PRESS RELEASE

Lysogene Reports LYS-SAF302 Biomarker Data Presented at the WORLDSymposium™ 2021

- **Evidence of positive biological response to LYS-SAF302 in patients treated in the AAVance clinical trial**
- **~30% decrease in pathological heparan sulfate in cerebrospinal fluid 12 months after treatment**
- **~40% decrease in pathological GM2 and GM3 gangliosides in cerebrospinal fluid 12 months after treatment**

Paris, France — 15 February 2021 at 08:00 am CET — Lysogene (FR0013233475 – LYS), a phase 3 gene therapy platform company targeting central nervous system (CNS) diseases, today reports biomarker data from the ongoing AAVance clinical trial with LYS-SAF302 for the treatment of MPS IIIA (NCT03612869) presented at the WORLDSymposium™ 2021 by Dr. Michaël Hocquemiller, Head of Non-Clinical Development, during the Late-Breaking Science session held on Friday, February 12, 2021.

Concentration of heparan sulfate (HS) in the cerebrospinal fluid (CSF) has been analyzed in 9 patients so far, with samples at baseline (n=9), 6 months (n=8) and 12 months (n=5) after LYS-SAF302 administration. The concentration of abnormally elevated HS-derived oligosaccharides in the CSF was reduced from baseline by 27% and 30% at 6 and 12 months, respectively ($p<0.005$ and $p<0.05$ by paired t-test vs baseline, respectively).

In contrast, changes in HS concentrations in serum samples from the same patients were not statistically significant, confirming that the reduction of HS in CSF after LYS-SAF302 treatment is linked to a reduction of HS entering the CSF from the brain parenchyma and not an indirect consequence of a reduction of HS entering the CSF from extra-parenchymal sources, such as choroid plexus or blood. Additionally, changes in dermatan sulfate (DS) and keratan sulfate (KS), which do not accumulate in MPS IIIA, were not statistically significant in serum and CSF, confirming the specificity of HS accumulation in the CSF.

Furthermore, the concentration of abnormally elevated GM2 ganglioside in CSF of the same patients was reduced from baseline by 7% and 40% at 6 and 12 months, respectively ($p<0.005$ by paired t-test vs baseline at 12 months), while the concentration of abnormally elevated GM3 ganglioside in CSF was reduced from baseline by 7% and 37% at 6 and 12 months, respectively ($p<0.005$ by paired t-test vs baseline at 12 months).

Ralph Laufer, Chief Scientific Officer at Lysogene said*: "The CNS-specific reduction of the disease biomarker HS is consistent with the mode of drug administration, directly into the brain, where accumulation of HS causes the predominantly neurological manifestations of MPS IIIA. The reduction in secondary storage products GM2 and GM3 gangliosides, which are thought to be possible contributors to neuronal damage in lysosomal storage diseases, confirms the biological activity and therapeutic potential of LYS-SAF302."*

The presentation is available on the "Events" page in the "Investors & Media" section of Lysogene's website (www.lysogene.com/events).

About the AAVance clinical trial

The AAVance Phase 2/3 clinical study is designed as an open-label, single-arm, multicenter study of LYS-SAF302 for the treatment of MPS IIIA. The study has been extensively discussed upfront with key opinion leaders, regulators and health technology assessment bodies, as well as with patient representatives. As of today, 19 patients have been treated. The primary objective is to assess the drug efficacy in improving the neurodevelopmental status of patients after 24 months, compared to the expected evolution based on natural history data. Safety, tolerability, effect on behavior, sleep and quality of life will also be collected as secondary endpoints. Lysogene has also set up the sub study, PROVide, collecting supportive video outcomes in the home environment.

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 genetic disorders of the CNS. A phase 2/3 clinical trial in MPS IIIA in partnership with Sarepta Therapeutics, Inc. is ongoing. An adaptative clinical trial in GM1 gangliosidosis is in preparation. In accordance with the agreements signed between Lysogene and Sarepta Therapeutics, Inc., Sarepta Therapeutics, Inc. will hold exclusive commercial rights to LYS-SAF302 in the United States and markets outside Europe; and Lysogene will maintain commercial exclusivity of LYS-SAF302 in Europe. 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 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 and (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 2019 universal registration document, registered with the French Markets Authorities on April 30, 2020, under number D.20-0427, 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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