PRESS RELEASE

Lysogene Provides Additional Update on AAVance Phase 2/3 Gene Therapy Clinical Trial with LYS-SAF302 in children with MPS IIIA

- **Positive biomarker data confirmed in additional subjects and at additional timepoints**
- **Stable or continuously increasing cognitive, language and motor functions observed in patients treated at ≤31 months of age, including subjects with SGSH mutations associated with the severe disease phenotype**
- **Full data analysis in Q3 2022 before discussions with regulatory authorities on next steps**

Paris, France — 07 July 2022 at 08:00 am CET — Lysogene (FR0013233475 – LYS), a phase 3 gene therapy platform Company targeting central nervous system (CNS) diseases, today communicates additional preliminary data from the AAVance Phase 2/3 gene therapy trial in MPS IIIA (NCT03612869). Data will be presented at the ADVANCE 2022 Sanfilippo Community Conference held on July 7-8, 2022, and at the 3rd Annual Gene Therapy for Neurological Disorders Europe held on July 11-13, 2022.

A positive effect of LYS-SAF302 on the MPS IIIA disease biomarker heparan sulfate (HS) in the cerebrospinal fluid (CSF) was confirmed in additional subjects and at additional timepoints relative to previously communicated partial data. Statistically significant decreases of about 20% in average levels of total HS-derived oligosaccharides in the CSF relative to baseline levels were observed at 6, 12 and 24 months after dosing with LYS-SAF302. HS levels at 24 months after dosing with LYS-SAF302 (1654 ± 497 ng/ml, mean ± SD, n=15) were decreased by 22% relative to baseline levels (2159 ± 589 ng/ml, mean ± SD, n=16), p=0.015 by Student's t test (preliminary analysis). No statistically significant effect on serum HS levels was observed at 6, 12 or 24 months after dosing with LYS-SAF302. These results confirm the biological activity of LYS-SAF302 gene therapy treatment. They are consistent with the

intraparenchymal mode of administration of LYS-SAF302, which is expected to lead to a specific decrease of HS in the brain, but not in the systemic circulation nor in other tissues, including the spinal cord.

The previous observation that treatment with LYS-SAF302 led to a transient increase in serum neurofilament light (NFL) levels, likely due to transient axonal damage caused by brain surgery, followed by a decrease below baseline levels, was confirmed in additional subjects and at additional timepoints. Moreover, a similar effect was demonstrated in the CSF. In the serum, NFL levels decreased by 33% (n=12, p=0.026) and 41% (n=16, p=0.0075) below baseline levels (113 ± 50 pg/ml, mean ± SD, n=19), 18 and 24 months after dosing with LYS-SAF302, respectively. In the CSF, NFL levels decreased by 33% (n=15, p=0.025) below baseline levels (3.7 ± 1.5 ng/ml, mean ± SD, n=17) 24 months after dosing with LYS-SAF302. All statistical analyses were done by Student's t test and are preliminary. These results suggest that treatment with LYS-SAF302 led to a decrease in neuronal damage relative to baseline at 18 and 24 months after drug administration.

Three subjects in AAVance, treated at 10, 13 and 31 months of age, present continuous increase of cognitive, language and motor functions 24 months after dosing with LYS-SAF302, as assessed by the BSID-III (Bayley's Scales of Infant Development, Third edition). Two of these subjects have a cognitive developmental age (DA) at 24 months after dosing with LYS-SAF302 that is 5-6 months higher (41 and 42, respectively) than the highest cognitive DA (35) observed in natural history studies of MPS IIIA (Shapiro et al, 2016; Wijburg et al 2022). Remarkably, one of these subjects is homozygous for a severe mutation (deletion) and the other subject is compound heterozygous for two severe mutations (a duplication and a deletion). The third subject with continuously increasing DA at 24 months after dosing with LYS-SAF302 is a compound heterozygote for a severe mutation and a S298P mutation, which may give rise to either a classical severe or an intermediate phenotype. Longer follow-up is warranted to confirm positive evolution of development in this patient. Three other subjects, treated at 24, 30 and 31 months of age, have stable cognitive DA relative to baseline, as assessed by the BSID-III scale, and stable or continuously increasing BSID-III language and motor development scores at 24 months after dosing with LYS-SAF302. Two of these subjects have SGSH missense mutations associated with the classical severe phenotype of MPS IIIA. One subject has a severe mutation on one allele and a mutation with unknown effect on disease severity on the second allele. The fact that developmental progression or stabilization is seen in subjects with mutations associated with the classical severe disease phenotype suggests that early therapeutic intervention with LYS-SAF302 can protect children with MPS IIIA from decline of cognitive, language, and motor functions.

The AAVance trial Month 24 database lock took place as planned on 1st of July 2022. Full study results are expected by mid-September 2022, along with results from the PROVide patient reported outcome videos study. Based on this comprehensive clinical data package, the company plans to initiate discussions with regulatory authorities in the US and in Europe to determine next steps.

"Preliminary data for AAVance indicates that subjects with MPS IIIA treated prior to 31 months of age not only continued with increasing developmental age, but exceeded developmental ages of any MPS IIIA subjects within the natural history cohorts. This data is highly suggestive of LYS-SAF302 efficacy in this treatment population, marking an important milestone as no treatment is currently available to slow the progression of MPS IIIA", said **Raymond Wang, M.D., Director, Foundation of Caring Multidisciplinary Lysosomal Disorder Program at CHOC Children's Specialists, Orange, CA, USA, and one of the principal investigators for the AAVance trial.**

"We are very pleased to confirm on a larger scale the encouraging data already observed earlier, notably stabilization or improvement in cognitive, language and motor functions in the younger patient population, even in those presenting with severe forms of the disease. We have recently locked the database of the 24-month post-treatment follow-up data. Full statistical analyses are underway with results expected in September this year. This represents a very exciting milestone as it completes years of efforts by the Lysogene team to bring a treatment to patients with MPSIIIA, a disease with a high unmet medical need. By Q3 2022, we should have the necessary elements to discuss the next steps with the regulatory authorities", said **Marie Trad, M.D. Chief Medical Officer** of Lysogene.

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. The Company also entered into an exclusive worldwide license agreement with Yeda, the commercial arm of the Weizmann Institute of Science, for a novel gene therapy candidate for neuronopathic Gaucher disease and Parkinson disease with GBA1 mutations. 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 2021 universal registration document, registered with the French Markets Authorities on April 19, 2022, 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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