ProMIS Neurosciences: “Best in Class” therapy for misfolded protein diseases, based on a proprietary discovery platform

Johanne Kaplan, PhD
Chief Development Officer

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

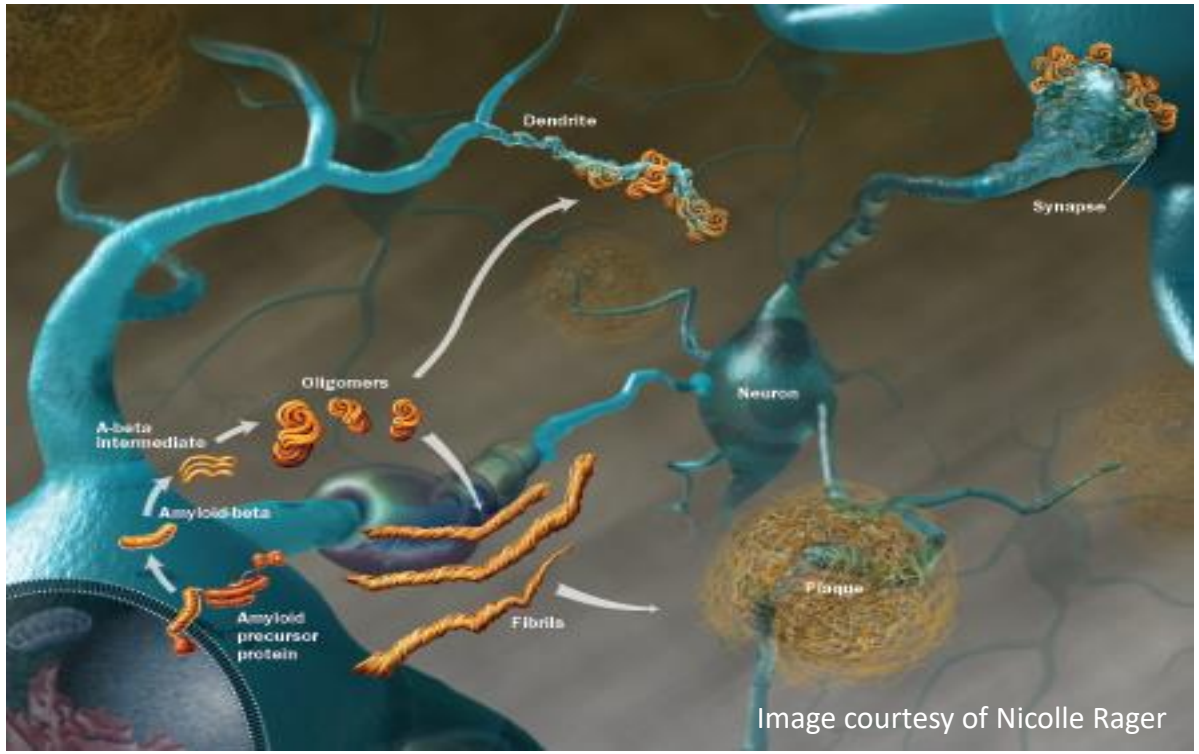
November 2019

Biogen's aducanumab is on track to be the first disease-modifying therapy in Alzheimer's…and ProMIS PMN310 has the potential to be better…

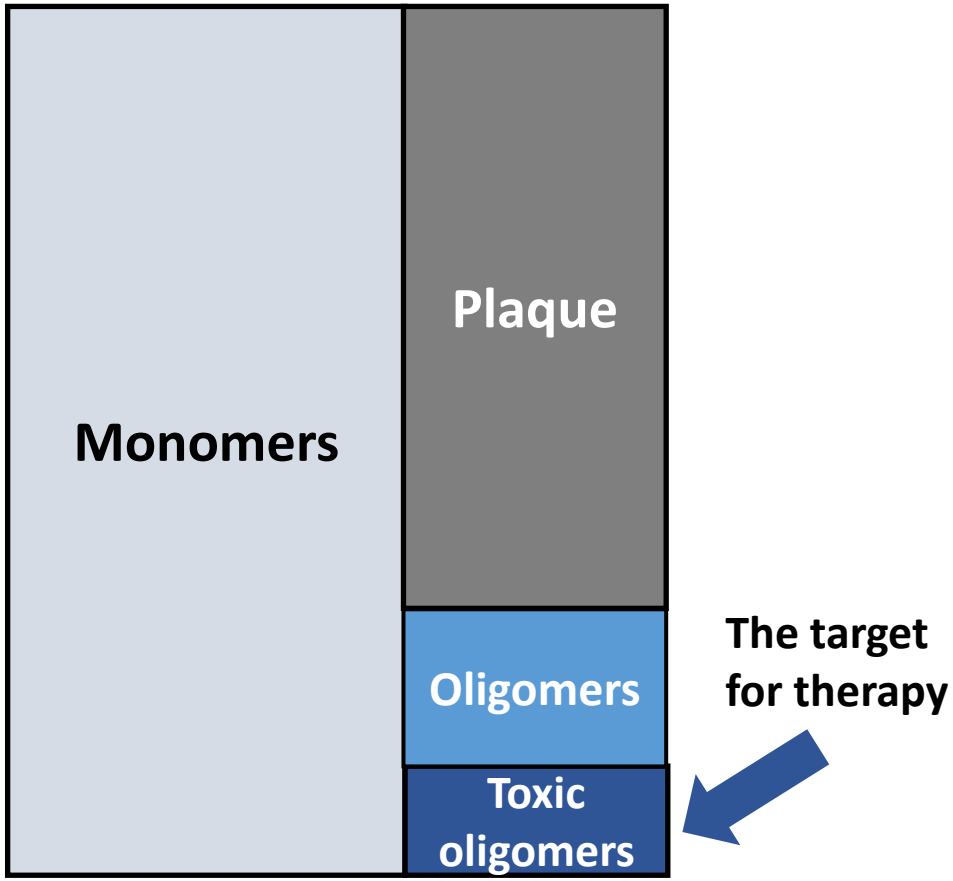
- Aducanumab, first ever amyloid-beta targeted therapy with positive Phase 1b data, in December 2014
- Biogen presents positive three year follow up data in November 2017 – still slowing disease progression
- Flawed futility analysis leads to discontinuation of Phase 3 trials in March 2019
- Inclusion of additional data collected between cut-off date of Dec. 2018 and March 2019 indicates that high dose aducanumab (10mg/kg) provides clinical benefit and is likely approvable - **October 22, 2019 announcement**
- Aducanumab high dose slows progression by 23% vs placebo, but with a 35% risk of ARIA-E (brain swelling side effect)
- ***ProMIS has created PMN310, designed to be clinically superior to aducanumab…"best in class"***

ProMIS™ Neurosciences

Selectivity for toxic Aβ oligomers is required for optimal safety and efficacy



Soluble Aβ oligomers now recognized as the most neuropathogenic Aβ species -> Spread in a prion-like manner



Specific targeting of toxic Aβ oligomers required for optimal efficacy and safety

ProMIS™ Neurosciences

Jacobsen et al, 22006, PNAS; Brier et al, 2016, Science Trans Med; Shankar et al, 2008, Nature Med; Cleary et al, 2005, Nature Neuroscience; Hong et al, 2016, Science; Benilova et al, 2012, Nature Neuroscience - Review; Lacor et al, 2007, J Neuroscience; Jin et al, 2011, PNAS; Lauren et al, 2009, Nature; [1]Balducci et al, 2010, PNAS

Alzheimer's amyloid failed programs were all designed 10-15 years ago and focused on the wrong forms of amyloid....*wrong target*

Product	Phase 3 Result	Monomer Binding/Targeting	Oligomer Binding	Plaque binding	Antibody Isotype	ARIA-E
Solanezumab	Failed	+++	+	None	IgG1	No
BACE inhibitors	Failed	+++	N/A	N/A	N/A	No
Bapineuzumab	Failed	++	++	+++	IgG1	Yes
Crenezumab	Failed	+	++	+++	IgG4	No
Aducanumab	Positive	None	+++	+++	IgG1	Yes
BAN2401	TBD	None	++	++	IgG1	Yes
PMN310	TBD	None	+++	None	IgG4	Not expected

ProMIS™ Neurosciences

Binding the right form of amyloid-beta is critical: the toxic oligomer is the target

Bapineuzumab
- Phase 2 failure
- Phase 3 failure
- ARIA-E side effect

Solanezumab
- Phase 2 failure
- Phase 3 failure

Aducanumab
- Phase 3 success
- ARIA-E side effect

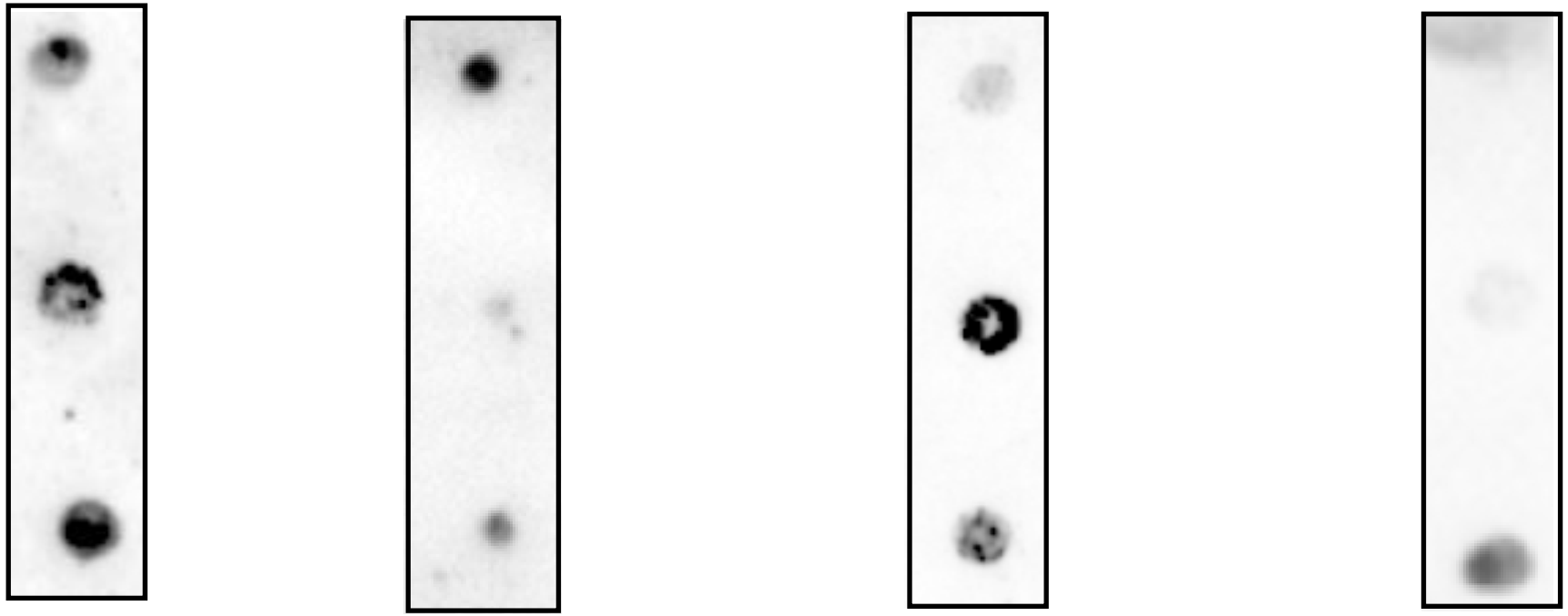
PMN310
- Selective binding to oligomers

-> Expected improvement in efficacy & safety

MONOMERS
- binding wastes therapeutic ammunition

FIBRILS (Plaque)
- binding wastes therapeutic ammunition
- contributes to ARIA-E side effect

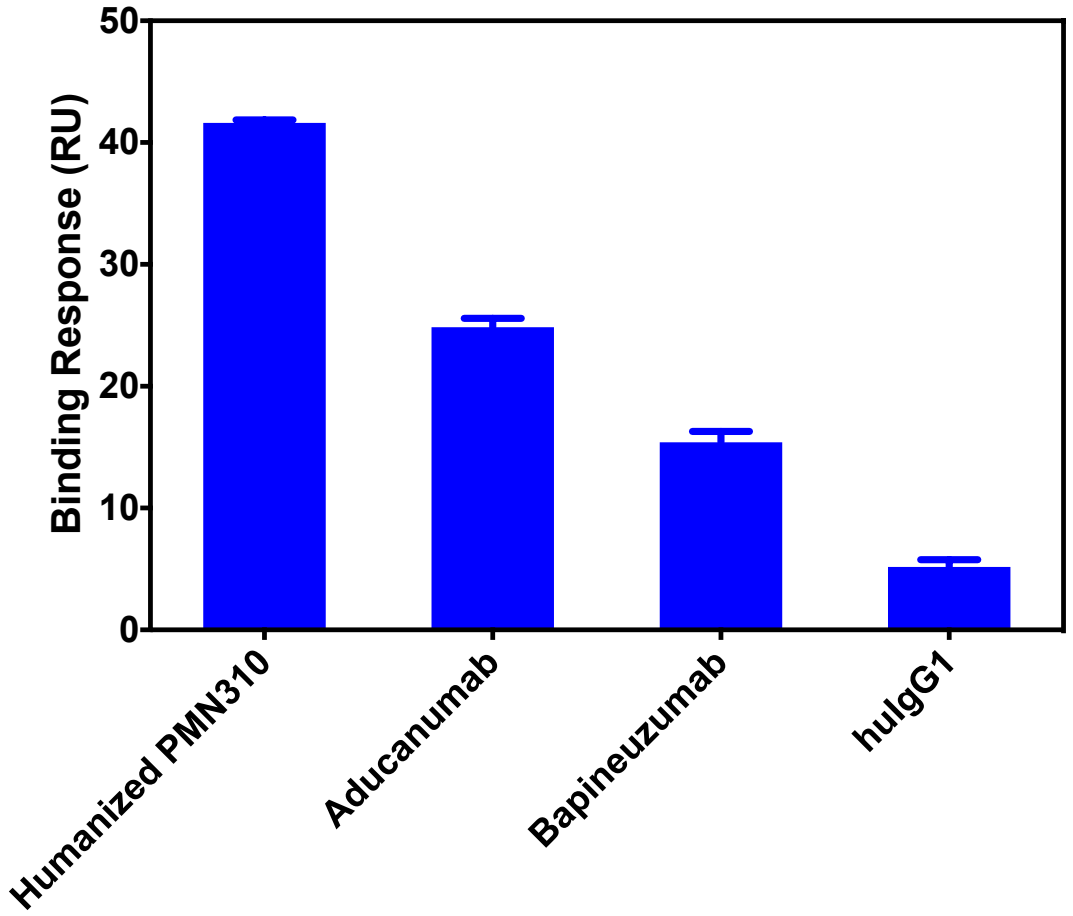
OLIGOMERS*
- the right target



ProMIS™ Neurosciences

* Synthetic oligomers

PMN310 shows superior binding to toxic oligomer-enriched fraction from human AD brains vs other antibodies directed against amyloid-beta



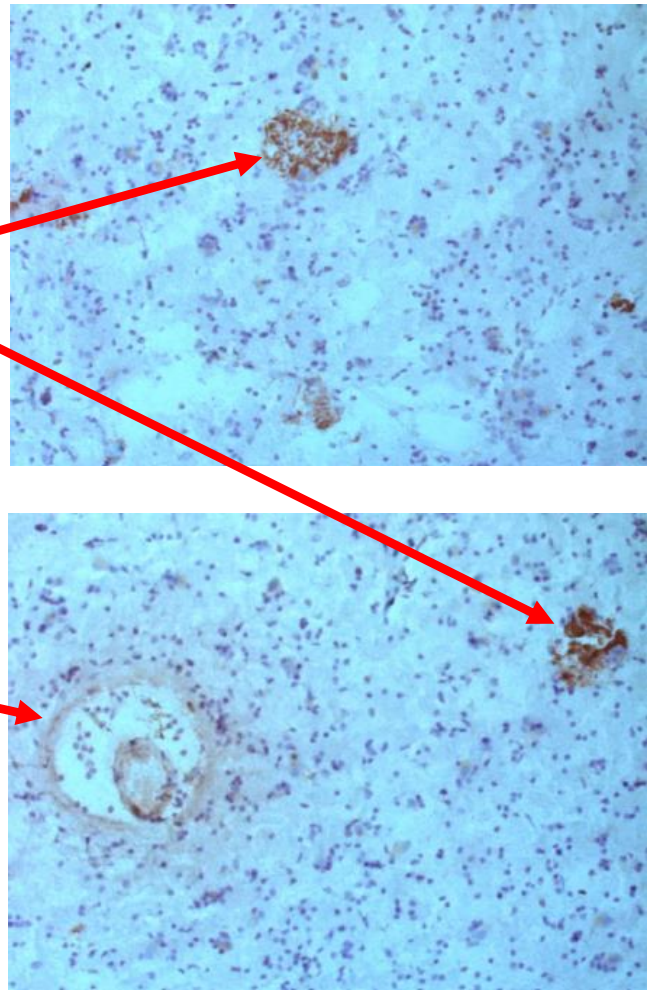
- Binding of antibodies to the toxic oligomer-enriched low-molecular weight fraction of soluble human AD brain extract was evaluated by surface plasmon resonance (SPR)
- Results representative of over 10 SPR runs with extracts from 11 different AD brains
- huIgG1 = Background control

ProMIS™ Neurosciences

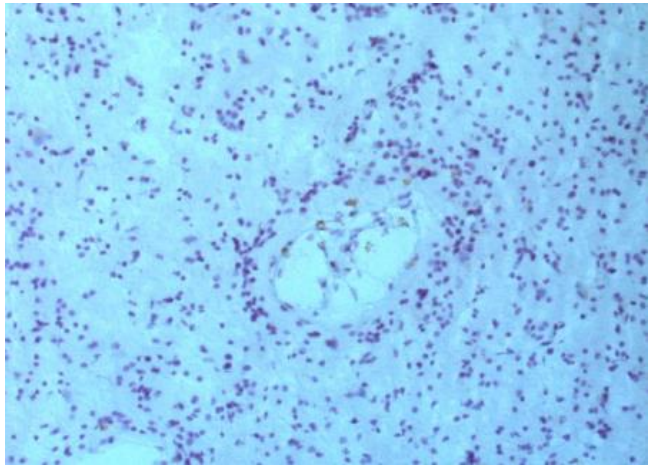
Source for comparative reagents: Creative Biolabs

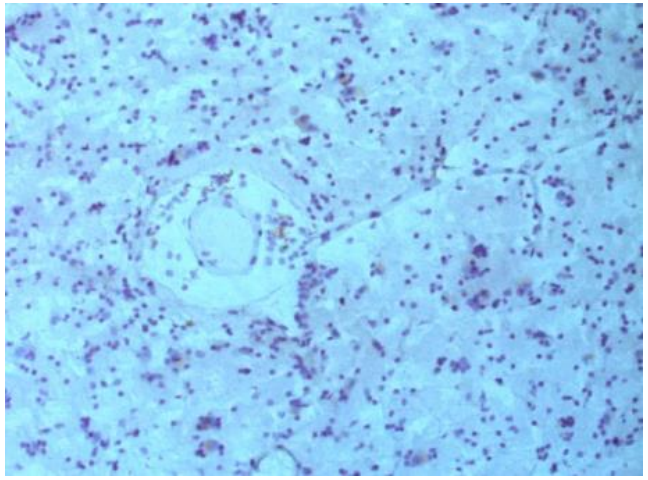
PMN310 does not bind to Aβ deposits, potentially reducing the risk of ARIA-E

Aducanumab



PMN310



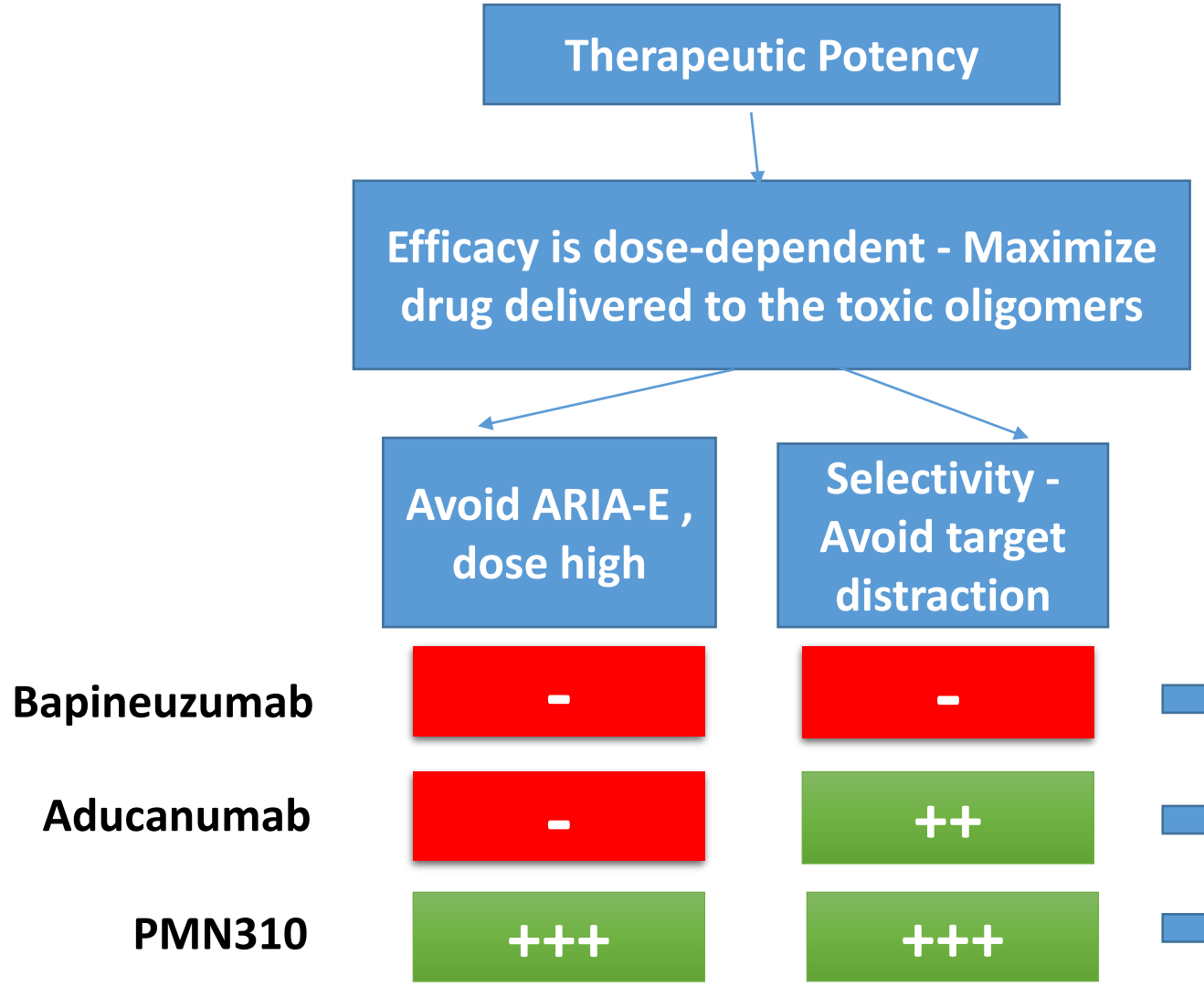


No binding to plaque or vascular deposits

*IgG4 isotype of PMN310 correlates with lack of ARIA-E

ProMIS™ Neurosciences

Properties of ProMIS PMN310 support better *Therapeutic Potency* vs Biogen's likely "First In Class" aducanumab



ProMIS™ Neurosciences

Summary - PMN310 may achieve better clinical outcome

- Most recent Phase 3 aducanumab data show a 23% reduction in cognitive decline in patients with longer term exposure at the high dose of 10 mg/kg.
- Clinical benefit might be improved by higher doses but not possible due to the high risk of ARIA-E (seen in 35% of patients at the doses tested)
- PMN310 designed to achieve greater therapeutic potency
  - No plaque binding -> Reduced risk of ARIA-E should allow for higher, more efficacious doses
  - Selectivity for toxic oligomers -> Reduced diversion from the target delivers full dose to the toxic oligomers driving disease
- Potential to safely administer higher, oligomer-targeted doses of PMN310 may achieve better clinical outcome