PRESS RELEASE

Lysogene Reports

Additional Positive Biomarker data with LYS-SAF302

and

Favorable Safety data with LYS-GM101

presented at the WORLDSymposium™ 2022

- **New positive biomarker data from 16 patients treated with LYS-SAF302 showing reduction in heparan sulfate and GM2 & GM3 ganglioside concentration in cerebrospinal fluid as well as neurofilament light concentration in serum**
- **Favorable preliminary safety data from 2 patients treated with LYS-GM101 showing no safety issue**

Paris, France — 11 February 2022 at 8:00 am CET — Lysogene (FR0013233475 – LYS), a phase 3 gene therapy platform company targeting central nervous system (CNS) diseases, today reports positive biomarker data from the ongoing AAVance clinical trial with LYS-SAF302 for the treatment of MPS IIIA (NCT03612869) as well as favorable safety data from the ongoing adaptative clinical trial with LYS-GM101 for the treatment of GM1 gangliosidosis (NCT04273269). Data were presented in oral presentations at the WORLDSymposium™ 2022, on February 10th, 2022. The presentations slides are available on the company's website at www.lysogene.com.

LYS-SAF302 biomarker data

Analysis of heparan sulfate (HS) concentration, the primary disease biomarker in MPS IIIA, in the CSF of all 16 patients analyzed at 6 and 12 months after treatment with LYS-SAF302 in AAVance showed 23% reductions relative to pre-treatment values. Furthermore, about 30% reductions in the concentration of secondary storage products GM2 and GM3 ganglioside, which are thought to be possible contributors to neuronal damage in lysosomal storage diseases, were observed in the CSF of treated patients at 12

months after treatment, relative to pre-treatment values. These results are consistent with the assumption that intraparenchymally administered LYS-SAF302 leads to a specific reduction of heparan sulfate and gangliosides entering the CSF from the brain parenchyma, with no effect on biomarkers entering the CSF from sources other than the brain, such as the spinal cord, choroid plexus or blood.

Serum concentrations of the axonal damage biomarker neurofilament light (NF-L) were increased in patients with MPS IIIA at baseline, relative to published values in children with no neurological disease, likely reflecting ongoing neurodegeneration associated with MPS IIIA. Following treatment with LYS-SAF302 in AAVance, mean serum NF-L concentrations increased, reaching about 2-fold above baseline at 6 months. This increase could be due to either disease progression or transient neuronal damage induced by intracranial surgery, as reported in other clinical trials with different drug products. At 12 months, mean NF-L levels returned to baseline values and then decreased to about 2-fold below baseline values at 18 and 24 months. A decrease of NF-L below baseline levels may indicate a positive effect of treatment.

LYS-GM101 safety data

The P1-GM-101 (NCT04273269) adaptive design gene therapy trial assessing safety and efficacy of intracisternal administration of LYS-GM101, an AAVrh10 vector carrying the GLB1 cDNA, in children with infantile GM1 gangliosidosis is ongoing. No adverse events linked to the intra-cisternal route of administration or the investigational gene therapy have been observed at more than 5 months post-dosing in the first two patients with late infantile GM1 gangliosidosis who have been treated. Based on a review of the initial safety data from these 2 subjects by the study Data Safety Monitoring Board, it has been decided that 2 subjects with early infantile GM1 gangliosidosis would receive LYS-GM101 in early 2022 to complete Stage 1. Consequently, the 3rd patient was treated in early February 2022. The enrollment of the 4th patient of the safety cohort is ongoing, following which Lysogene will initiate the treatment of the 12 patients of the efficacy confirmatory cohort.

"*These very encouraging results confirm and extend evidence of positive biological responses to LYS-SAF302 treatment in patients enrolled in the AAVance trial which had previously been observed in a smaller number of patients. The extent of reduction of the disease biomarker HS is consistent with Lysogene's unique intra-parenchymal mode of administration, which delivers the drug directly into the brain, where accumulation of HS causes the predominantly neurological manifestations of MPS IIIA. The reduction relative to baseline of the secondary storage products, GM2 and GM3 ganglioside 12 months after treatment, as well as the decrease of the axonal damage biomarker neurofilament light from 18 months onward, confirm the biological activity and therapeutic potential of LYS-SAF302. We look forward to confirming these results in additional patients and timepoints"* said **Dr. Ralph Laufer, Chief Scientific Officer of Lysogene.** *"We are also very encouraged with the DSMB's confirmation of LYS-GM101 safety profile and plan to complete Stage 1 of the study in the coming weeks"*.

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 a delivery of gene therapies to the CNS to treat lysosomal diseases and other genetic 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 collaborating with an academic partner to define the strategy of development 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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