Chelsea's Hope
Lafora Children Research Fund

Lafora Therapeutic Pipeline

An Update on Therapies in Development from the 2025 Lafora Science Symposium

Antisense Oligonucleotide Therapies

What is it? Antisense Oligonucleotides (ASOs) bind specific transcribed genes (mRNA), making the RNA unable to make protein. This reduces protein levels in the patient, which slows/halts glycogen accumulation to slow/halt disease progression

ION283 Gys1 ASO Updates:

- 10 patients are enrolled in the Safety Study at UTSW
- $1.32 million raised, $1.5 million needed to complete the study
- 15mg dose of ION283 has been well-tolerated in patients but has not halted disease progression
- 30mg dose is predicted to be an efficacious dose, which could slow/halt disease progression
- The FDA approved the dose escalation if a patient has already had 3x lower doses
- The team at UTSW agreed to share data with Noventia so that they can accelerate a clinical trial in Europe
- Noventia has not released any updates to the community since our open letter this summer. As of the Symposium, they were still negotiating with Telethon, which would be the foundation helping to design and run the clinical trial. Until that contract is signed, nothing can move forward with Noventia.

Stay up to date on our website: https://chelseashope.org/safety-study/

Gene Therapies in Development

What is it? Gene therapy is designed to replace the mutated versions of a gene in patients with the correct version, allowing the gene to be transcribed into a functional protein.

EPM2A and EPM2B-Targetting Updates:

- Dr. Serratosa's lab has developed a gene therapy for EPM2A and EPM2B
- Both therapies have shown in mice that EEG signals in the hippocampus were restored to normal levels
- Treatment did not reduce damage to the astrocytes but did reduce neurodegeneration in the mouse hippocampus
- Researchers are continuing to work to improve the distribution of the drug. They need to make sure it reaches all regions of the brain.
- Barriers to treatment: It is expensive to manufacture this drug, and data was shared from UTSW that overexpression of EPM2A could have potential toxic effects, so the toxicity needs to be carefully monitored in future experiments.

Gene Therapy 101: https://chelseashope.org/wp-content/uploads/2022/06/Gene-Therapy-101.pdf

Antibody Enzyme Fusion Therapies

What is it? Antibody Enzyme Fusion (AEF) is a type of Enzyme Replacement Therapy that uses an antibody to deliver an enzyme (i.e. a protein) where it is needed to perform its necessary function in the patient. The enzyme is lab-made and administered through IV or ICV injection.

VAL-0417 AEF Updates:

- Successfully degrades Lafora Bodies and restores normal metabolism in mouse models
- VAL-0417 was given to a canine with Lafora disease using a delivery mechanism directly to the brain. Data is still being collected, but the owner reports that the dog is in good health.
- Tests in more canines are required to have enough data to show the drug is effective. Data could be used to apply for a clinical trial.
- Barriers to the trial: The IP belongs to Valerion (now Parasail), which went bankrupt, so the use of the drug would have to be negotiated in the US (this is not a problem in Europe), and the community would likely need to pay 100% of the trial costs

VAL-1221 AEF Updates:

- 8 patients have now used this drug through a compassionate use option
- Shown to be effective in animal models when administered directly to the brain, but the drug is only approved for IV administration in humans, and the data from the compassionate use patients shows that the drug does not get to the brain.
- To be effective, this drug needs to obtain approval for a different type of administration that allows the drug to reach the brain
- Barriers to trial: This IP is also owned by Valerion/Parasail, so if the company is not interested in developing the drug, we would need to develop it in Europe to avoid IP issues.

hTfR Amylase AEF Updates:

- This is a new AEF under development, with the IP owned by the University of Florida and Harvard
- It is similar to VAL-0417 and VAL-1221. However, it has a third component that allows it to interact with the Transferrin Receptor (TfR) and cross the blood-brain barrier, so it could be administered through an IV and still reach the brain.
- Works similarly to VAL-1221 and VAL-0417 in mouse models
- Barriers to trial: Still needs about a year of preclinical work to determine the minimum effective dose and maximum tolerance levels