



*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

6<sup>th</sup>

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

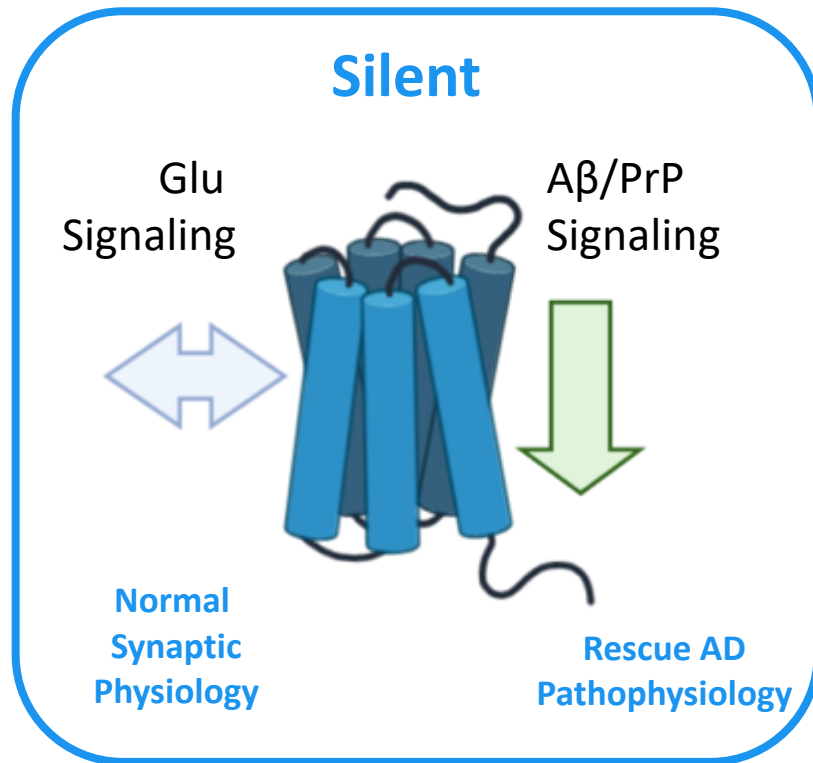
- 1 Targeting synapse loss is required as it is the underlying driver of disease progression
- 2 Conduct animal studies in a manner that best models human disease progression and clinical treatment paradigms with replication across multiple models
- 3 Utilize PET imaging biomarkers as a powerful means 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



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



Model: APP/PS1

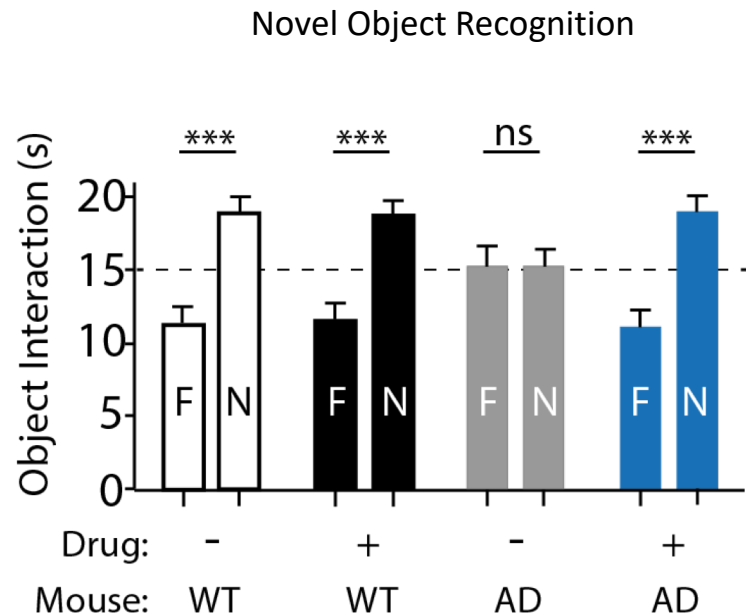
Age: 12-month old

Status: Established AD Phenotype

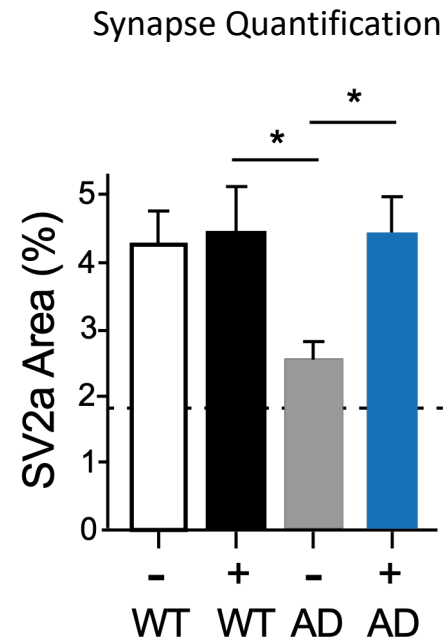
Treatment: 3.75 mg/kg BID

Duration: 1-Month

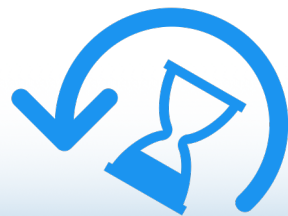
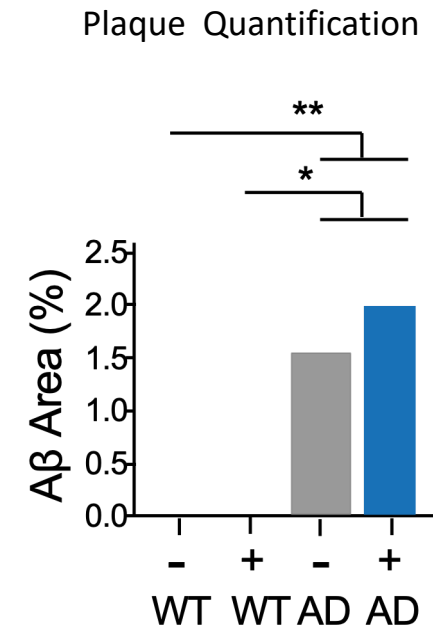
## Rescues Memory Deficit



## Reverses Synapse Loss



## A $\beta$ Plaque Levels Are Unchanged



ALX-001 Reverses Disease In Preclinical Models



# Translatable Imaging Technologies Mitigate Clinical Risk

Non-Clinical

Safety Study in HV

Phase 1a

Ongoing

Safety Study in AD Patients

Phase 1b

PoC Study in AD Patients

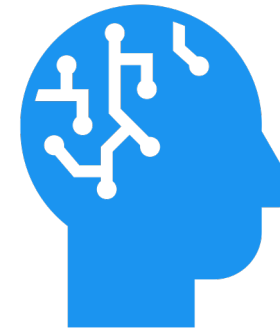
Phase 2



mGluR5 PET

Early Clinical Development

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



Synapse Targeting PET

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 A $\beta$  or Tau lowering technologies

Genetic link to GWAS AD risk variant

Expedited and capital efficient plan to Proof of Concept

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