Cyclerion Therapeutics Receives U.S. FDA Orphan Drug Designation for Zagociguat for the Treatment of Mitochondrial Diseases

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CAMBRIDGE, Mass., March 27, 2023 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company on a mission to develop treatments for serious diseases, today announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation to zagociguat (previously CY6463) for the treatment of mitochondrial diseases.

Zagociguat is the first CNS-penetrant sGC stimulator to be developed as a symptomatic and potentially disease-modifying therapy for serious diseases that involve the CNS. In an open-label, 29-day study in patients with MELAS*, zagociguat treatment was associated with improvements in multiple disease-relevant biomarkers: mitochondrial function, inflammation, cerebral blood flow, functional brain connectivity, and visually evoked brain activation. These data coupled with data from preclinical studies in cells from mitochondrial disease patients and in zebrafish disease models support the potential of zagociguat as a treatment for MELAS/mitochondrial diseases.

“Orphan drug designation underscores the FDA’s recognition of zagociguat’s potential promise as a first-ever therapy for patients with MELAS, a rare, genetic mitochondrial disease,” said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion. “Cyclerion is working expeditiously to advance this potential treatment to help address the immense unmet needs of patients with MELAS, a patient population in desperate need of therapies.”

The FDA's Orphan Drug Designation program provides orphan status to drugs defined as those intended for the treatment, diagnosis or prevention of rare diseases that affect fewer than 200,000 people in the United States. Orphan drug designation qualifies the sponsor of the drug for certain development incentives, including tax credits for qualified clinical testing, prescription drug user fee exemptions, and seven-year marketing exclusivity upon FDA approval.

About MELAS

MELAS is a complex orphan disease affecting multiple organ systems, including the CNS, with different degrees of severity, and no approved therapies. MELAS, one of the most common primary mitochondrial diseases (PMDs), is caused by mitochondrial DNA mutations resulting in large clusters of familial cases. It is estimated that about 1 in 4,300 individuals has a mitochondrial disease, and ~80% of individuals with mitochondrial disease have CNS symptoms. The unmet need in MELAS is immense, symptoms can affect virtually any organ and cause intense fatigue, muscle weakness, and pain in addition to neurological manifestations, including stroke-like episodes, encephalomyopathy, seizures, and headaches. Life expectancy is estimated at ~17 years from onset of CNS symptoms. The disease impedes the individual’s ability to live independently and leads to social isolation and overall reduced quality of life.

About Zagociguat

Zagociguat is the first CNS-penetrant sGC stimulator to be developed as a symptomatic and potentially disease-modifying therapy for serious diseases that involve the CNS. The nitric oxide (NO)-soluble guanylate cyclase (sGC)-cyclic guanosine monophosphate (cGMP) signaling pathway is a fundamental mechanism that precisely controls key aspects of physiology throughout the body. In the CNS, the NO-sGC-cGMP pathway regulates diverse and critical biological functions including mitochondrial function, neuronal function, inflammation, and vascular dynamics. Although it has been successfully targeted with several drugs in the periphery, this mechanism has yet to be fully leveraged therapeutically in the CNS, where impaired NO-sGC-cGMP signaling is believed to play an important role in the pathogenesis of many neurodegenerative and neuropsychiatric diseases. As an sGC stimulator, CY6463 acts as a positive allosteric modulator to sensitize the sGC enzyme to NO, increase the production of cGMP, and thereby amplify endogenous NO signaling. By compensating for deficient NO-sGC-cGMP signaling, CY6463 may have broad therapeutic potential as a treatment to improve cognition and function in people with serious diseases that involve the CNS, including mitochondrial diseases.

About Cyclerion Therapeutics

Cyclerion Therapeutics is a clinical-stage biopharmaceutical company on a mission to develop treatments for serious diseases. Cyclerion’s portfolio includes novel sGC stimulators that modulate a key node in a fundamental signaling network in both the CNS and the periphery. The multidimensional pharmacology elicited by the stimulation of sGC has the potential to impact a broad range of diseases. Zagociguat is a CNS-penetrant sGC stimulator that has shown rapid improvements across a range of endpoints reflecting multiple domains of disease activity, including mitochondrial disease-associated biomarkers. CY3018 is a CNS-targeted sGC stimulator in preclinical development that preferentially localizes to the brain and has a pharmacology profile that suggests its potential for the treatment of neuropsychiatric diseases and disorders. Praliciguat is a systemic sGC stimulator that is licensed to Akebia and being advanced in rare kidney disease. Olinciguat is a vascular sGC stimulator that the Company intends to out-license for cardiovascular diseases. For more information about Cyclerion, please visit https://www.cyclerion.com/ and follow us on Twitter (@Cyclerion) and LinkedIn (www.linkedin.com/company/cyclerion).

Forward Looking Statement

Certain matters discussed in this press release are “forward-looking statements”. We may, in some cases, use terms such as “predicts,” “believes,” “potential,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should”, “positive” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to, being able to complete clinical studies for zagociguat for the treatment of mitochondrial diseases, including submitting additional regulatory applications in other countries; ability to demonstrate effectiveness of zagociguat in treating mitochondrial disease in patients; ability to maintain and expand related intellectual property portfolio; and statements regarding the timing of regulatory filings regarding

development programs. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. The forward-looking statements are made only as of the date of this press release and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

* MELAS (Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes syndrome)

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