ProMIS™ Neurosciences

Developing Therapies Selectively Targeting the Believed Root Cause of Alzheimer's Disease

ProMIS is developing effective therapies that target the root cause of neurodegenerative disorders including Alzheimer's disease (AD, lead focus), ALS, and Parkinson's disease
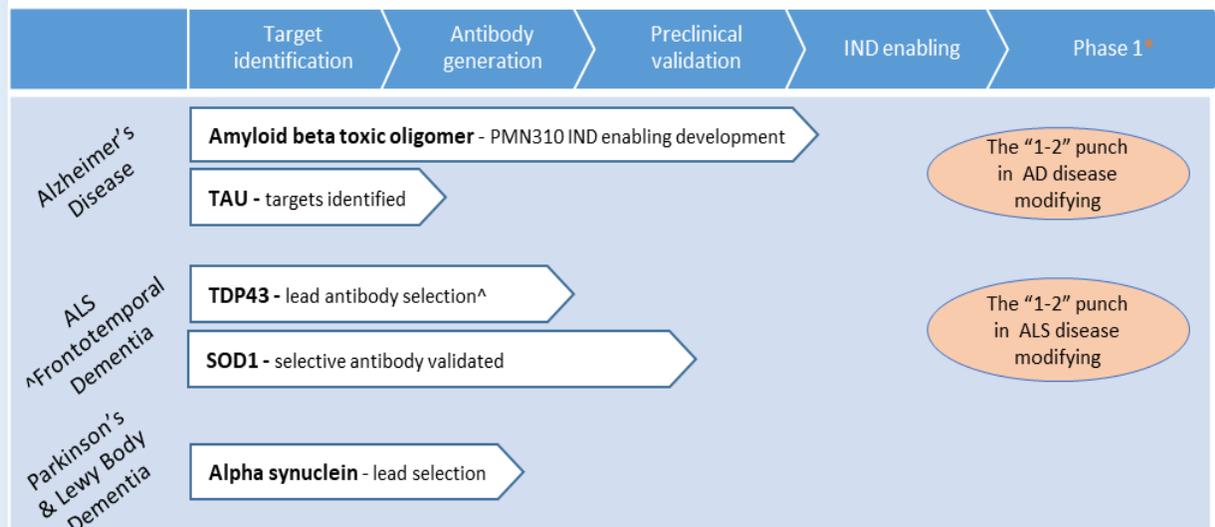
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Exquisite Selectivity for the Toxic Oligomer

Hundreds of studies show the toxic oligomer is a root cause of several neurodegenerative diseases, including Alzheimer's, Parkinson's and ALS. ProMIS' lead program, PMN310, offers unique and exquisite selectivity for the toxic oligomers of amyloid beta (Aβ) without binding to non-toxic forms. Preclinical results suggest safe administration of high doses with greater efficacy than current late-stage drug candidates in development.

Novel Platform for Neurodegenerative Diseases

Traditional methods to develop antibodies cannot produce therapies that bind the toxic oligomer with adequate precision. ProMIS' novel drug discovery and development platform offers exquisite precision for the toxic oligomer, marking a critical shift in the opportunity to develop an effective disease-modifying therapy for several neurodegenerative diseases.

Product Pipeline & Stage of Development

	Target identification	Antibody generation	Preclinical validation	IND enabling	Phase 1*
Alzheimer's Disease	**Amyloid beta toxic oligomer** - PMN310 IND enabling development				The "1-2" punch in AD disease modifying
	TAU - targets identified				
ALS ^Frontotemporal Dementia	**TDP43** - lead antibody selection^				The "1-2" punch in ALS disease modifying
	SOD1 - selective antibody validated				
Parkinson's & Lewy Body Dementia	**Alpha synuclein** - lead selection				

*Multiple dose phase 1 to include biomarkers for early evaluation of potential signs of neuronal protection

Potential near term catalysts

- Results of preclinical comparison of ProMIS oligomer selective antibodies vs other monoclonal antibodies (mAbs) targeting AD, PD & ALS
- Potential partnering deals for PD & ALS programs

- New targets and IP submissions on-going
  - TDP43 (ALS)
  - Tau (AD, other dementias)
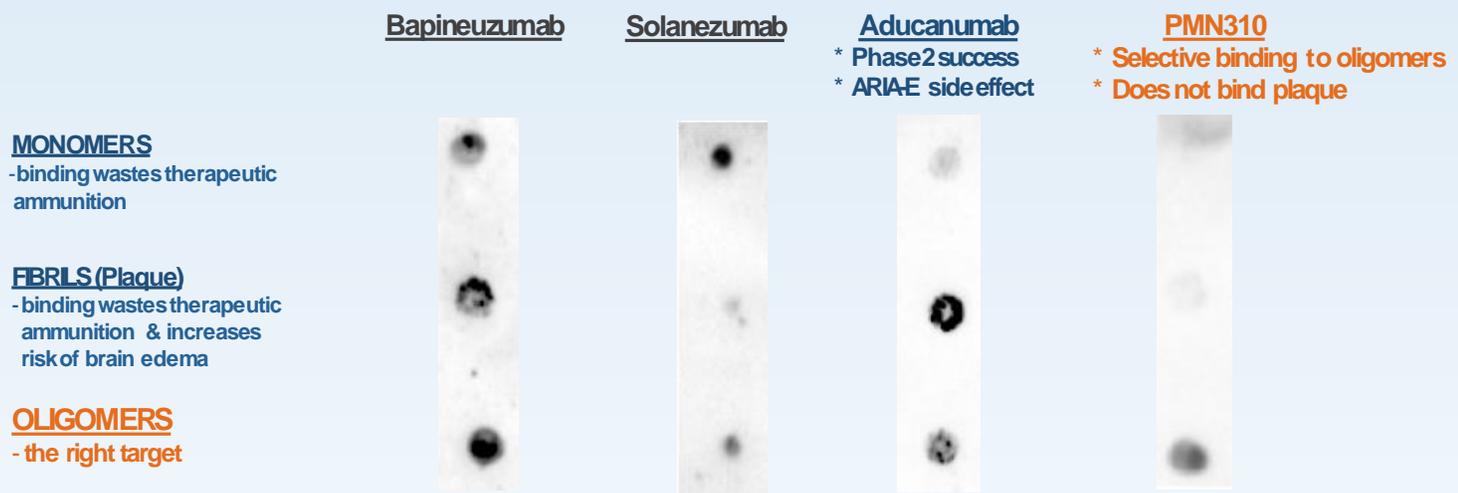 - Alpha synuclein (Parkinson's disease)

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"A common mechanism underlies the top three neurodegenerative disorders, including Alzheimer's: monomers aggregate into oligomers that are toxic to synapses and propagate in a prion-like fashion[1]"
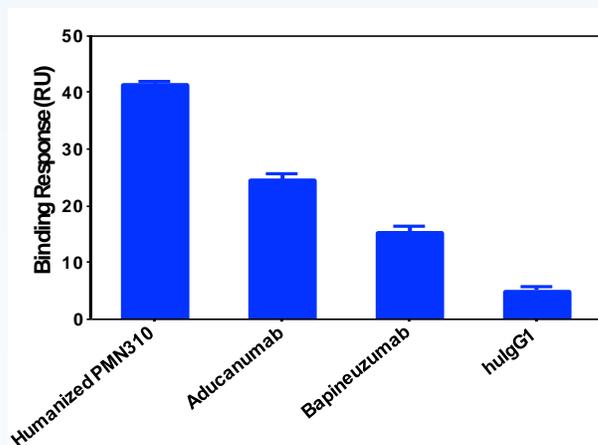
[1]Eliezer Mazliah, Director, Division of Neuroscience at National Institute on Aging
American Academy of Neurology, April 22-28, 2017

PMN310 best-in-class profile versus other antibody therapies targeting Amyloid beta for Alzheimer's Disease (AD)

- Selective targeting of the toxic oligomer form of Amyloid beta
- No binding to amyloid plaque to avoid dose-limiting brain swelling (unlike aducanumab, BAN2401)
- Significantly better binding to, and greater selectively for the toxic oligomers, now considered a root cause of AD

	Bapineuzumab	Solanezumab	Aducanumab	PMN310
			* Phase 2 success	* Selective binding to oligomers
			* ARIA-E side effect	* Does not bind plaque

MONOMERS
- binding wastes therapeutic ammunition

FIBRILS (Plaque)
- binding wastes therapeutic ammunition & increases risk of brain edema

OLIGOMERS
- the right target

PMN310 shows greater selectivity for toxic oligomers, compared to other antibody therapeutics

Bar chart: Binding Response (RU) on y-axis (0–50) for Humanized PMN310 (~41), Aducanumab (~24), Bapineuzumab (~15), huIgG1 (~5)

- Binding of antibodies to the toxic oligomer fraction of human AD brain extract was evaluated by surface plasmon resonance

- Results show greater binding of aducanumab to the toxic oligomer fraction compared to bapineuzumab, in line with the greater therapeutic benefit of aducanumab seen in clinical trials

- Importantly, PMN310 showed even greater binding (~1.5-2 fold) compared to aducanumab

Kaplan et al. Humanized PMN310 Shows Enhanced Therapeutic Potential by Binding Toxic Low Molecular Weight Amyloid β Deposits in AD Patient Brains. Poster Presented at AAIC 2018