal insufficiency, monitor for clinical signs of acute adrenal insufficiency.

Sodium Imbalance in Patients with Acquired HO and Central Diabetes Insipidus: Patients with acquired HO and concomitant central diabetes insipidus (DI)/arginine vasopressin (AVP) deficiency reported hyponatremia in 6% of IMCIVREE-treated patients and 2% of placebo-treated patients and hypernatremia in 5% of IMCIVREE-treated patients and 4% of placebo-treated patients. Monitor serum sodium levels with changes in fluid intake and hydration status. Adjust the doses of concomitant therapies for DI/AVP deficiency as needed.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥20% in at least 1 indication) 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 +1 (833) 789-6337 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch. See section 4.8 of the Summary of Product Characteristics for information on reporting suspected adverse reactions in Europe.

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 safety, efficacy, potential benefits of, and clinical design or progress of any of our products or product candidates at any dosage or in any indication; the publication of a new Bardet-Biedl Syndrome diagnostic algorithm in the *American Journal of Medical Genetics*; our inaugural MOMENTUM MC4R Pathway Summit on Friday, June 12 in Chicago, ahead of The Endocrine Society's Annual Meeting, including the content, date and timing of any of the foregoing. Statements using words such as "expect", "anticipate", "believe", "may", "will" and similar terms are also forward-looking statements. Such statements are subject to numerous risks, uncertainties and other important factors, including those discussed under the caption "Risk Factors" in Rhythm's Quarterly Report on Form 10-Q for the three months ended March 31, 2026, 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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