Oscotec R&D Day

April 15, 2024

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CEO

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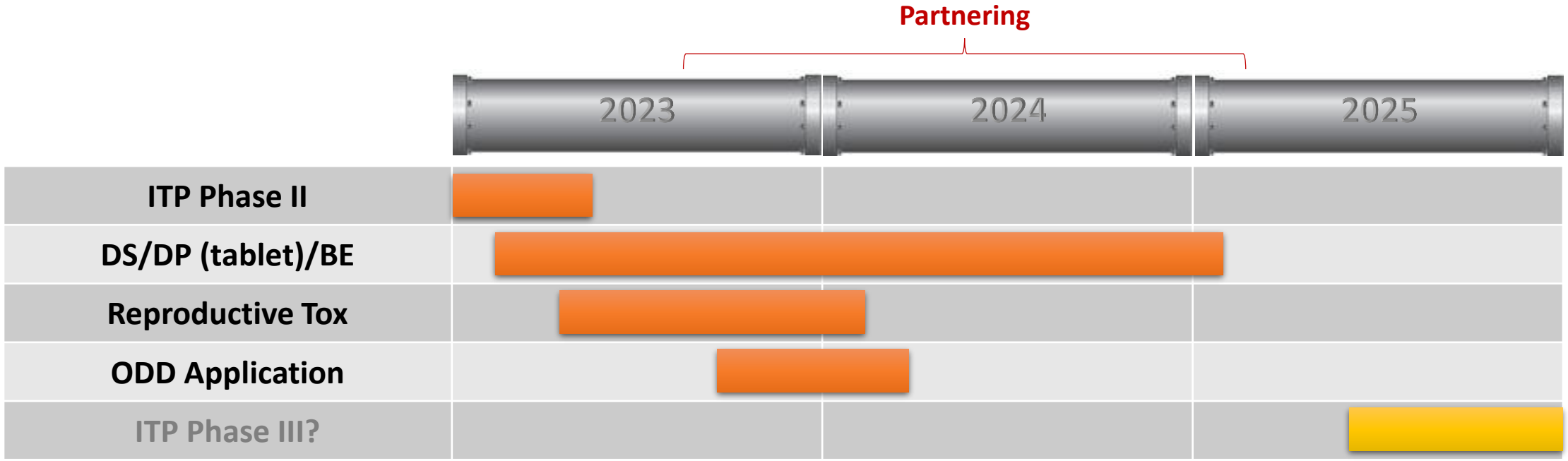
Agenda

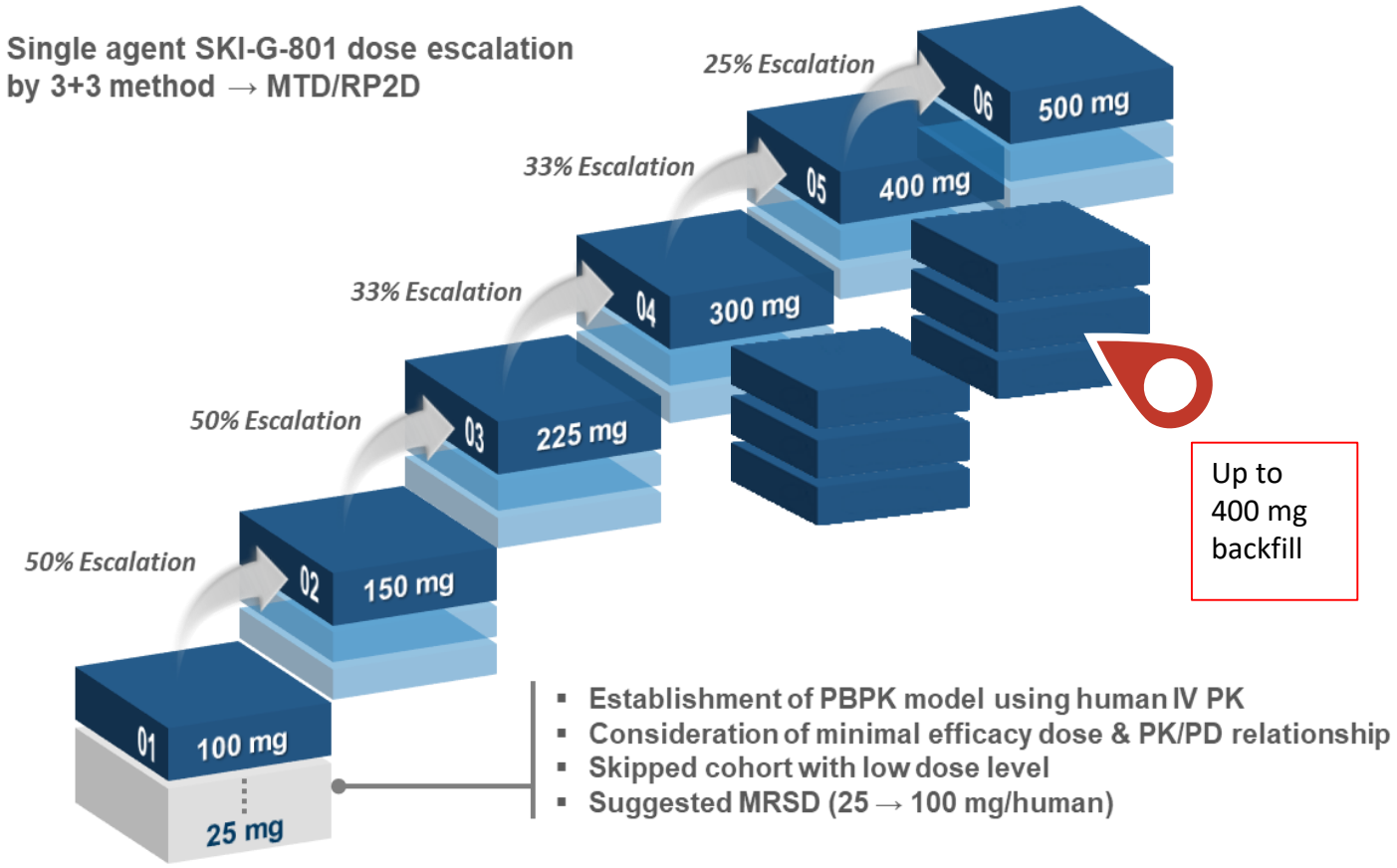
- Oscotec Pipeline Update
  - Cevidoplenib (SKI-O-703) in partnering discussions
  - Denfivontinib (SKI-G-801) wrapping up P1a study in solid tumors
  - ADEL-Y01 P1a study underway (Cohort 2)
  - OCT-598 completes GLP tox studies; CMC development ongoing
- Spotlight on ADEL-Y01
  - Alzheimer drug development landscape
  - The promises and pitfalls of tau immunotherapy
  - ADEL-Y01, the best-in-class anti-tau antibody
- Under the Hood
- Q&A

Cevidoplenib; Immune Thrombocytopenia and Beyond



- Successful completion of Phase 2 study in patients with chronic ITP
- Completed reproductive toxicology
- **Orphan drug designation by FDA**
- **Large potential for indication expansion**
- **Partnering discussions ongoing**

Denfivontinib Clears the Safety Bar in P1a



Aims

Dose finding
Safety, PK

Main Eligibility

Refractory
Solid Tumor

Safety Review

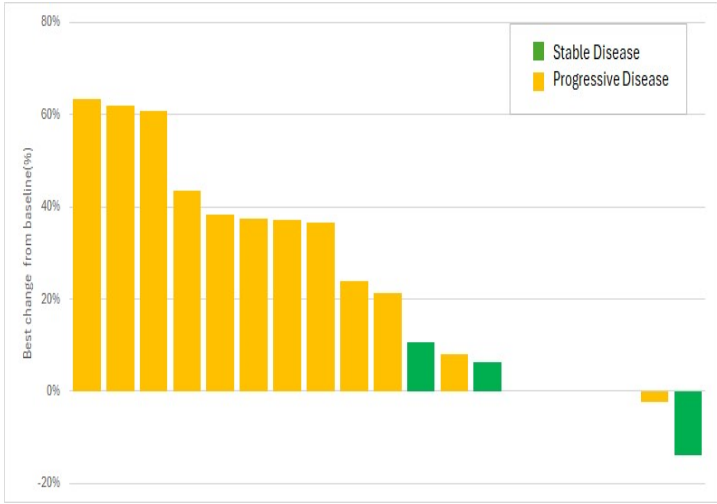
SRC review prior to dose escalation

Safety profile

- MTD not reached (400 mg)
- 2 DLTs reported
- 3 SAEs reported
- No new safety signals

Efficacy signal

- Little antitumor activity observed as a single agent

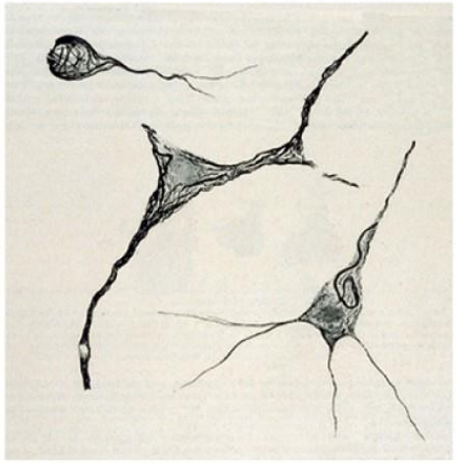


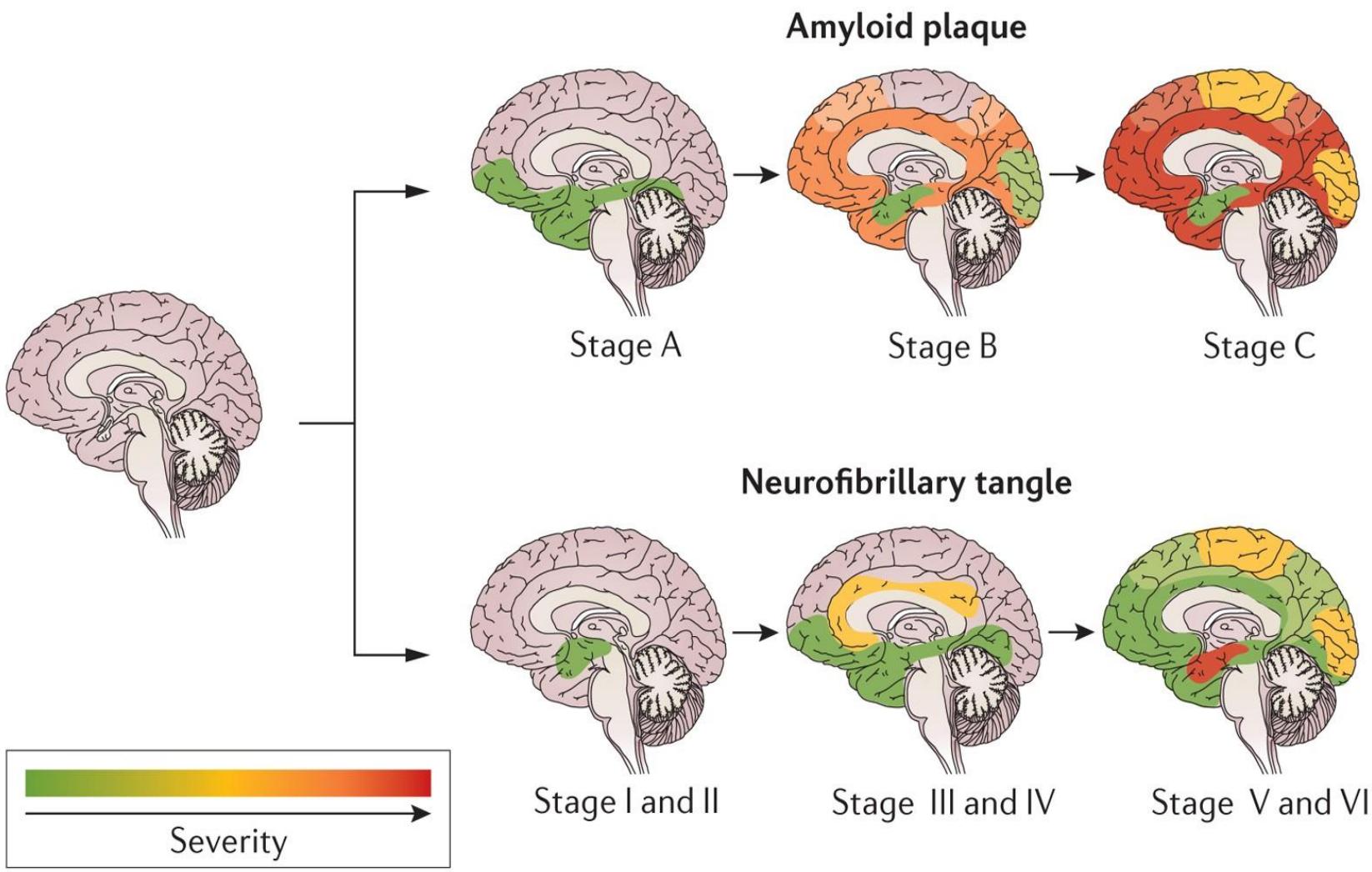
ADEL-Y01
for Alzheimer's Disease

Alzheimer Disease

Amyloid plaque

Neurofibrillary tangle

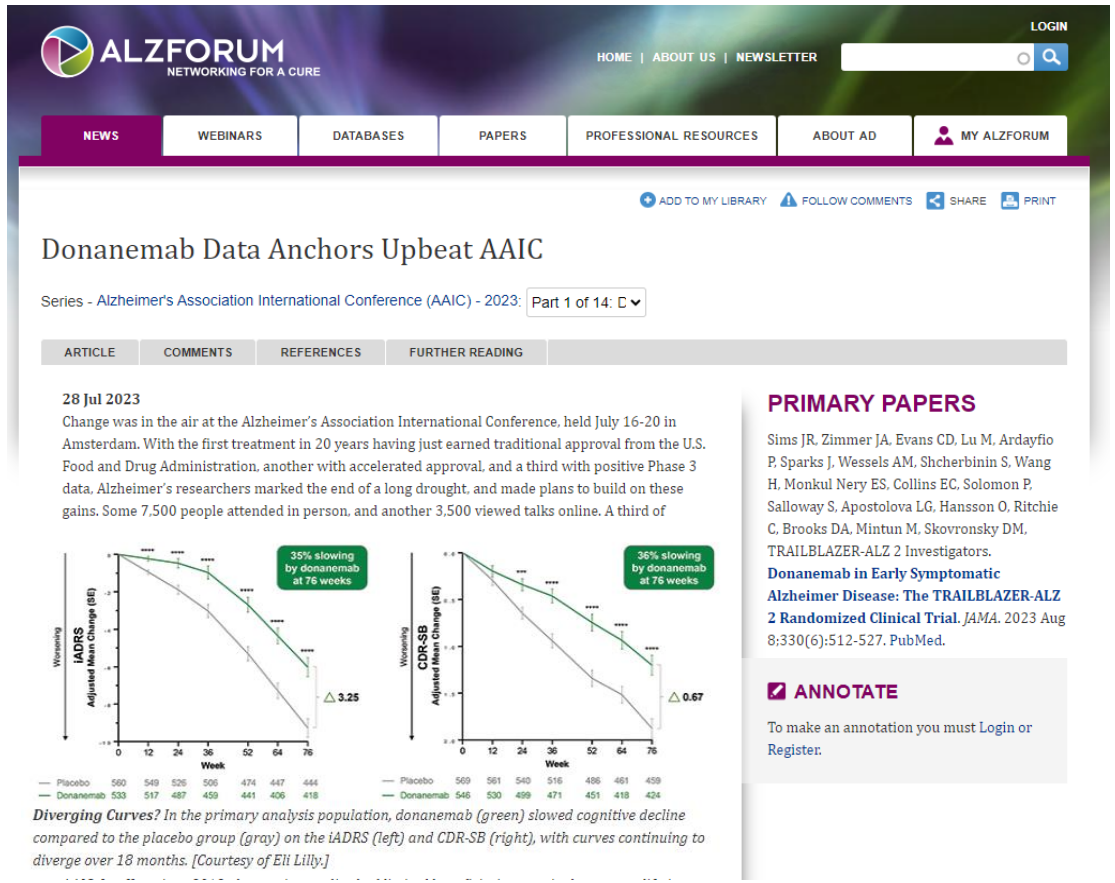




Nature Reviews | Disease Primers

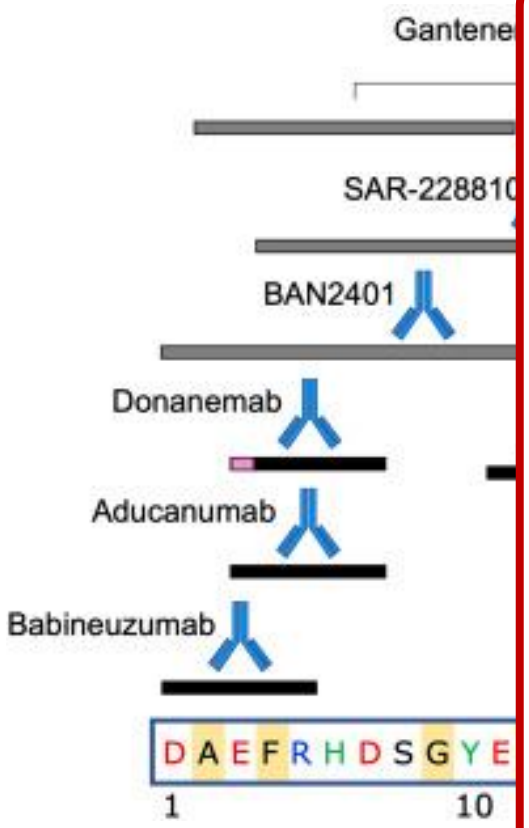
After Decades of Failures, Anti-Aβ Drugs Coming Through

- Lecanemab (Leqembi®, Eisai/Biogen) fully approved
- Donanemab (Eli Lilly) has shown good efficacy in P3 (esp. in low-tau patients)

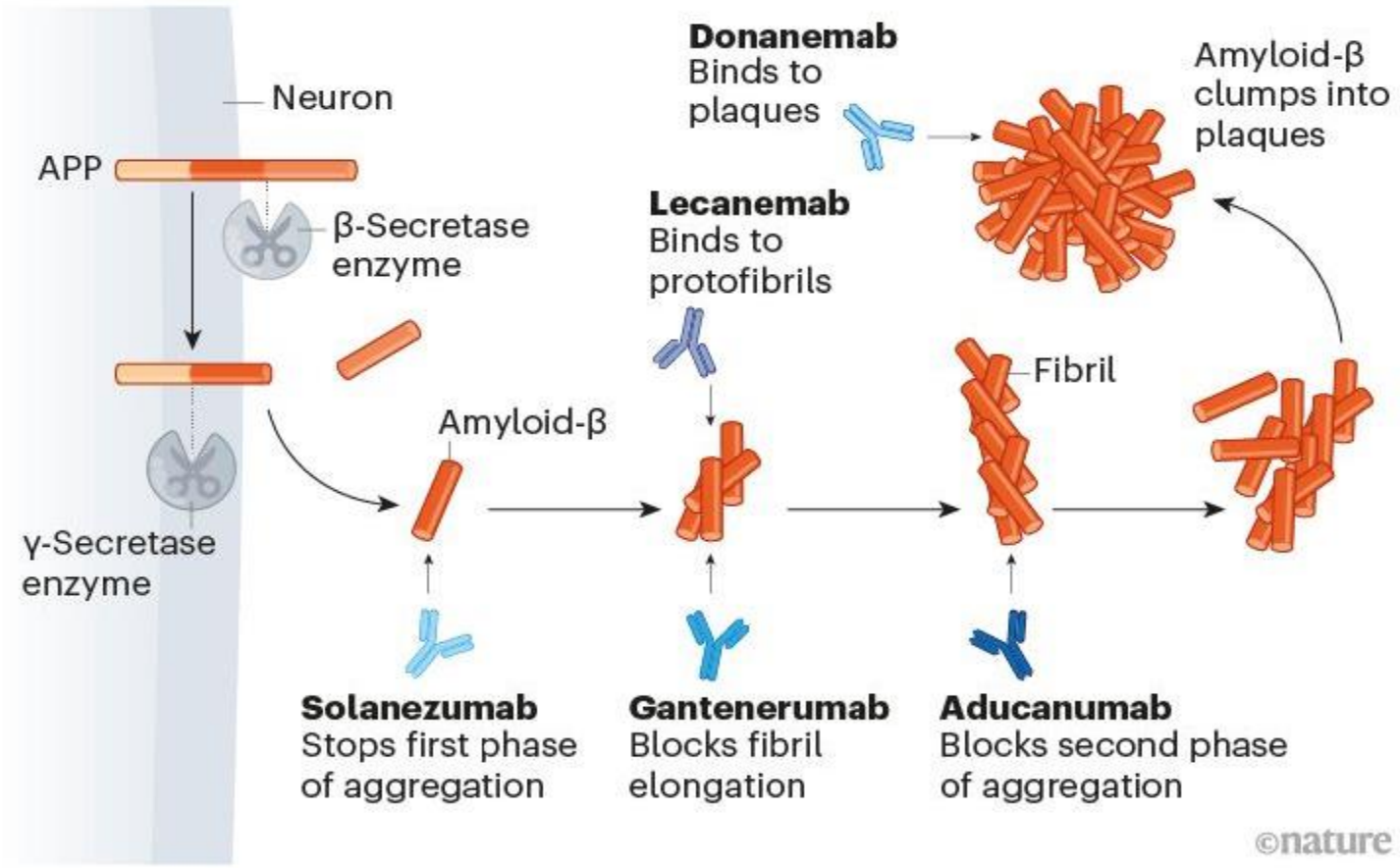


The Secrets of Success

Antibodies binding to different regions of amyloid beta peptide

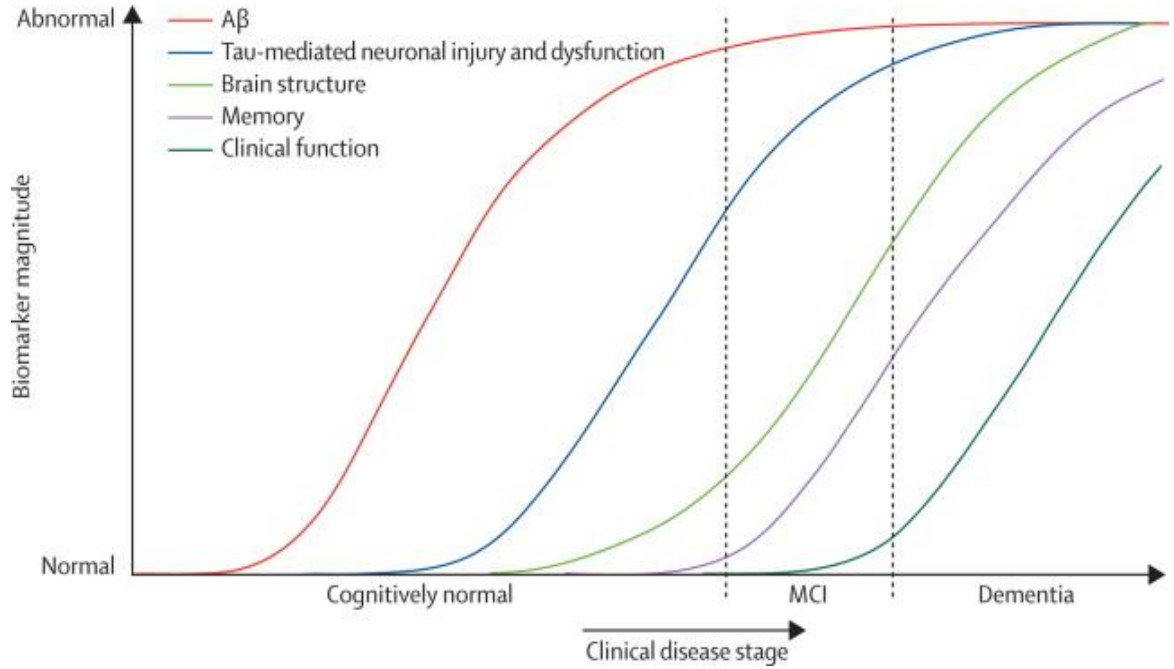


Antibodies clearing different 'species' of amyloid beta

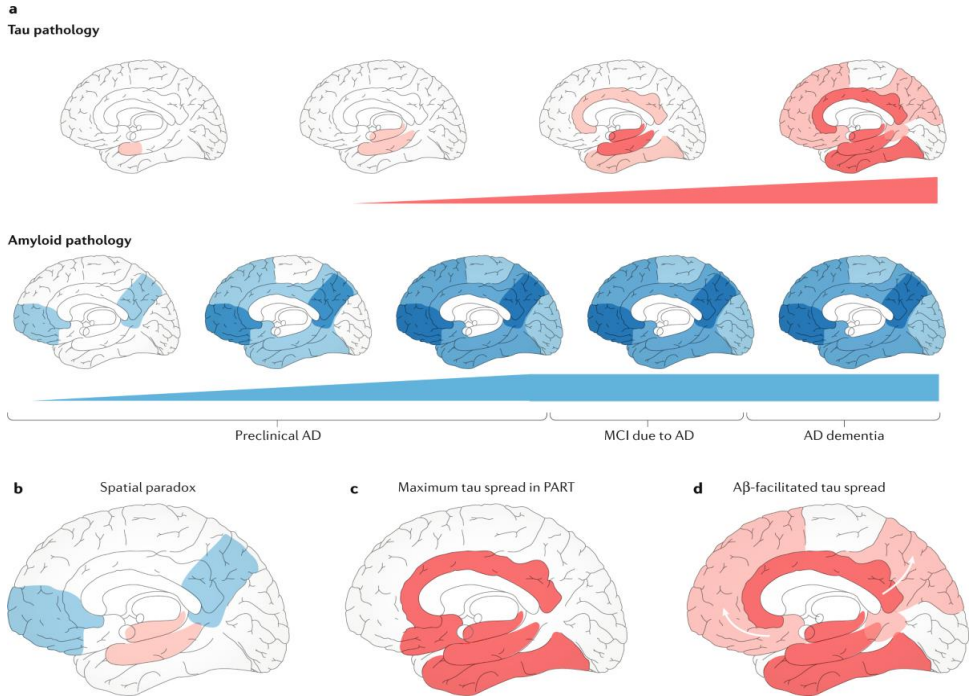


Next in Line; Anti-Tau Therapy

- What we learned from anti-Aβ therapies
  - Not all anti-Aβ antibodies are created equal; targeting the right epitope matters
  - Lowering Aβ is more effective in earlier AD patients, “before it bothers tau”
  - Tau deposits are the best indicator of cognitive decline
- **Targeting tau is the logical next step toward improved outcomes**



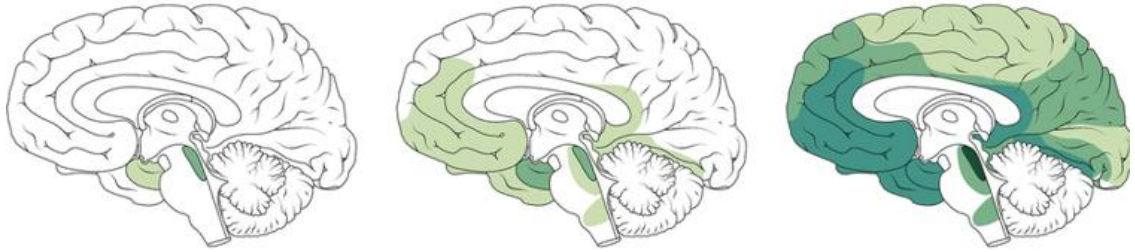
Lancet Neurol 2013



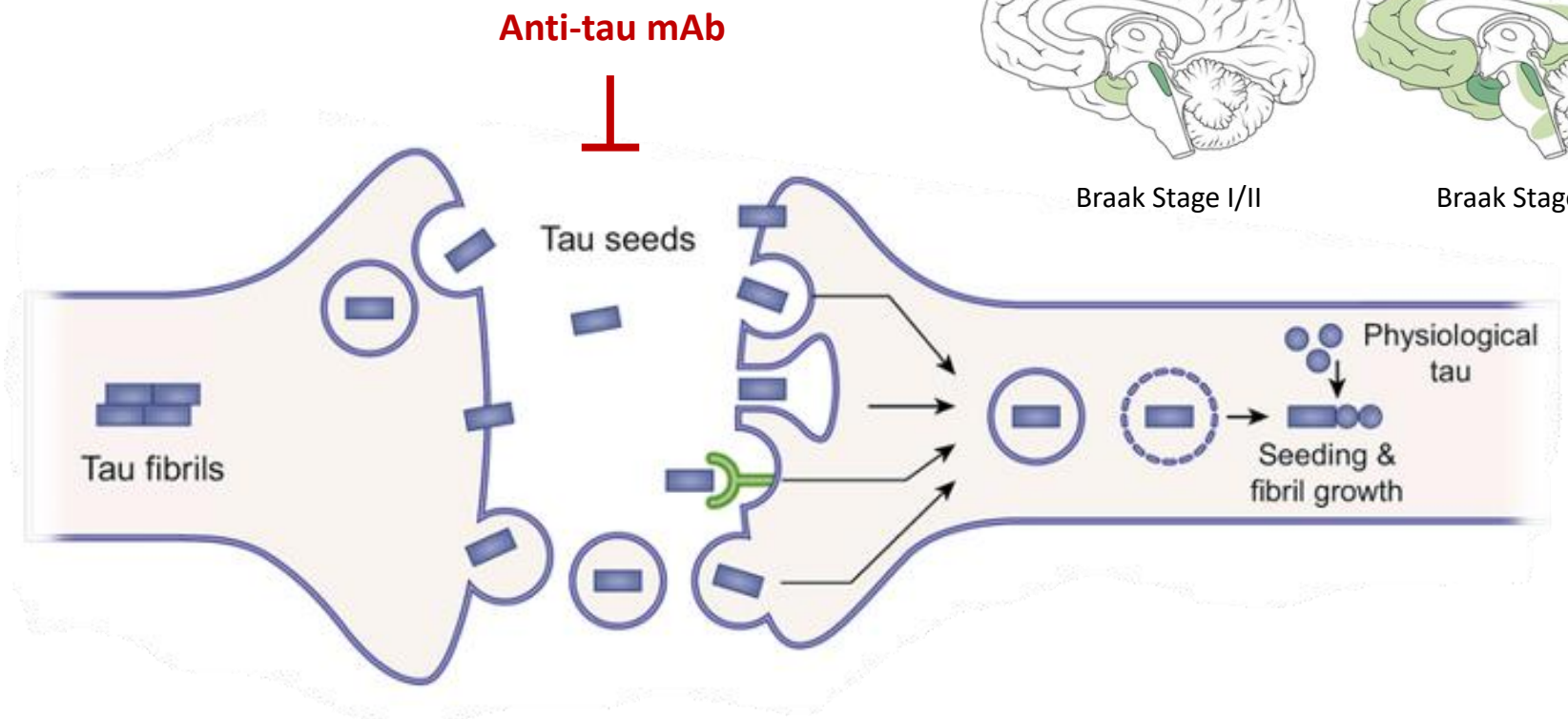
Nat Rev Neurosci 2019

Tau Immunotherapy; Blocking Tau Spreading

- Tau tangles spread from entorhinal to limbic to cortical regions as AD progresses
- Cell to cell transmission through specific neuronal networks
- Presynaptic release and postsynaptic uptake followed by prion-like seeding



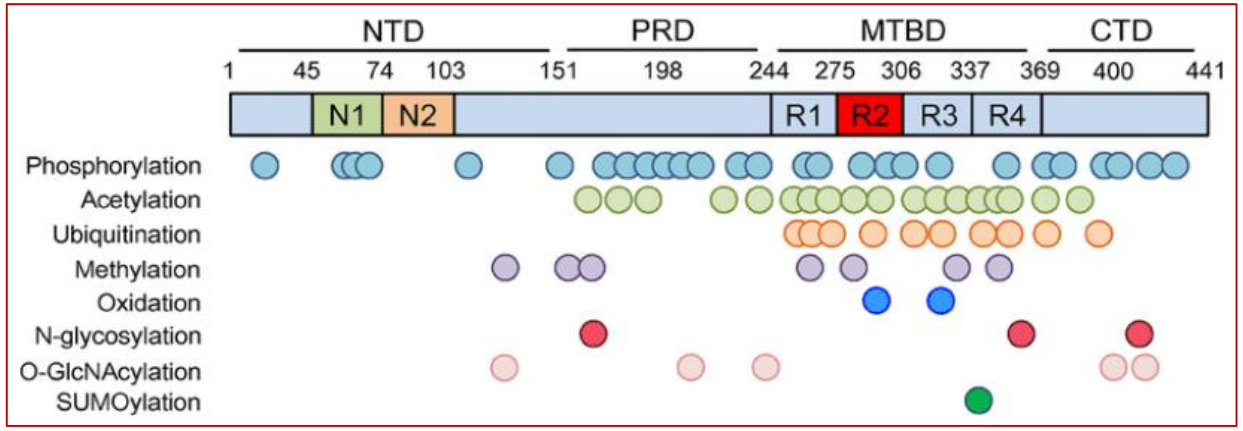
Braak Stage I/II | Braak Stage III/IV | Braak Stage V/VI



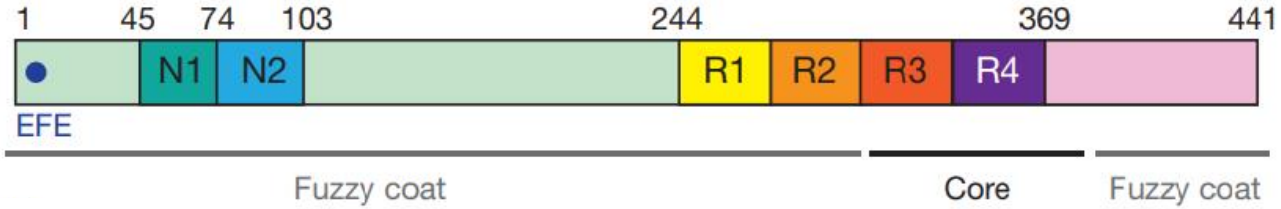
J Neural Transmission 2020

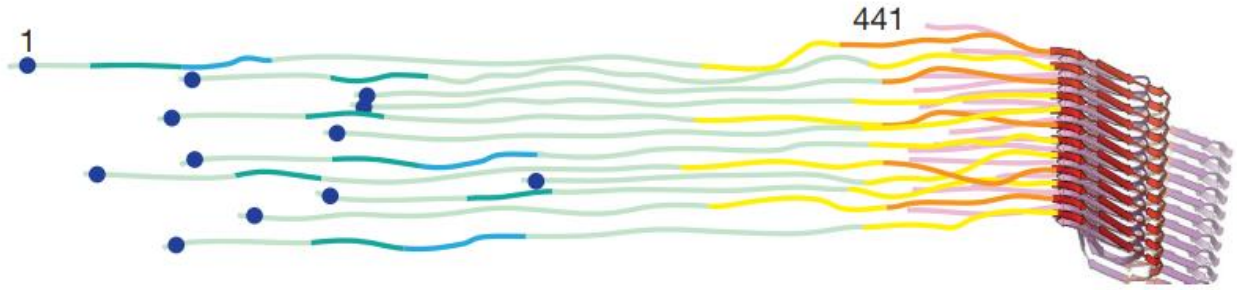
Targeting Tau Protein

- Tau is a 441-aa-long, intrinsically disordered protein (IDP)
- Infinite number of possible combination of post-translational modifications (PTMs)
- Certain mutations/PTMs can stabilize certain aggregation-prone conformations
- R3/R4 domains of MTBR (microtubule-binding region) form the fibrillar core
- Extensive hydrolysis of fuzzy coat
- Diverse core structures (“tau strains”)



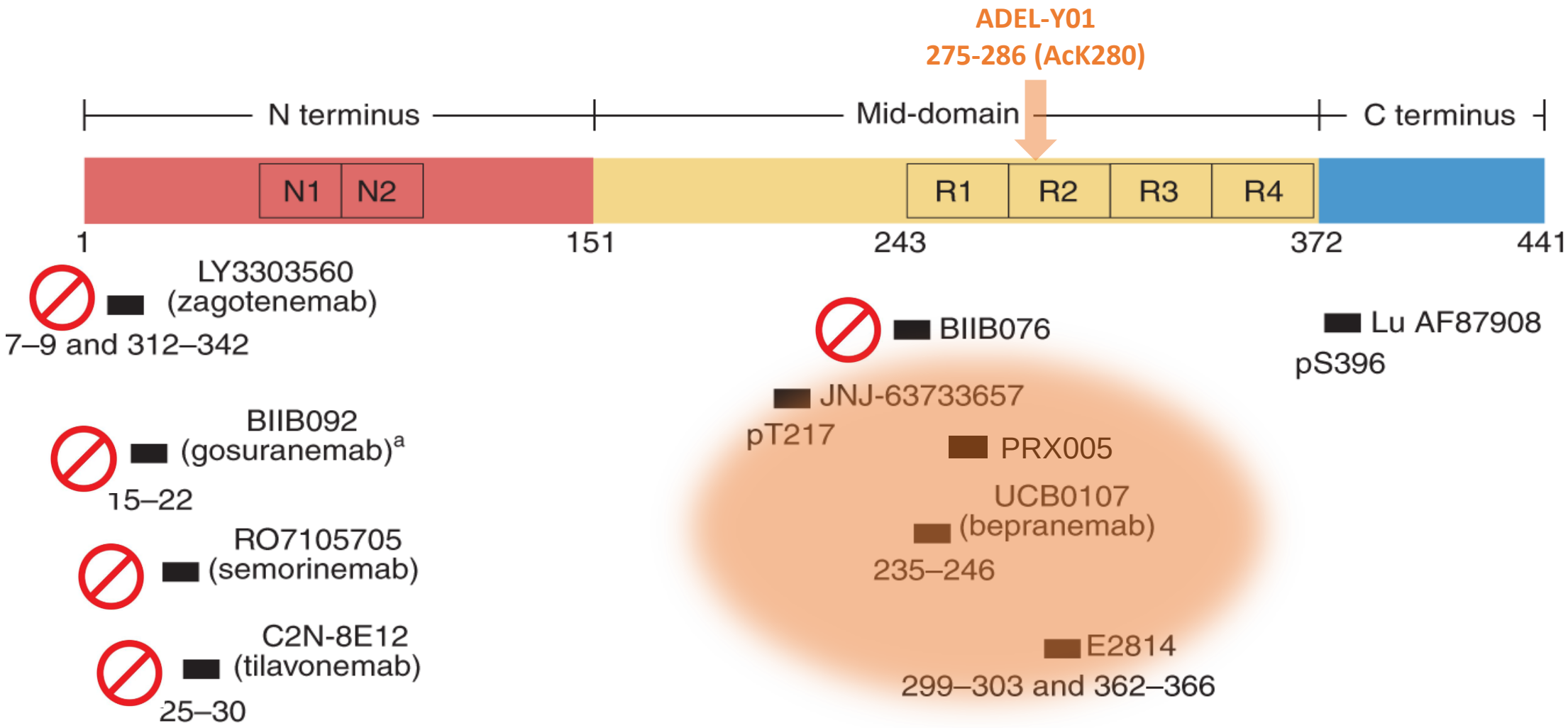
J Mol Neurosci 2022





Nature 2017

Anti-Tau Antibodies in the Clinic

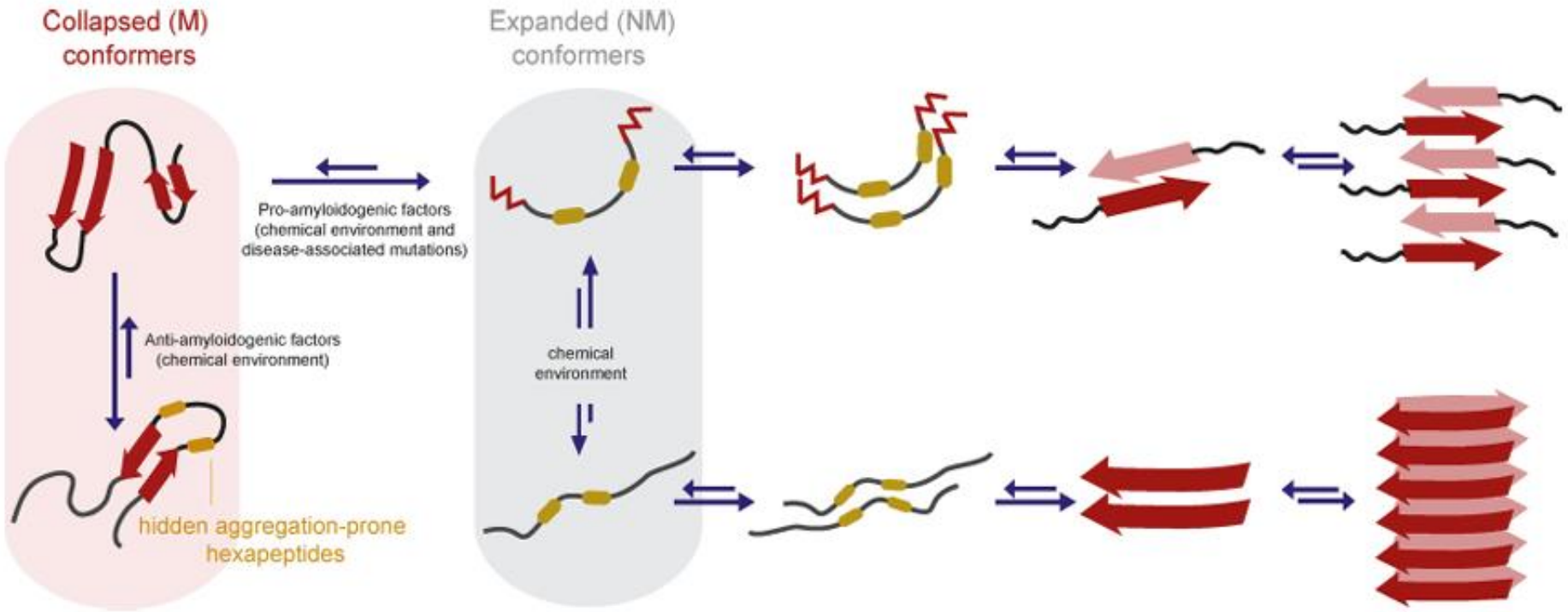


MTBR tau antibodies awaiting clinical proof-of-concept

Modified from Nat. Med. 2021

VQIINK^{280} is Critical for Tau Aggregation

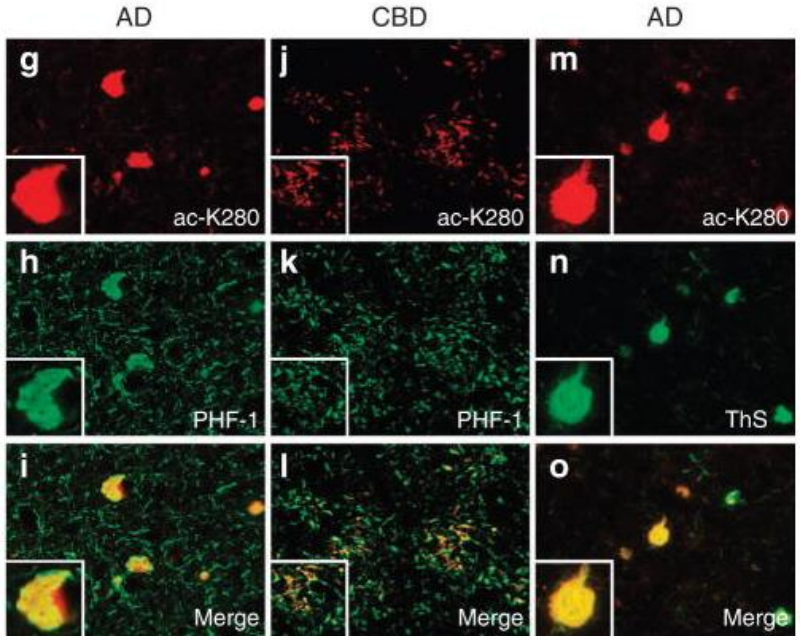
- VQIINK^{280}-VQIVYK^{311} (R2/R3) hexapeptide controls aggregation propensity
- Extended conformation of the hexapeptide drives aggregation
- Disease-associated acetylation stabilizes tau fibrils (Li et al., Structure 2023)



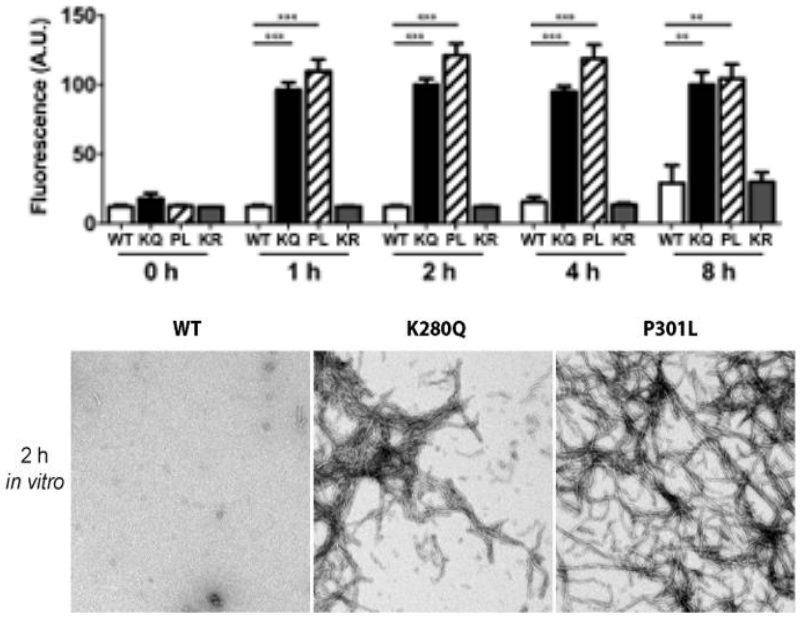
Angew Chem Int Ed Eng 2022

Rationale for Targeting K280-Acetylated Tau (AcK280)

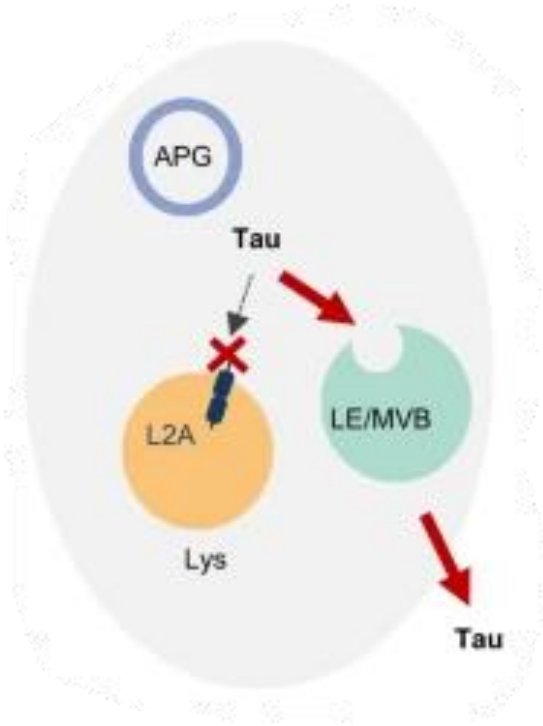
- Tau K280 acetylation is a pathological PTM (undetectable in normal brain)
- AcK280 (or K280Q) dramatically accelerates tau aggregation
- Tau acetylation impairs autophagic flux and promotes tau secretion



Nat Commun 2011



Sci Rep 2017

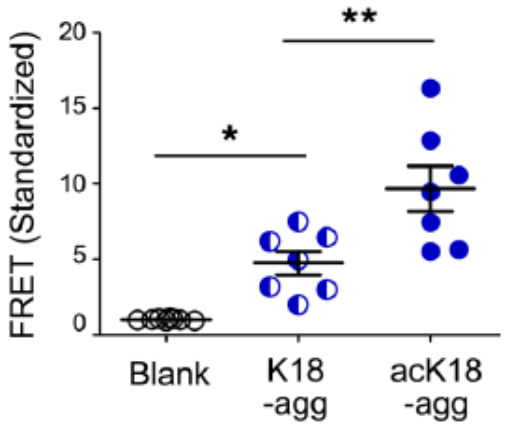


Nat Commun 2021

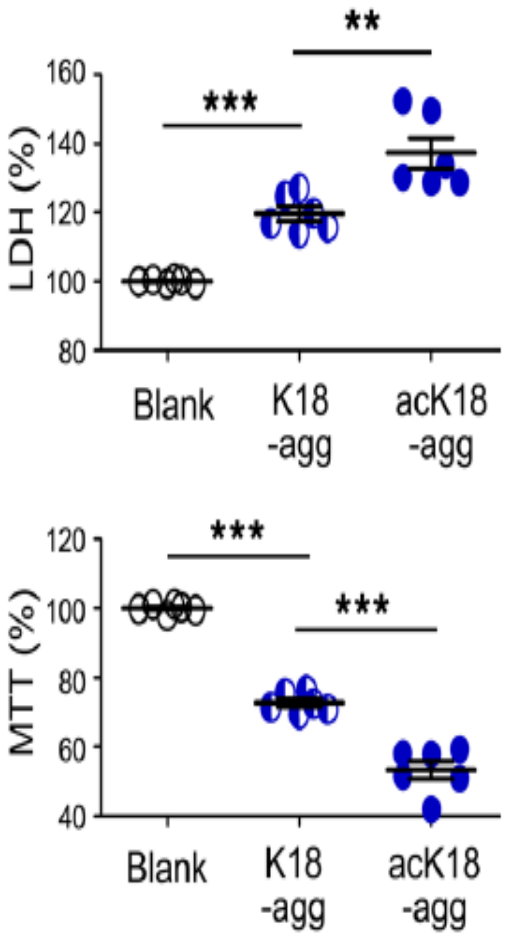
Tau Acetylation Enhances Pathogenicity

ADEL
We dream of a world without dementia.

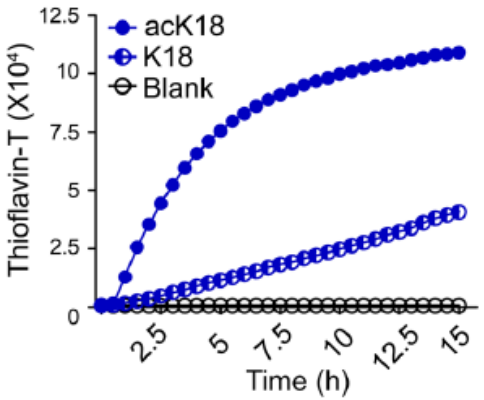
Seeding



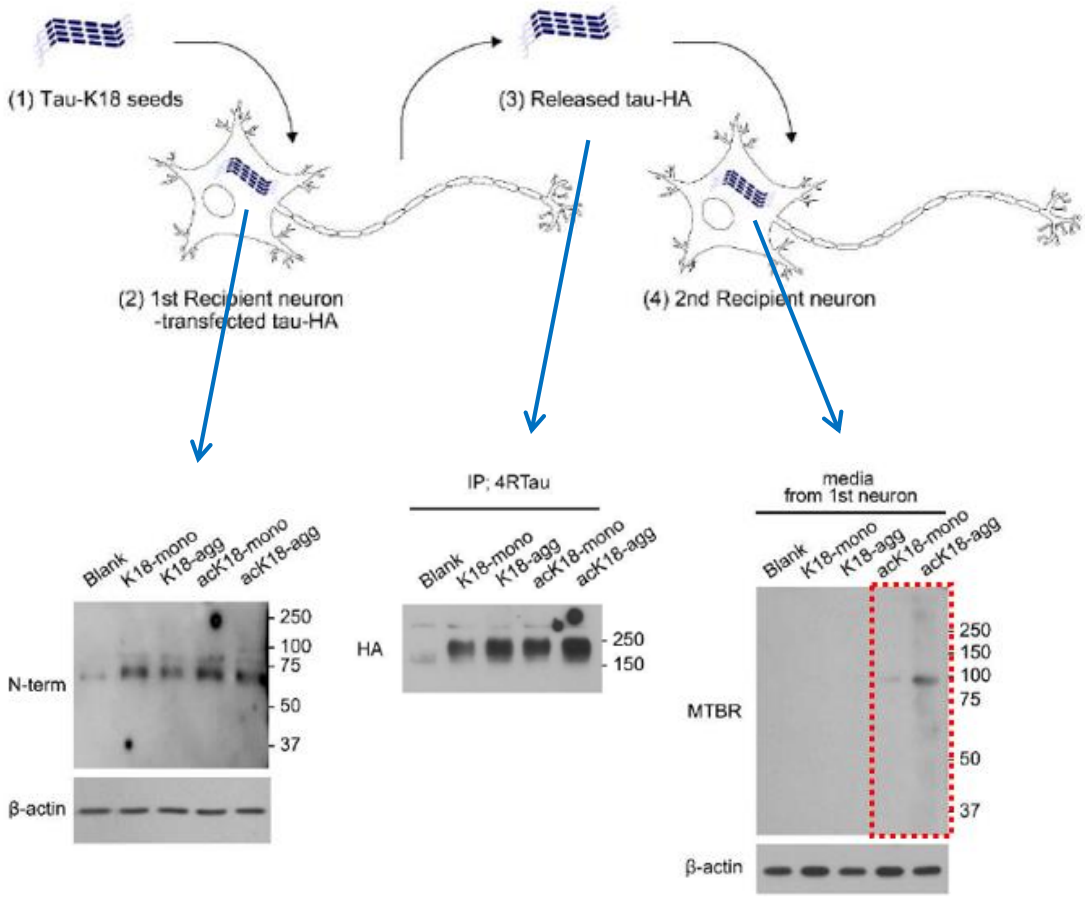
Neurotoxicity



Aggregation



Propagation

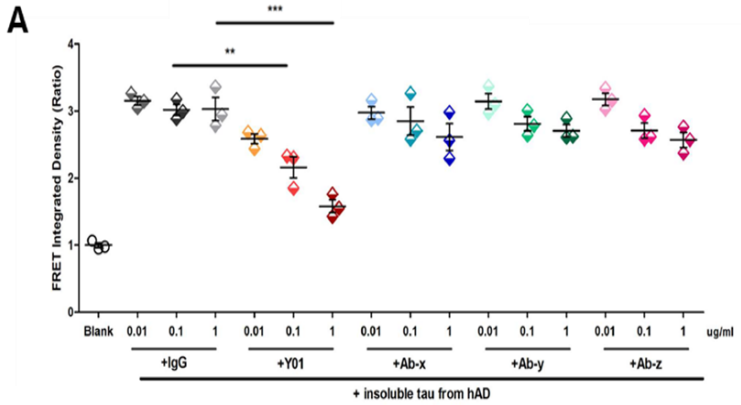


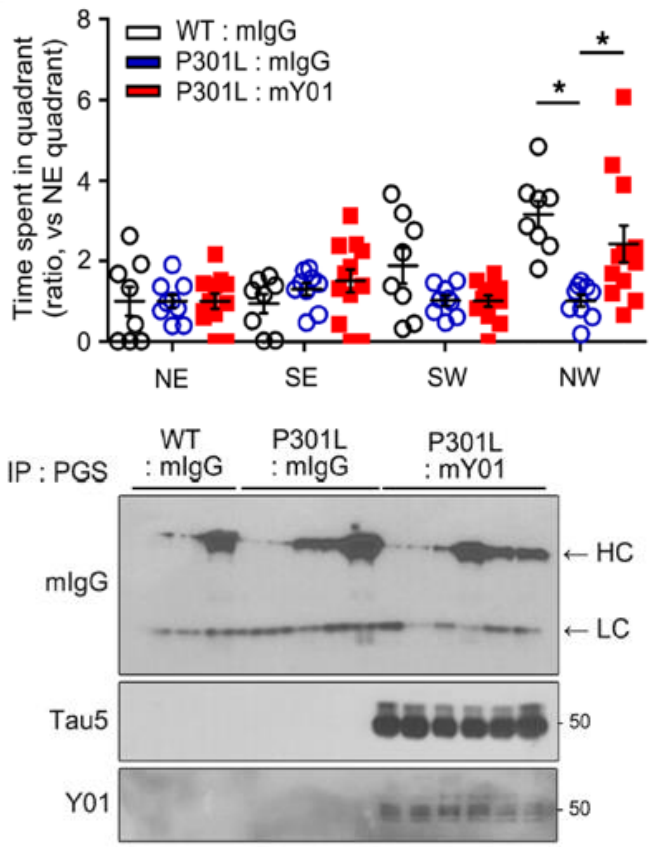
J Clin Investigation 2023

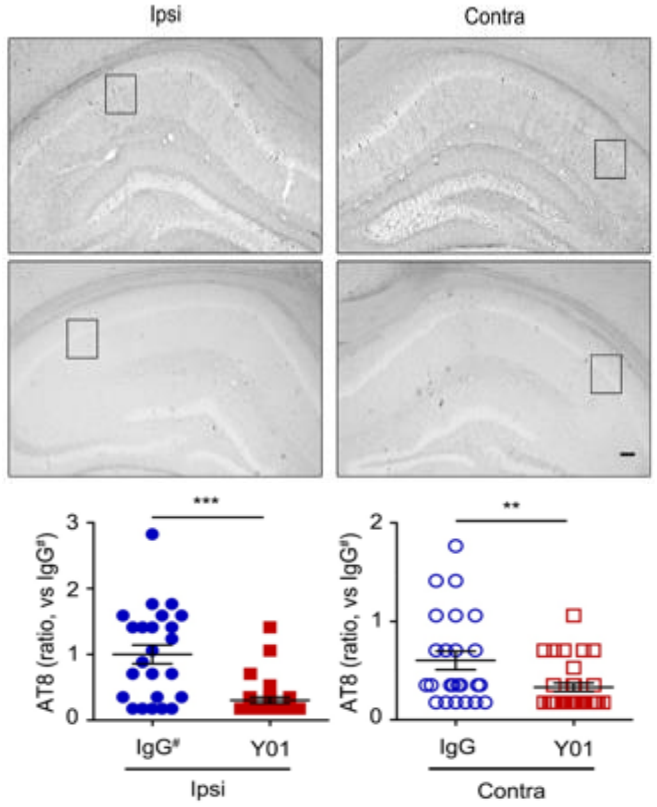
ADEL-Y01; Best-in-Class Anti-Tau Antibody

ADEL
We dream of a world without dementia.

- Superior in vitro activities (seeding, aggregation) to competitors'
- Improved behaviors and brain tau pathology in mouse tauopathy models (P301L)
- Inhibited propagation of human tau tangle in P301S mice



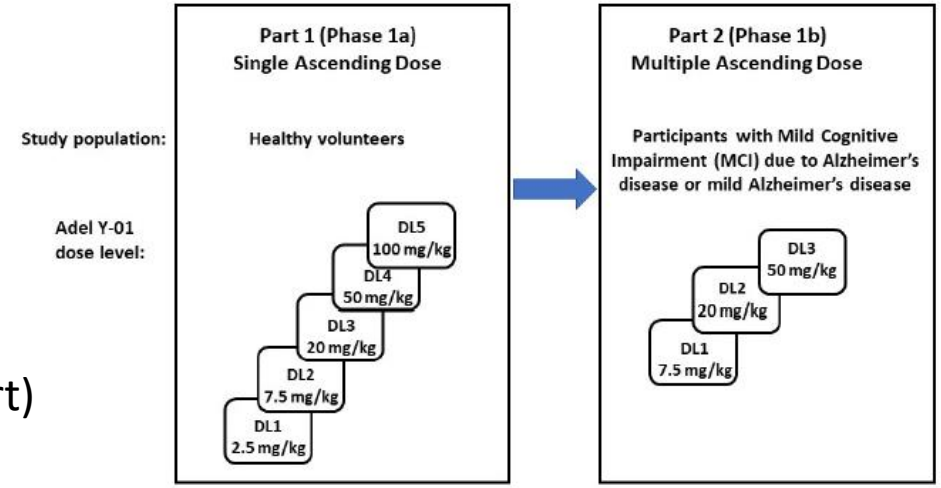




J Clin Investigation 2023

ADEL-Y01; First-in-Human Clinical Trial Commenced

- First in Human, Phase Ia/Ib study for safety, tolerability, pharmacokinetics, and clinical activity evaluation of ADEL-Y01 in healthy participants and in participants with Mild Cognitive Impairment due to Alzheimer's disease or mild Alzheimer's disease
- Objectives
  - Primary; safety, tolerability and pharmacokinetics
  - Secondary; PD effects in patients (CSF/plasma biomarkers)
- Study design
  - Part I; SAD in HV (5 dose levels, 8 subjects per cohort)
  - Part II; MAD in MCI/AD (3 dose levels, 11 subjects per cohort)
- Timeline



Phase 1		2023				2024				2025			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
IND (US FDA)													
Part I (SAD)	Healthy volunteers (n = 40)												
Part II (MAD)	MCI from AD or mild AD (n = 33)												

The Best is Yet to Come

- **Clinical Pipeline**
  - Cevidoplenib for ITP and others
  - SKI-G-801 for solid tumors
  - ADEL-Y01 for Alzheimer disease
- **Preclinical Pipeline**
  - OCT-598 for solid tumors (IND in 2024/5)
- **Discovery Pipeline**
  - A novel cancer/fibrosis program (candidate selection in 2024)
  - A novel cancer therapy resistance target (lead in 2024; Galux collaboration)
  - First-in-class targets from BioRevert collaboration
- **Platform Technologies**
  - Undruggable targets
  - Transformative screening technology

Q & A