Cyclerion Therapeutics and Ariana Pharma Announce an Artificial Intelligence-driven Precision Medicine Collaboration

Collaboration to identify patient-selection biomarkers for Cyclerion's investigational therapeutics in neurological and neuropsychiatric diseases associated with cognitive impairment

Cambridge, Mass. and Paris, France, February 23, 2022 -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN) and Ariana Pharma (Cambridge, MA and Paris, France) today announced an artificial intelligence-driven, precision medicine collaboration. This collaboration is expected to identify biomarkers of response to refine patient selection to guide and accelerate the clinical development of Cyclerion's investigational therapeutics for neurological and neuropsychiatric diseases associated with cognitive impairment.

Ariana Pharma's proprietary KEM® (Knowledge Extraction and Management) eXplainable Artificial Intelligence (xAI) technology aims at significantly increasing success rates and accelerating clinical development timelines by fully evaluating complex clinical study data, including the discovery of hidden pharmacological and efficacy signals that may be beyond the reach of conventional statistical analyses. This approach enables identification of specific target patient populations, as well as biomarkers of therapeutic response for future clinical studies.

Ariana Pharma and Cyclerion will initially focus on supporting the development of CY6463, Cyclerion's lead clinical program. The collaboration will analyze data from completed Phase 1 clinical studies of CY6463, including a completed translational pharmacology study in healthy elderly subjects, as well as an ongoing study in Cognitive Impairment Associated with Schizophrenia (CIAS). Insights from these analyses are expected to accelerate and support further clinical development of CY6463.

CY6463 is an oral, first-in-class, central nervous system (CNS)-penetrant sGC stimulator that is being developed for neurological and neuropsychiatric diseases associated with cognitive impairment. CY6463 was designed to address multiple pathophysiological features of these disorders. Results from initial CY6463 clinical studies have demonstrated favorable safety and tolerability and pharmacologically relevant drug exposure in the cerebral spinal fluid. Furthermore, promising impacts on EEG measures, neuroinflammation, and other measures support the current clinical development of CY6463. In addition to the ongoing study in CIAS, studies to evaluate CY6463 safety and signals of clinical activity are also ongoing in participants with Alzheimer's Disease with vascular pathology (ADv) and Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS). Cyclerion expects to obtain clinical results from the MELAS and CIAS studies in Q2 2022 and 2H 2022, respectively. The ADv study initiated patient dosing in January 2022 and enrollment is ongoing.

"Ariana integrates disease biology, mechanism information, and pre/clinical data in their AI platform. This multidimensional machine learning approach, based on Formal Concept Analysis, identifies all possible relationships, the strongest of which may form the basis of drug-specific patient selection and/or surrogate pharmacology/efficacy markers and identify additional indications. We believe that Ariana's extensive drug development experience in the CNS and the application of this technology to our innovative pipeline may be quite powerful in guiding efficient drug development, and we look forward to a productive collaboration focused on successfully advancing CY6463 for diseases associated with cognitive impairment," said Andy Busch Ph.D., Chief Scientific Officer of Cyclerion Therapeutics.

"We are eager to apply our pioneering eXplainable AI platform KEM® to support the development of Cyclerion's promising therapeutic candidates. We believe that our platform has the capacity to help guide

the selection of patients who may benefit most from the therapy, by identifying patient-selection biomarkers, and the right measure of therapeutic efficacy, by identifying pharmacodynamic biomarkers, and optimal endpoints for future clinical development. We are excited about the prospect of using our xAI to accelerate the precision medicine development of CY6463 towards effective treatments against devastating neurological and neuropsychiatric diseases" said Mohammad Afshar, M.D., Ph.D., Chief Executive Officer of Ariana Pharma.

About Cyclerion Therapeutics

Cyclerion Therapeutics is a clinical-stage biopharmaceutical company on a mission to develop treatments that restore cognitive function. Cyclerion is advancing novel, first-in-class, CNS-penetrant, sGC stimulators that modulate a key node in a fundamental CNS signaling pathway. The multidimensional pharmacology elicited by the stimulation of sGC has the potential to impact a broad range of CNS diseases. The most advanced compound, CY6463, has shown rapid improvement in biomarkers associated with cognitive function and is currently in clinical development for Alzheimer's Disease with Vascular pathology (ADv), Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS), and Cognitive Impairment Associated with Schizophrenia (CIAS). Cyclerion is also advancing CY3018, a next-generation sGC stimulator.

For more information about Cyclerion, please visit https://www.cyclerion.com/ and follow us on Twitter (@Cyclerion) and LinkedIn (www.linkedin.com/company/cyclerion).

About Ariana Pharma

Ariana Pharma is a leading Artificial Intelligence (AI) drug development company. Using its KEM® Artificial Intelligence (xAI) technology, Ariana helps its partners introduce personalized medicine clinical trial design into their protocols and optimize clinical endpoints, identify biomarkers of therapeutic response and potential synergistic therapies. Ariana routinely collects and combines clinical data with omic data, immunological readouts (such as Fluorescence-Activated Cell Sorting (FACS)), microbiota, Patient Reported Outcomes (PRO) as well as Real World Evidence (RWE) data. Combining advanced data analytics, drug development, and regulatory expertise, Ariana helps translate findings into innovative clinical development plans and regulatory approvals. With a growing number of successful therapeutic development programs, KEM® is an FDA-assessed technology that systematically explores combinations of biomarkers, producing more effective biomarker signatures for precision medicine. Ariana has developed Onco KEM®, the most advanced, clinically tested, oncology therapeutic decision support system. Founded in 2003 as a spin-off of the Institut Pasteur, Paris, France, the company operates a subsidiary in the United States since 2012. Further information is available at www.arianapharma.com.

Forward Looking Statement
This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. We may, in some cases use terms such as "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "may," "could," "might," "likely," "will," "should" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks listed under the heading "Risk Factors" and elsewhere in Cyclerion's 2020 Form 10-K filed on February 25, 2021, and subsequent SEC filings including the Form 10-Q filed on April 30, 2021, July 29, 2021 and

November 9, 2021. Investors are cautioned not to place undue reliance on these forward-looking statements. These forward-looking statements (except as otherwise noted) speak only as of the date of this press release, and Cyclerion undertakes no obligation to update these forward-looking statements, except as required by law.

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