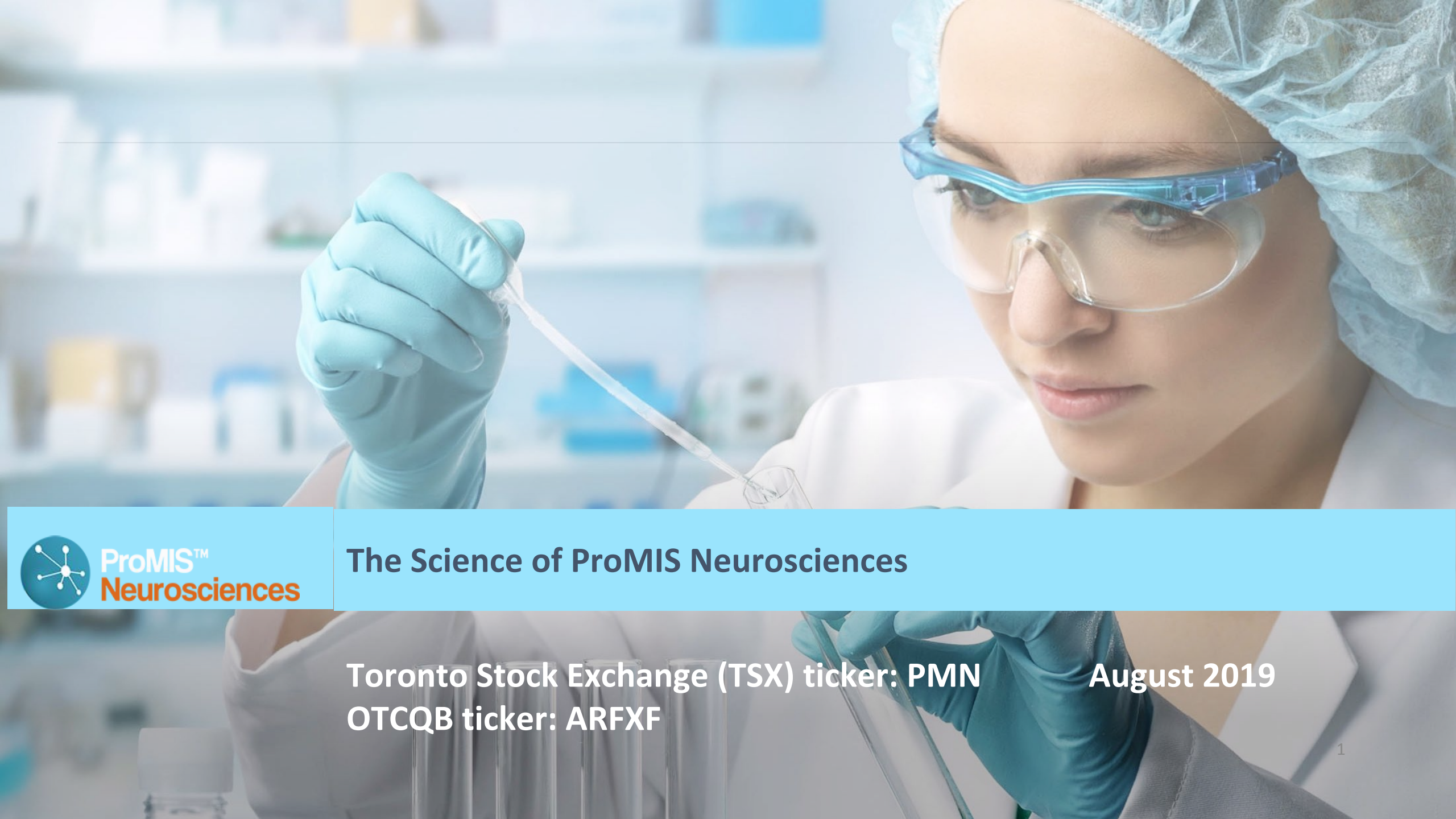


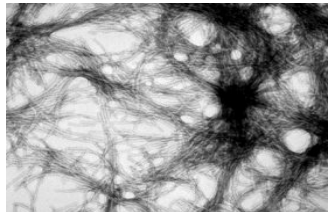
The Science of ProMIS Neurosciences

Toronto Stock Exchange (TSX) ticker: PMN
OTCQB ticker: ARFXF

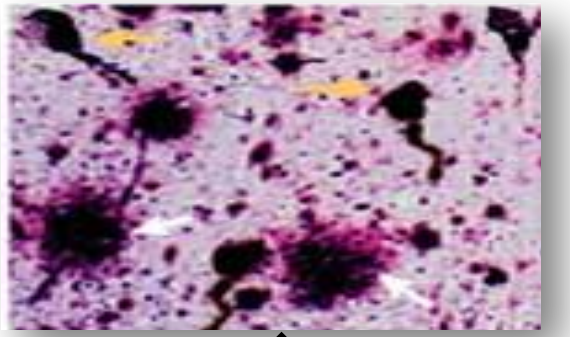
August 2019

The universe of propagated protein misfolding diseases includes Alzheimer and Parkinson diseases, amyotrophic lateral sclerosis

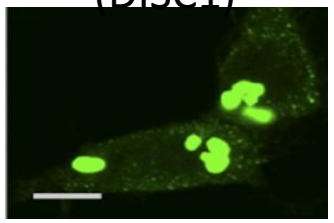
Huntington's disease
(huntingtin)



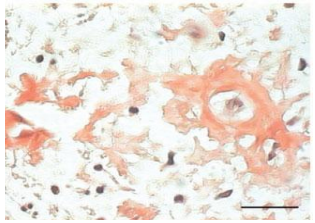
Alzheimer's diseases
(Abeta and tau)



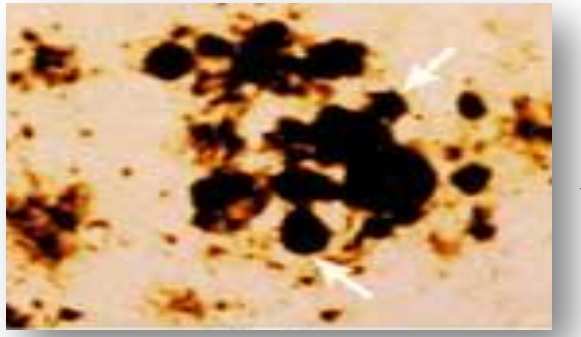
Schizophrenia
(DISC1)



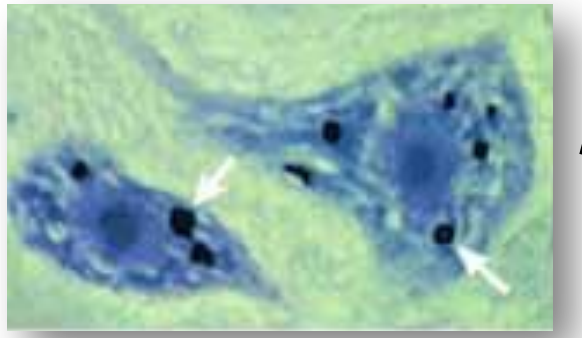
senile amyloidosis
(transthyretin)



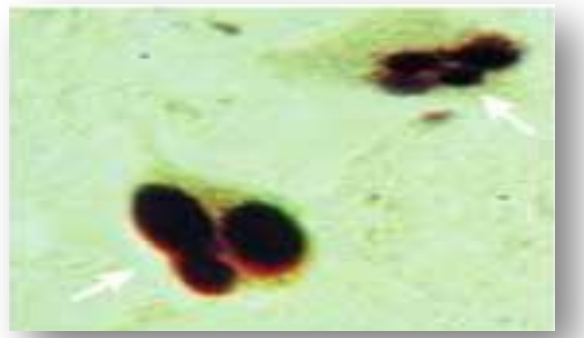
Type 2 diabetes
(amylin)



Prion diseases
(prion protein)

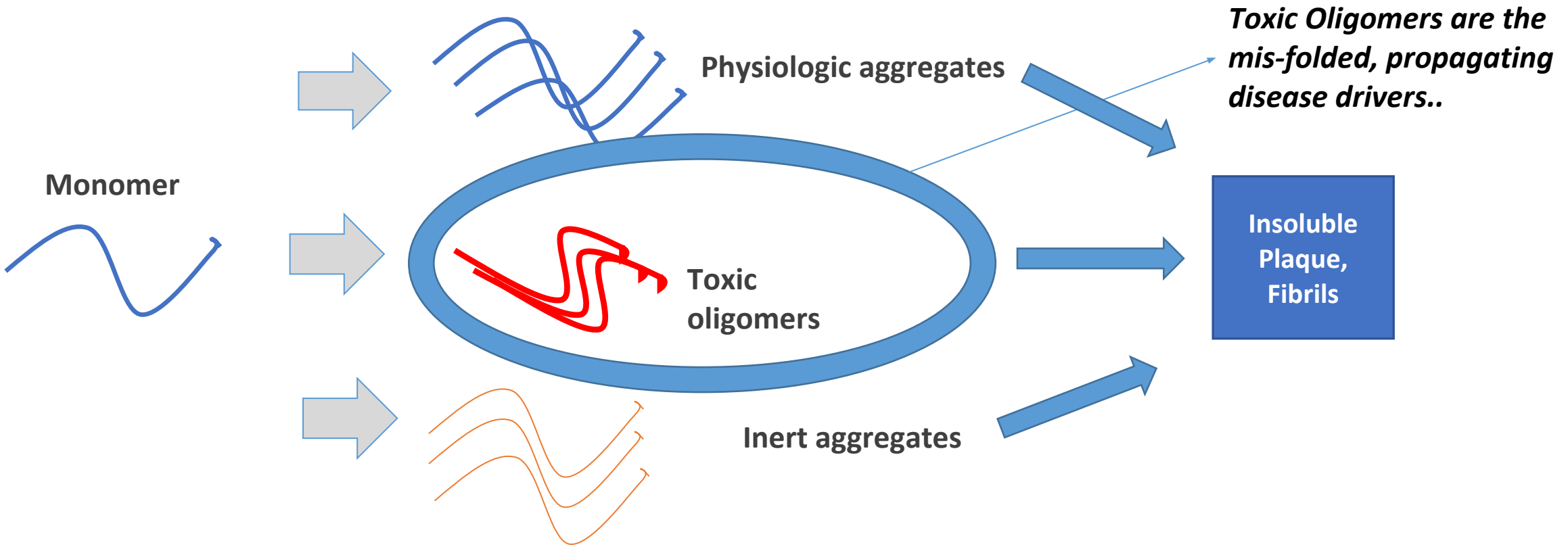


ALS
(TDP43, SOD1, FUS)



Parkinson-like diseases
(alpha synuclein)

Neurodegenerative protein molecular species start as monomer and then aggregate…..into soluble forms *with different biologic roles…..*



ProMIS™ Neurosciences

ProMIS technology platform has a spectacular track record of creating highly selective antibodies at the molecular species level

Total of 15 *Amino Acid Sequences with at least one conformational scaffold predicted for amyloid, tau, alpha synuclein, TDP43, and SOD1*

15/15 led to at least one, if not dozens of antibody candidates with desired molecular species selectivity

- 100% success rate

22 *immunizations, in some cases with more than one conformational scaffold, for amyloid, tau, alpha synuclein, TDP43, and SOD1*

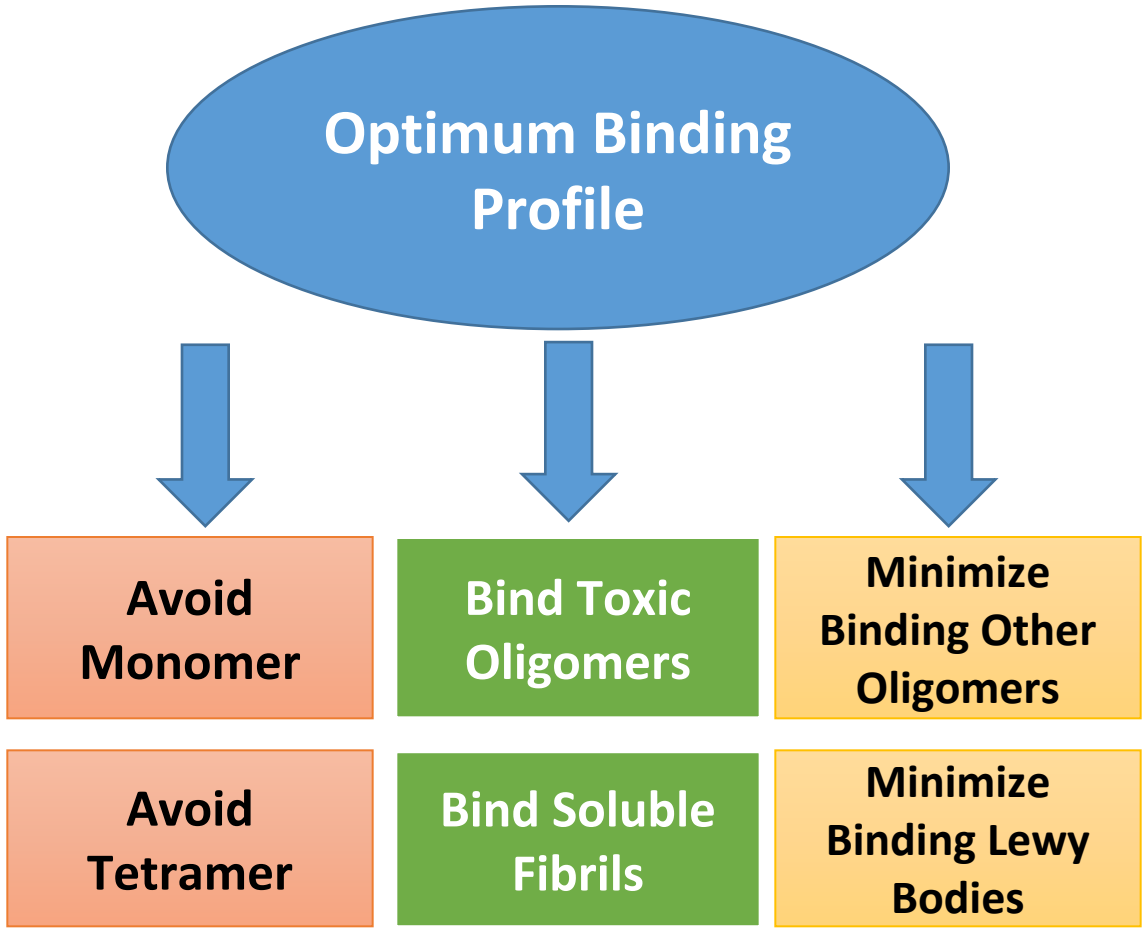
21/22 led to at least one, if not dozens of antibody candidates with desired molecular species selectivity

- 95.4% success rate

ProMIS™ Neurosciences

Protein/ Molecular Species Binding Target	Immunizations Epitope-conformation	mAbs selective for toxic species	Current status
Amyloid-beta BIND – Toxic Oligomers AVOID – Monomer - Plaque	EP-300 EP-301 EP-302 EP-303 EP-304 EP-305	✓ ✓ ✓ ✓ ✓ ✓	Lead selected Clinical candidate (PMN310) Lacks biological activity Lead selected Lacks biological activity Lead selected
Tau BIND – Toxic Oligomers AVOID – Monomer, tangles	EP-501a EP-501b EP-501c	✓ ✓ ✓	Initial candidates
Alpha-synuclein BIND – Toxic Oligomers - Soluble Fibrils AVOID – Monomer - Physiologic Tetramer - Lewy Bodies	EP-401a EP-401c EP-402a EP-402b	✓ ✓ ✓ ✓	2 candidates + additional under evaluation 2 candidates + additional under evaluation 2 candidates + additional under evaluation 1 candidate + additional under evaluation
TDP43 BIND – Toxic Oligomers AVOID – Monomer, Native Dimer	EP-201a EP-201b EP-201c EP-202a EP-202b EP-203	✓ X ✓ ✓ ✓ ✓	1 candidate --- 3 candidates 2 candidates 1 candidate 3 candidates
SOD1 BIND – Toxic Oligomers AVOID – Native Dimer	EP-101 EP-102 EP-103	✓ ✓ ✓	Lead selected Lead selected Lead selected

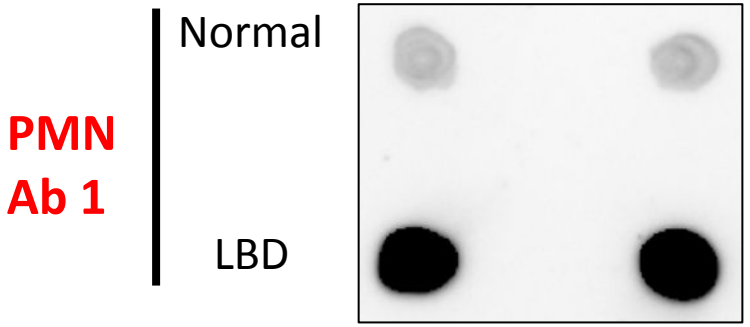
Alpha synuclein: an example of the need for antibody specificity

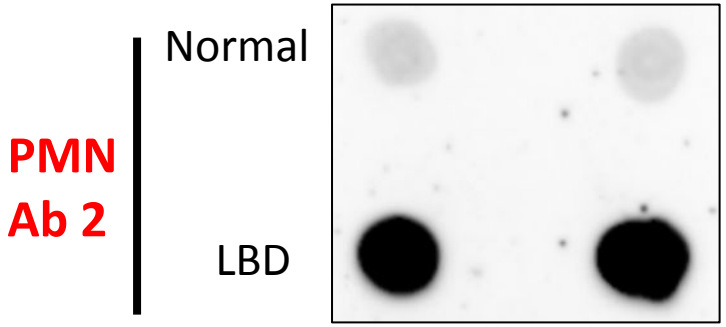


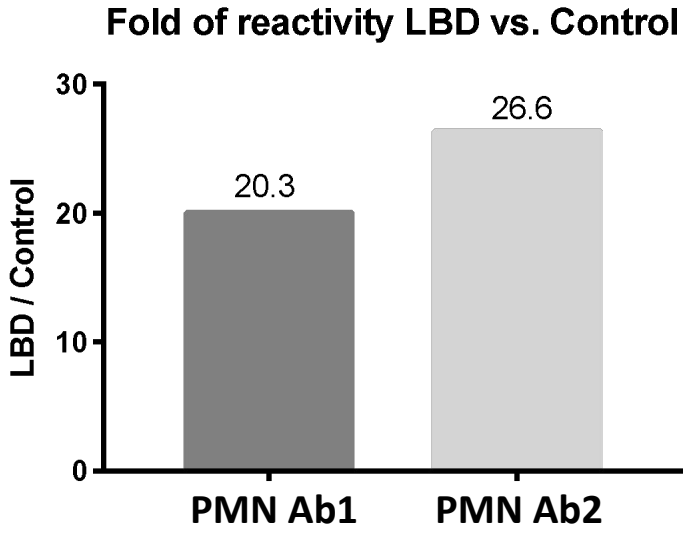
PMN unique technology platform has created antibodies that achieve the targeted binding profile….better than other α-synuclein-directed antibodies

Target Properties	PMN Antibodies	Prothena/ Roche	BioArctic/ ABBVIE	Neurimmune/ Biogen
No binding to monomers	✓	X	+/-	X
No binding to physiological tetramers	✓	X	+/-	X
Binding to oligomers/small soluble fibrils	✓	✓	✓	✓
Binding to native toxic α-syn in LBD/PD brain extract	✓	✓	✓	✓
Little or no binding to insoluble fibrils (Lewy bodies)	✓	X	X	X

Alpha synuclein PMN antibodies react with diseased brain but not normal control brain



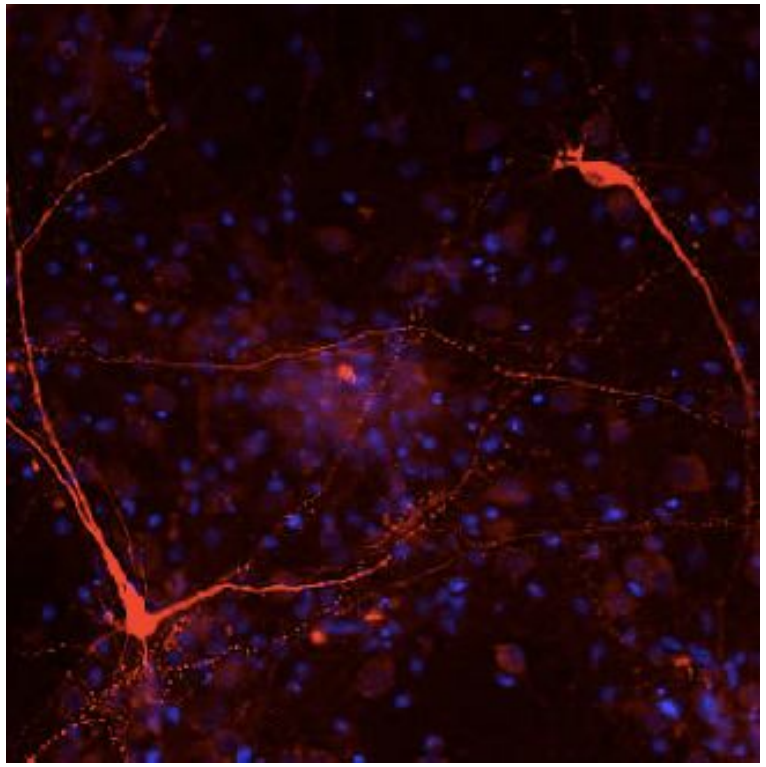




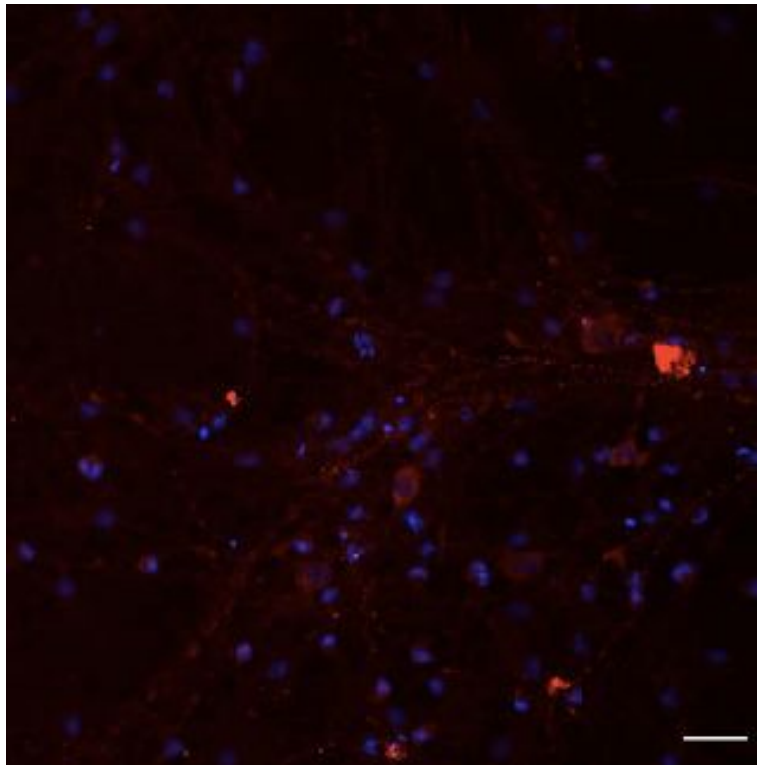
- Source of extract: Brain frontal cortex sample of LBD and normal 58 year old control
- Preparation of extract: Triton-X100 extract of high speed pellet from brain homogenate. Expected to contain fibrillar fragment material.
- 10 ug protein dotted and probed with test antibodies and control antibodies

Alpha synuclein PMN antibodies protect cultured nerve cells from oligomer toxicity

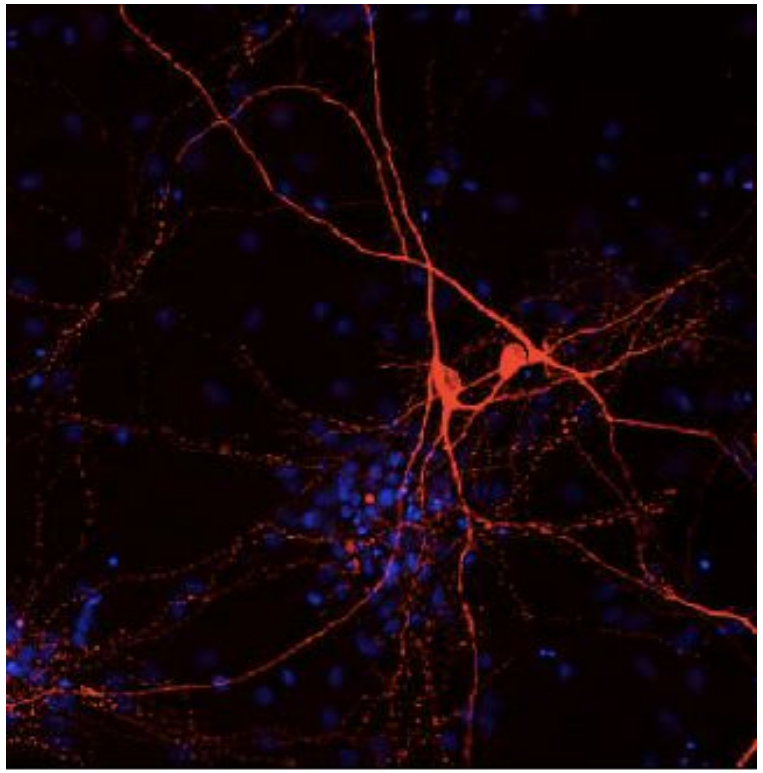
CONTROL



α-SYN OLIGOMERS



PMN ANTIBODY + α-SYN OLIGOMERS



ProMIS™ Neurosciences

ProMIS Scientific Thesis/Strategy – Developing a Portfolio of Disease Modifying Therapies in Neurodegenerative Disease

The right target for therapy needs to be specified at the molecular species level
→ not just any form of amyloid, tau, synuclein or TDP43, but the specific toxic species

High selectivity for the toxic target is critical for clinical success since the toxic species are relatively rare
→ indiscriminate binding leads to "dose reduction" and adverse events

Successful development will be greatly enhanced by the emergence and usage of fluid based biomarkers that reflect disease modifying treatment effects

Thank You

We appreciate your interest in ProMIS Neurosciences. Please feel free to contact us with any additional questions.

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