NTSAD

SAM PARKER
Chief Patient Access Officer

APRIL 12, 2019
...HOW IT ALL STARTED...
## Lysogene Today: Focus in Orphan CNS Diseases

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>PROGRAM</th>
<th>VECTOR</th>
<th>ENZYME</th>
<th>POC</th>
<th>PRE-CLINICAL</th>
<th>PHASE 1/2*</th>
<th>PIVOTAL</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanfilippo A (MPS IIIA)</td>
<td>LYS-SAF302</td>
<td>AAVrh10</td>
<td>N-sulfoglycosamine sulphohydrolase</td>
<td></td>
<td></td>
<td></td>
<td>green</td>
<td>PIVOTAL TRIAL START H2 2018 (FPI**)</td>
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<tr>
<td>GM1 Gangliosidosis</td>
<td>LYS-GM101</td>
<td>AAVrh10</td>
<td>Beta-galactosidase-1</td>
<td></td>
<td>blue</td>
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<td>Phase 1/2 trial IND submission</td>
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<tr>
<td>Fragile X syndrome (FXS)</td>
<td>FXS01</td>
<td>AAV</td>
<td>5’-truncated Diacylglycerol Kinase Kappa (Dgkk)</td>
<td></td>
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<td>Pre-clinical proof of concept</td>
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*MPS IIIA Phase 1/2: LYS-SAF301, first generation program  
** FPI : « First Patient In »: First Patient Enrolled
A single therapy is anticipated to compensate for the genetic abnormality

The goal of therapy is a steady state, rather than varying levels of the therapy over time as with recombinant protein therapy

Intra-CSF administration: Preferred RoA for indications with CNS including spinal cord & cerebellum involvement

- Intracisternal
- Intrathecal (lumbar)
- Intracerebroventricular

Adeno-associated virus

4.5 kb genome

promoter

normal βgal gene coding sequence

LYSOGENE
Gene therapy for GM1 Gangliosidosis

**GM1 Gangliosidosis**

GM1 gangliosidosis disease is caused by the absence or significantly reduced level of the enzyme beta-galactosidase (GLB1).

Severe GM-1 ganglioside build up causes progressive neurodegeneration.

The later onset forms of GM1 occur when the mutations allow the GLB1 enzyme to function a little bit.

Just a small increase in GLB1 activity is enough to delay the onset and slow the progression of symptoms.

**Project: LYS-GM101**

**Mechanism of action:**
Replacement of βgal, reducing GM1 ganglioside accumulation

**Administration route**
intrathecal (cisternal)

**Special regulatory status:**
Orphan Drug Designation – FDA Rare Pediatric Disease Designation
AAVrh.10 βgal corrects lysosomal pathology in GM1 animal models

AAVrh.10βgal treatment of GM1 mice and GM1 cats:

- Significantly increases βgal activity in the brain and reduces lysosomal storage throughout CNS compartments
- Produces long-term βgal expression

In addition, have shown that LYS-SAF302 yields broad distribution of SGSH enzyme activity in brain, cerebellum and spinal cord of non-human primate.
## Study design

Will primarily look at speech and motor Natural history data, potentially serving as external control, already published and ongoing

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<tbody>
<tr>
<td>Sample size</td>
<td>18 GM1 patients</td>
</tr>
<tr>
<td>IND open</td>
<td>2020</td>
</tr>
<tr>
<td>Study duration</td>
<td>24 months follow-up</td>
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<tr>
<td>Sites</td>
<td>USA and Europe</td>
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Responsibility and Purpose

- Create and work beside global networks of patients, experts, clinicians, policy makers and regulators
- Patient centric: create therapies that will offer a better life for patients
We thank the children, their parents and families for their continued contribution, time and energy to progressing research in finding treatments.