PRESS RELEASE

Lysogene Publishes Positive Preliminary Preclinical Results in the Treatment of Fragile X Syndrome

Paris, France — 21 April 2022 at 08:00 am CEST — Lysogene (FR0013233475 – LYS), a phase 3 gene therapy platform Company targeting central nervous system (CNS) diseases, announced today the publication of a peer-reviewed article in EMBO Molecular Medicine (Habbas et al., EMBO Mol Med (2022) e14649) showing that adeno-associated viral (AAV) vector-delivered diacylglycerol kinase (DGKk) achieves long-term rescue of fragile X syndrome (FXS) in a mouse model of disease.

The article can be accessed at: https://www.embopress.org/doi/full/10.15252/emmm.202114649.

FXS is a rare genetic condition that affects approximately 1 in 4,000 to 5,000 boys and 1 in 8,000 girls. It is estimated to affect about 110,000 people in Europe and about 70,000 people in the US. FXS is caused by a mutation of the FMR1 gene that provides instructions for production of the Fragile X Mental Retardation Protein (FMRP). This protein plays a key role in developing synapses, the connections between nerve cells that relay nerve signals. Inadequate or disrupted FMRP production affects nervous system function, leading to both cognitive and behavioral issues in patients.

The lab of Dr. Hervé Moine at the IGBMC in Strasbourg, France, discovered that diacylglycerol kinase kappa (DGKk), a main mRNA target of FMRP in cortical neurons and a master regulator of lipid signaling, is downregulated in the absence of FMRP in the brain of the Fmr1-KO mouse model. The studies, which are the result a collaboration between Lysogene and Dr. Moine's lab, the CNRS, INSERM, and ICM, show that AAV vector delivery of a modified and FMRP-independent form of DGKk corrects abnormal cerebral diacylglycerol/phosphatidic acid homeostasis and FXS-relevant behavioral phenotypes in the Fmr1-KO mouse.

These data suggest that DGKk is an important factor in FXS pathogenesis and provide preclinical proof of concept that its replacement could be a viable therapeutic strategy in FXS.

Ralph Laufer, CSO of Lysogene, commented: *"These preclinical results confirm the validity of our innovative approach targeting DGKk for the treatment of FXS, a CNS pathology with high unmet medical need. We are looking forward to expanding these results in further preclinical studies."*

About Lysogene

Lysogene is a gene therapy Company focused on the treatment of orphan diseases of the central nervous system (CNS). The Company has built a unique capability to enable delivery of gene therapies to the CNS to treat lysosomal diseases and other disorders of the CNS. A phase 2/3 clinical trial in MPS IIIA is ongoing. An adaptive clinical trial in GM1 gangliosidosis is also ongoing. Lysogene is also developing an innovative AAV gene therapy approach for the treatment of Fragile X syndrome, a genetic disease related to autism. www.lysogene.com.

Forward Looking Statement

This press release may contain certain forward-looking statements, especially on the Company's progress of its clinical trials and cash runway. Although the Company believes its expectations are based on reasonable assumptions, all statements other than statements of historical fact included in this press release about future events are subject to (i) change without notice, (ii) factors beyond the Company's control, (iii) clinical trial results, (iv) increased manufacturing costs, (v) potential claims on its products. These statements may include, without limitation, any statements preceded by, followed by or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "objective", "project," "will," "can have," "likely," "should," "would," "could" and other words and terms of similar meaning or the negative thereof. Forward-looking statements are subject to inherent risks and uncertainties beyond the Company's control that could cause the Company's actual results, performance or achievements to be materially different from the expected results, performance or achievements expressed or implied by such forward-looking statements. A further list and description of these risks, uncertainties and other risks can be found in the Company's regulatory filings with the French Autorité des Marchés Financiers, including in the 2020 universal registration document, registered with the French Markets Authorities on April 12, 2021, under number D.21-0296, and future filings and reports by the Company. Furthermore, these forward-looking statements are only as of the date of this press release. Readers are cautioned not to place undue reliance on these forward-looking statements. Except as required by law, the Company assumes no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future. If the Company updates one or more forward-looking statements, no inference should be drawn that it will or will not make additional updates with respect to those or other forward-

looking statements.
This press release has been prepared in both French and English. In the event of any differences between the two texts, the French language version shall supersede.

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