Rhythm Pharmaceuticals and Axovia Therapeutics Announce Joint Research Collaboration in Bardet-Biedl Syndrome

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BOSTON and LONDON, Oct. 24, 2024 (GLOBE NEWSWIRE) -- Rhythm Pharmaceuticals, Inc. (Nasdaq: RYTM) and Axovia Therapeutics Ltd. today announced a joint research collaboration designed to advance the understanding of Bardet-Biedl syndrome (BBS).

“We believe there is a significant need and opportunity with the growing awareness of BBS to better understand the disease and its epidemiology,” said Prof. Phil Beales, Axovia Therapeutics’ Chief Executive Officer and Co-Founder. “At Axovia, we are utilizing gene therapy to address the loss of sight and obesity experienced by patients with BBS, and we are pleased to be collaborating with Rhythm, a global company that has pioneered research in the melanocortin-4 receptor pathway and developed the first and only commercially available drug to help treat hyperphagia and severe obesity in patients living with BBS. Rhythm and Axovia Therapeutics are natural collaborators in such an effort.”

“Prof. Beales is a leading expert on BBS and was involved in creating the original diagnostic criteria for patients living with this disease,” said David Meeker, M.D., Chairman, Chief Executive Officer and President of Rhythm. “We are excited to work together with Axovia Therapeutics to advance our shared understanding of the disease and pool the knowledge we have gained from our respective screening efforts with the goal of further improving the lives of patients and their families living with BBS.”

About Bardet-Biedl syndrome (BBS)
BBS is a rare autosomal recessive ciliopathy that presents with a variety of signs and symptoms that evolve over time including visual impairment, renal disease, polydactyly, genital abnormalities, cognitive impairment, hyperphagia and early-onset, severe obesity arising from impairment of the hypothalamic MC4R pathway. In the United States, BBS affects approximately 4,000 to 5,000 individuals with similar prevalence in Europe.

About Axovia Therapeutics
Axovia Therapeutics is leading the development of therapies that address the genetic causes of blindness and obesity which are driven by ciliopathies. Ciliopathies are a group of more than 50 inherited genetic diseases linked to more than 950 genes that impact the function of cilia which are critical for protein transport and cellular signaling. The company is positioned to initiate clinical studies for its lead program for Bardet-Biedl Syndrome (BBS), AXV-101, in mid-2025 based on robust preclinical data, scaled manufacturing and established patient registries. The initial subretinal study is designed to halt photoreceptor cell death and retinal degeneration and the CNS delivery program, which will begin in 2026, will seek to address hyperphagia and obesity. AXV-101 has achieved U.S. Food and Drug Administration Orphan Drug Designation and Rare Pediatric Disease Designation. Axovia was formed following decades of work on ciliopathies at University College London by co-founders Professor Phil Beales and Dr. Victor Hernandez.

About Rhythm Pharmaceuticals
Rhythm is a commercial-stage biopharmaceutical company committed to transforming the lives of patients 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. The EC has also authorized setmelanotide for control of hunger and treatment of obesity in children as young as 2 years old, living with BBS or POMC, PCSK1, or LEPR deficiency. 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, 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 Europe, 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.

To report SUSPECTED ADVERSE REACTIONS, contact Rhythm Pharmaceuticals at +1 (833) 789-6337 or FDA at 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.

Please see the full U.S. Prescribing Information and EU Summary of Product Characteristics 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, potential regulatory submissions, approvals and timing thereof of setmelanotide and our other product candidates, and our business strategy and plans, the potential benefits of a joint research collaboration between Rhythm and Axovia Therapeutics, and the potential of Rhythm's and Axovia Therapeutics' drug candidates to provide treatment options for patients with BBS. 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 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 ability to successfully commercialize setmelanotide, our liquidity and expenses, our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel, 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 three months ended June 30, 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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