AT-1501

“The most effective potential treatment tested at the ALS Therapy Development Institute.”

- Steve Perrin, Ph.D. CEO/CSO

ALS THERAPY DEVELOPMENT INSTITUTE
An Unmet Need
ALS is a progressive, fatal, neurodegenerative disease, typically causing death within 3-5 years of diagnosis. The only FDA approved drug for ALS is Riluzole, which at best prolongs life by 90 days. There are few potential treatments in ALS clinical trials.

What we know
Based on our data, about 70% of people with ALS have an immune response at some point during its progression. ALS tends to progress and then plateau, progress and then plateau. The immune system may be highly active during the progression stages and less active during the plateau stages. The immune system appears to be involved in both familial and sporadic forms of ALS. These findings make targeting immune response in ALS extremely important in developing effective treatments quickly for everyone with ALS.

What is AT-1501?
AT-1501 is an antibody therapeutic with comprehensive and promising preclinical data. It blocks specific immune cell activation and may protect nerves against the progression of ALS.

Why we are excited about AT-1501
In preclinical testing, AT-1501 produced the most exciting outcomes we have seen in the over 300 drugs tested since the inception of ALS TDI. In the gold standard SOD1 mouse model:

- AT-1501 extended life span significantly; beyond any other drug that has been advanced into human ALS clinical trial.
- AT-1501 delayed disease onset.
- AT-1501 improved body weight, signaling that muscle is healthier.
- AT-1501 improved the percentage of neuromuscular junctions that remain intact, allowing muscle to remain functional.
- AT-1501 decreased indications of inflammation in nerves and spinal cord.

All of these data have been consistently reproduced, enhancing our excitement and confidence that AT-1501 is one of the best drug candidates ever developed for advancement to clinical trial for ALS.

What is needed to advance it?
We have been developing AT-1501 since 2013. Currently it is being evaluated for safety in non-human primates. To move AT-1501 through a Phase 2 clinical trial, we will need to raise $30 million.
We believe that in ALS, there are two distinct disease-driving events that can potentially be slowed down or halted by AT-1501.

By blocking CD40 Ligand on T cells, AT-1501 is inhibiting both events by:

1. Helping to keep the connection at the neuro-muscular junction intact because it prevents macrophages from attacking it.

2. Helping to decrease a different population of T cells that cause neuro-inflammation and neuro-toxicity. So instead of activating the natural immune cells in the spinal cord, it keeps them quiet so that they don’t attack the neuron and eliminate it.

Work to date

2008
Completed the first unbiased comprehensive study of 12 tissues in the mouse over time and identified pathway. Sourced antibodies to explore if blocking the pathway in mice would produce a result. Tested the hypotheses and saw that drug was slowing disease down. Repeated the experiment. 3 months later, the results from the repeat were the same!

2008-2010
Spent two years investigating exactly how the antibody blocked the pathway in mice. Discovered that 1) it improves the percentage of neuro-muscular junctions that do not die, 2) It decreases the macrophage attack on nerves, and 3) It decreases the activation of microglia and astrocytes.

2011
Tested versions of mouse antibodies to see if they would work. Made human antibody that blocks CD40 Ligand.

2013
Began working with our own human version of the antibody, confirming its impact in mice and confirming its potential in clinical trials for people with ALS.

2014
Settled on the final analog of the antibody.

2015
Signed the manufacturing contract with Lonza.

2016
In late summer, Lonza work resulted in stable and scalable manufacturability of AT-1501.

2017
Non-human primate studies began to ensure safety of drug before human clinical trials.
WHERE DO WE GO FROM HERE?

A QUICK LESSON ON PRE-CLINICAL AND CLINICAL TRIALS

Pre-clinical research does not involve testing in humans and is a stage of research that begins before clinical trials. Clinical trials are conducted in a series of steps, called “phases.” Each phase is designed to answer a separate research question.

Phase I: Researchers test a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.

Phase II: The drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.

Phase III: The drug or treatment is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely.

Phase IV: Studies are done after the drug or treatment has been marketed to gather information on the drug’s effect in various populations and any side effects associated with long-term use.

It is important to keep in mind that timelines in the world of drug development can change frequently and significantly. The pace of drug development can be impacted by such variables as:

- The reality that there are sometimes unexpected outcomes in the scientific process.
- The amount of funding in place to advance from one stage to the next.

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$300K
Formulation
i.e. optimization of drug stability after purification and making it last as long as possible.

$300K
Lyophilization
i.e. turning drug from liquid form to powder, as powder is more stable, and stability testing.

$1.6M
Make an 800L GMP** grow that will be of suitable quality for humans.

$300K
Ship drug to vialer, who then ships worldwide for trials.

$150K
Develop process to vial AT-1501

$750K-$1.5M
File IND*** w/ FDA.

$250K
Non-human primate PK Study* to help us learn how to dose AT-1501

$1.5M
Non-human primate Tox Study, where dose levels are similar to/higher than what would be administered to humans, in order to gauge effect of dose.

$1.5M
Phase 1 clinical trial

$24M
Phase 2 clinical trial

Q1 2017 Q2 2017 Q3 2017 Q4 2017 Q1 2018 Q2 2018 Q3 2018 Q4 2018 Q1 2019 Q2 2019

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*PK Study = Pharmacokinetic Study
**GMP = Good Manufacturing Practice
***IND = Investigational New Drug Application

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