Protecting Synapses to Treat Neurodegenerative Diseases
Allyx Therapeutics Founding Team

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ALZHEIMER’S DISEASE
BY THE NUMBERS

5.8 Million Patients in the US

40% Patients in MCI Stage of Disease

6th Leading Cause of Death in US

17 Million Patients in US by 2050

Currently No Disease Modifying Therapies Available
Tenets of Allyx
Path to Developing a Disease Modifying AD Therapy

1. Targeting synapse loss is required as it is the underlying driver of disease progression

2. Conduct animal studies in a manner that best models human disease progression and clinical treatment paradigms with replication across multiple models

3. Utilize PET imaging biomarkers as a powerful means to de-risk clinical development and validate mechanism of action

4. Leverage non-dilutive funding available from the NIH at each stage of the development process to maximize investor equity and returns
ALX-001 – mGluR5 Silent Allosteric Modulator (SAM)
Optimized Mechanism of Action and TPP for AD Therapy

mGluR5 is Essential for Cognition
Central Receptor for Pathophysiological Synapse Dysfunction and Loss

Silent
Glu Signaling
Aβ/PrP Signaling

Normal Synaptic Physiology
Rescue AD Pathophysiology

In-licensed portfolio of mGluR5 allosteric modulators from BMS
Highly potent and selective small molecule. Preferentially delivered to the brain.
Solid oral formulation and expected QD dosing
Disease reversal demonstrated in 3 different mouse models of Alzheimer’s disease
Wide therapeutic window validated by primate receptor occupancy study

IND activated March 2021 with Phase 1a currently underway at the Yale Alzheimer’s Disease Research Center
ALX-001 **Restores** Learning and Memory Deficit in Mouse Model of AD and **Reverses** Synapse Loss

**Rescues Memory Deficit**

- Novel Object Recognition

**Reverses Synapse Loss**

- Synapse Quantification

**Aβ Plaque Levels Are Unchanged**

- Plaque Quantification

**ALX-001 Reverses Disease In Preclinical Models**

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**Model:** APP/PS1  
**Age:** 12-month old  
**Status:** Established AD Phenotype  
**Treatment:** 3.75 mg/kg BID  
**Duration:** 1-Month
**Translatable Imaging Technologies Mitigate Clinical Risk**

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### Early Clinical Development

**mGluR5 PET**

*Title: Early Clinical Development*

Measure ALX-001 target engagement at predicted therapeutic concentrations and relationship with safety.

### Late Clinical Development

**Synapse Targeting PET**

*Title: Late Clinical Development*

Establish proof of concept by tracking synapse preservation with ALX-001 treatment in patients.
Focus on neuronal synapse protection and rescue

Distinct mechanism of action from Aβ or Tau lowering technologies

Genetic link to GWAS AD risk variant

Expedited and capital efficient plan to Proof of Concept

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