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THERAPEUTICS

Multiple System Atrophy (MSA)

New Opportunity with Rapid Entry to Clinic

- Orphan disease: ~3 in 100,000 over age 50
- Mean survival time: 5-10 years
- An aggressive form of Parkinson's disease
- Rapid progression due to prion-like propagation of toxic oligomers of α-synuclein (αS)

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Experienced Leadership Team

Enrique Alvarez DVM, MA
Co-Founder
VP Research and Development

Susan Froshauer, PhD
Chief Executive Officer

Andrew Miranker, PhD
Co-Founder
Chief Scientific Officer

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Pangolin Tackles Misassembled Oligomers

- *In vivo*, most of the human proteome is unstructured
- Unstructured proteins tend to self-associate into oligomers
- Misassembled oligomers are toxic
- Pangomer™ chemistry enables the creation of novel agents that selectively neutralize these toxins
- New drugs will be first-in-class with potential for disease-modification

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Pangolin Tackles Misassembled Oligomers

Many diseases are caused by the missassembly of multiple copies of unstructured proteins

Key Examples	Unstructured Target
Multiple System Atrophy (MSA)	αS
Type II diabetes	IAPP
Alzheimer's	Aβ
Amyotrophic lateral sclerosis (ALS)	SOD
Traumatic Brain Injury (TBI)	Tau

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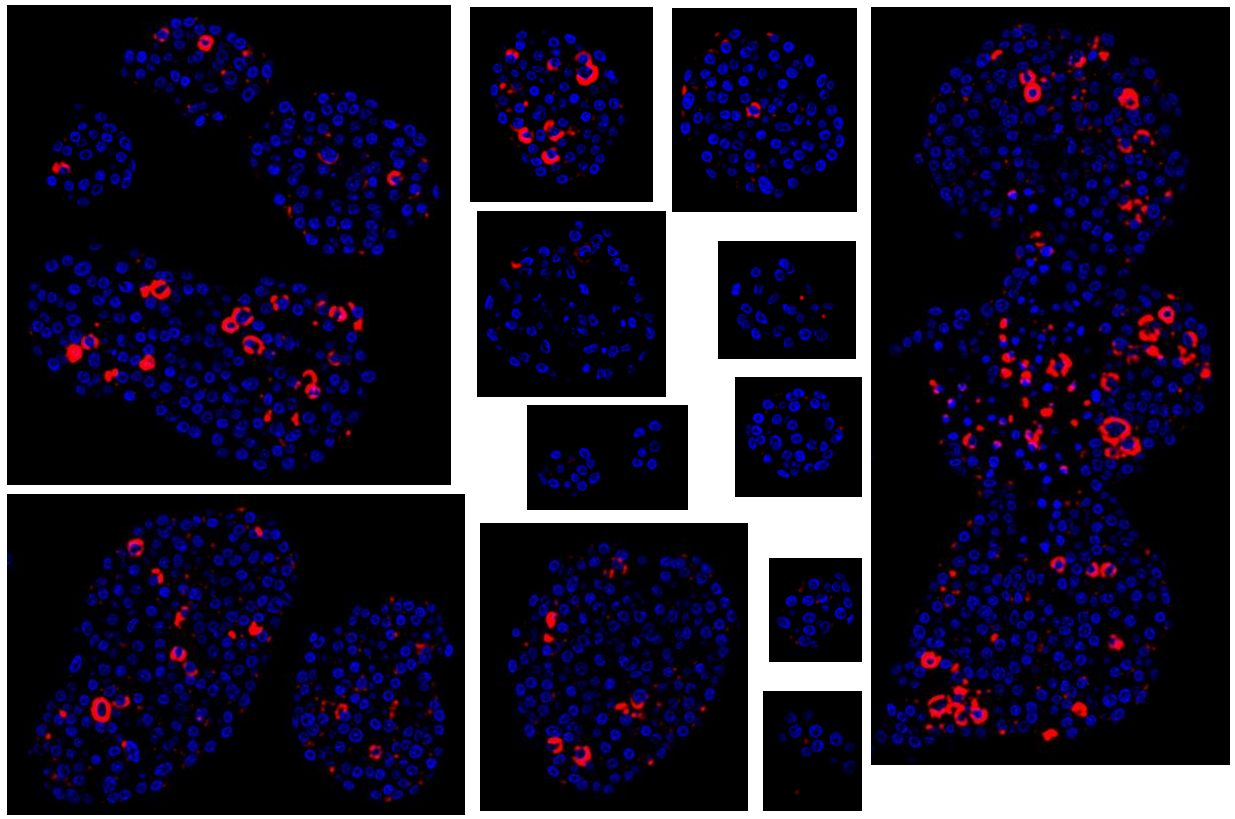
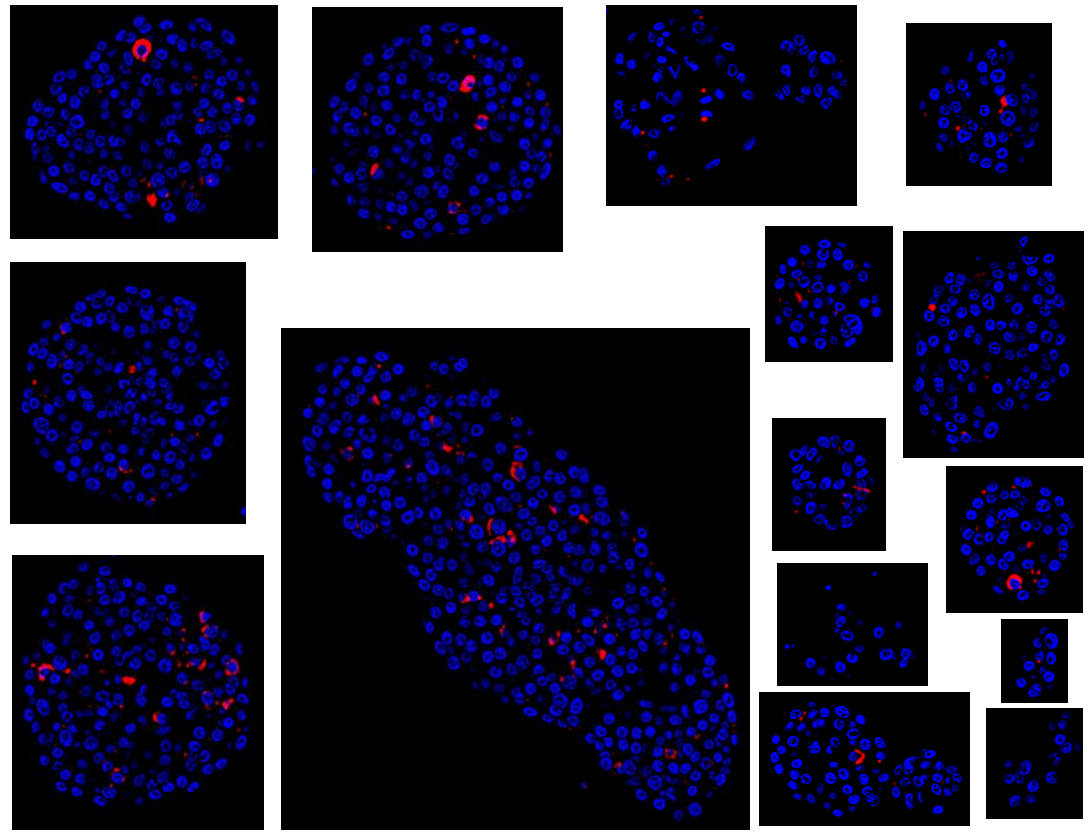
Pangolin Technology in Action

Rescue of Human Insulin Secreting Cells with a Diabetes Specific Pangomer™



+ Vehicle



Human islets challenged with high glucose for seven days stained for Death Receptor and Nuclei

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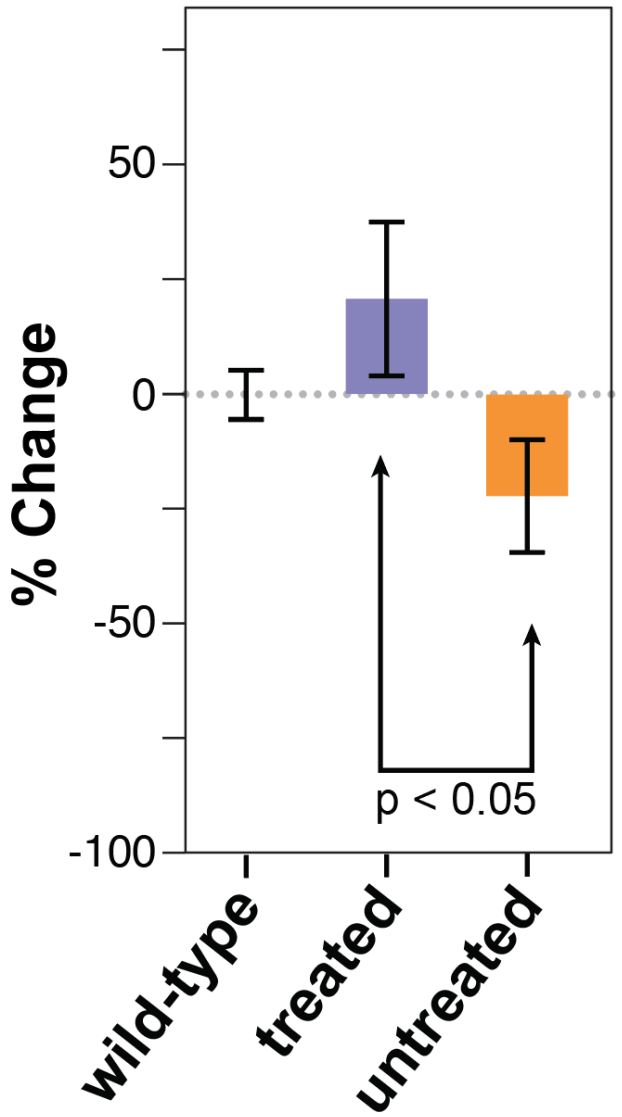
Pangolin Technology in Action

In vivo rescue of insulin secretion function in transgenic, diabetic mice treated with disease-specific Pangomer analogue ADM-116



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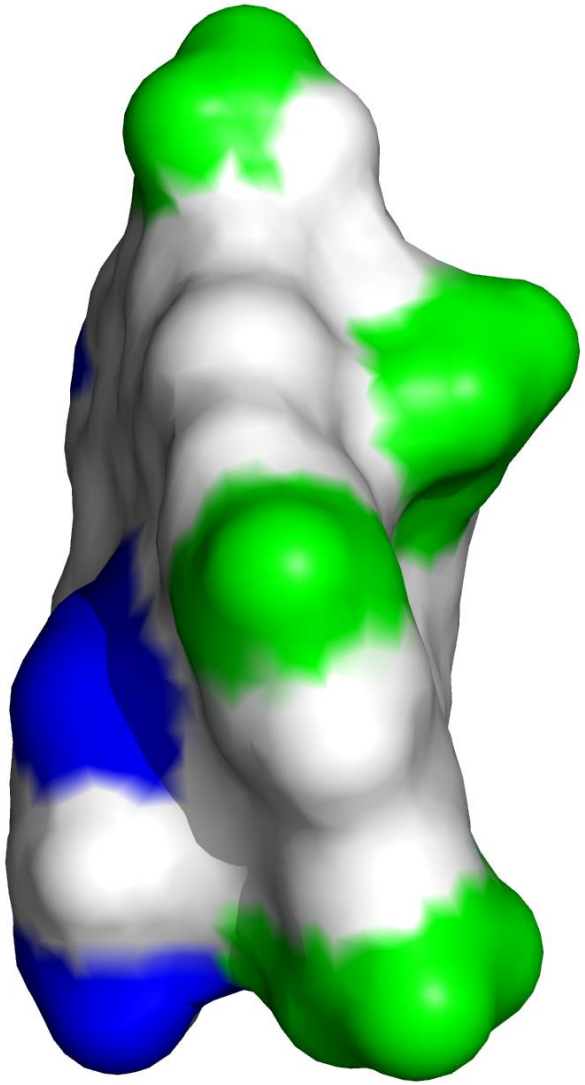
The Pangomer™ Drug Design Platform

The Pangomer™ IP is a small molecule, foldamer-scaffold that can be modified without impacting its core fold



locations that uniquely allow for optimization of pharmacodynamic, biodistribution, formulation properties without affecting target binding

locations can be modified to create selective binders to new disease targets

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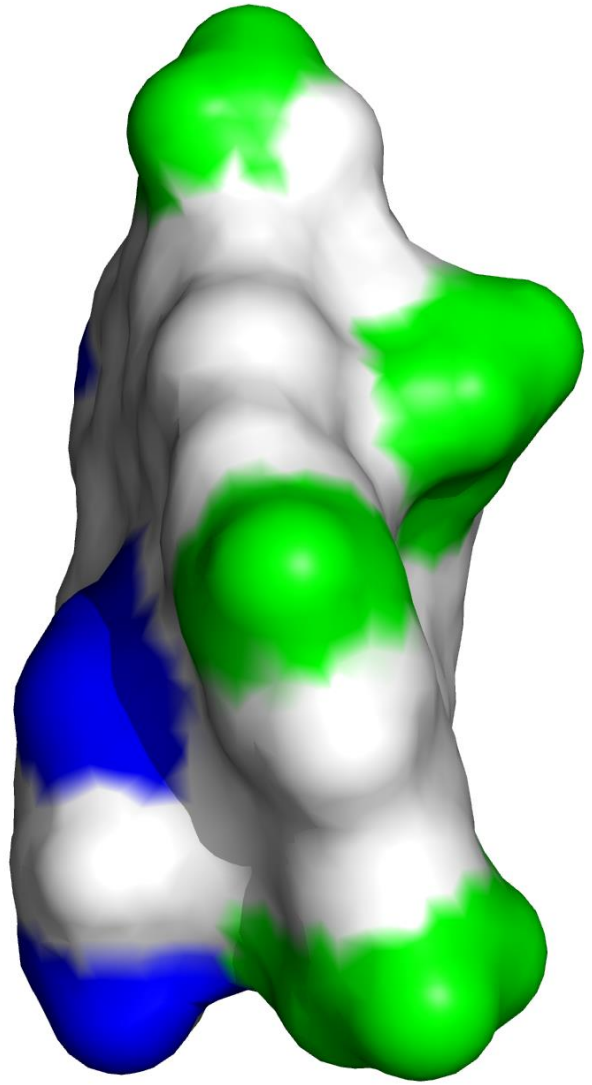
Fundamentals of the Pangomer™ Scaffold

- Achieves disease-specificity by inducing structure in the target protein
- Foldamer class: small molecules that can function like proteins
- Defined folded structure with a grease stabilized core and derivitizable surface
- Water soluble analogues (>20mM) can cross cell membranes
- Designed to avoid common classes of false-positive binders



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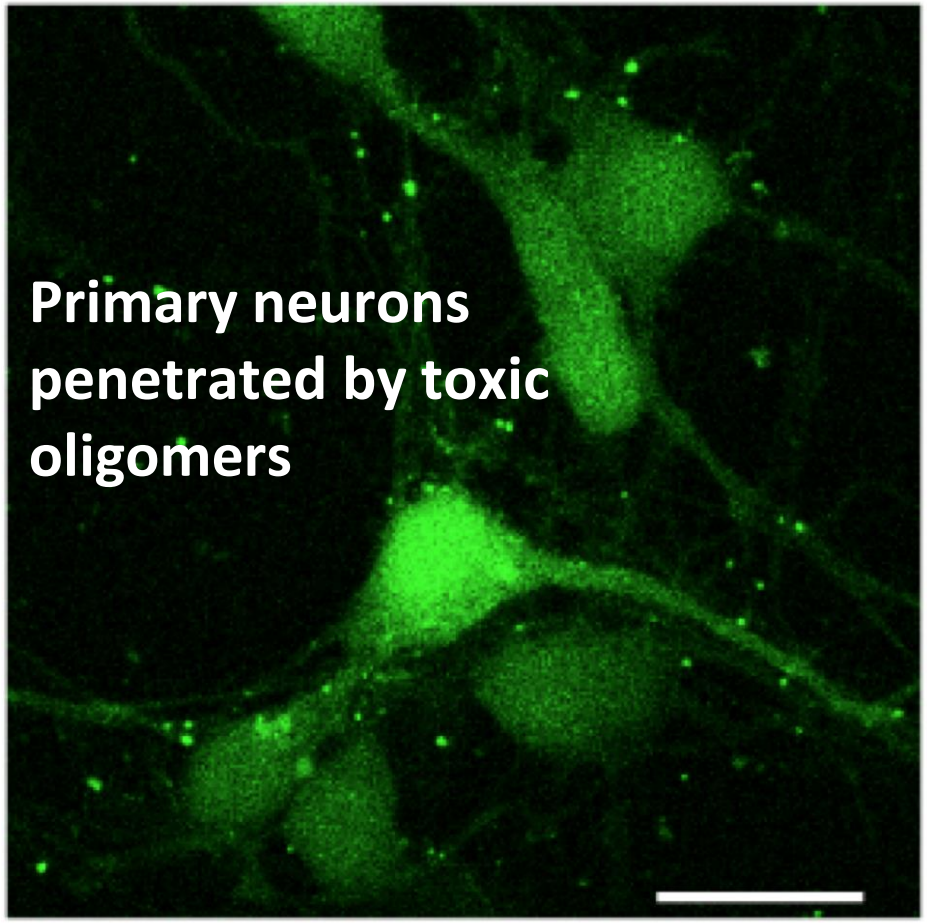
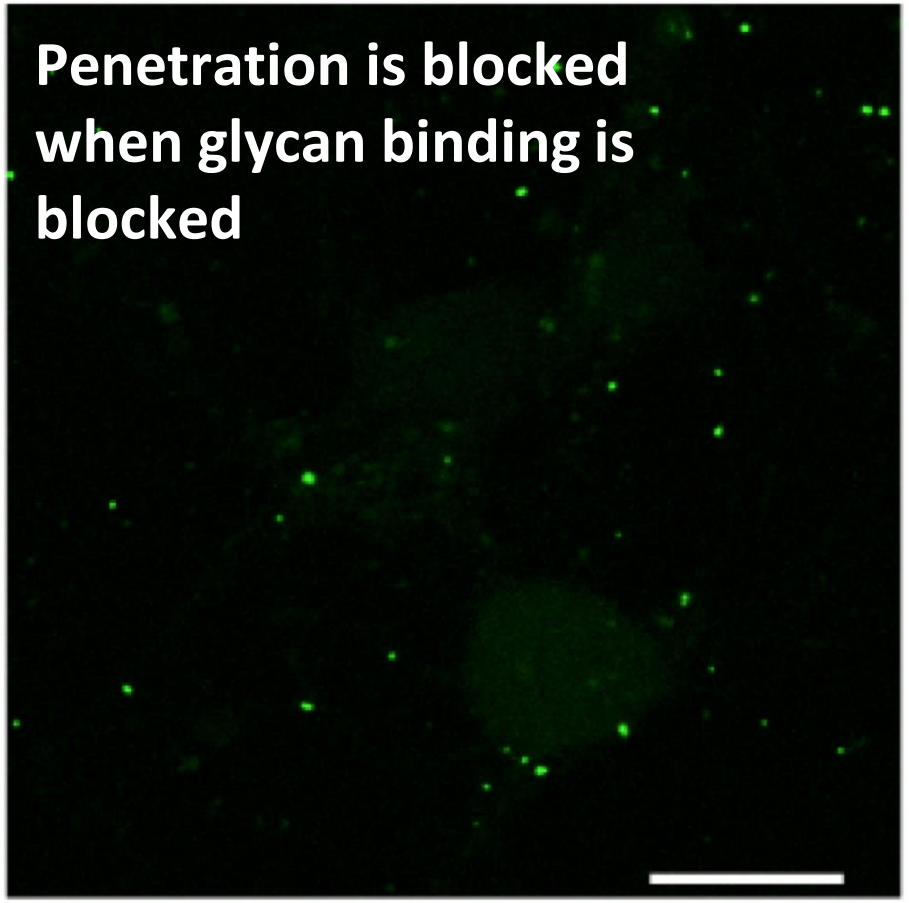
Pangolin in Unique Position to Address MSA

MOA: toxic oligomers of α-Synuclein propagate through the brain





Our discovery: **neuron specific glycans are required**

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Pangomer™ Design Step 1
Identify a Disease-Relevant Region

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Pangomer™ Design Step 2
Computer impose an α-helix conformation

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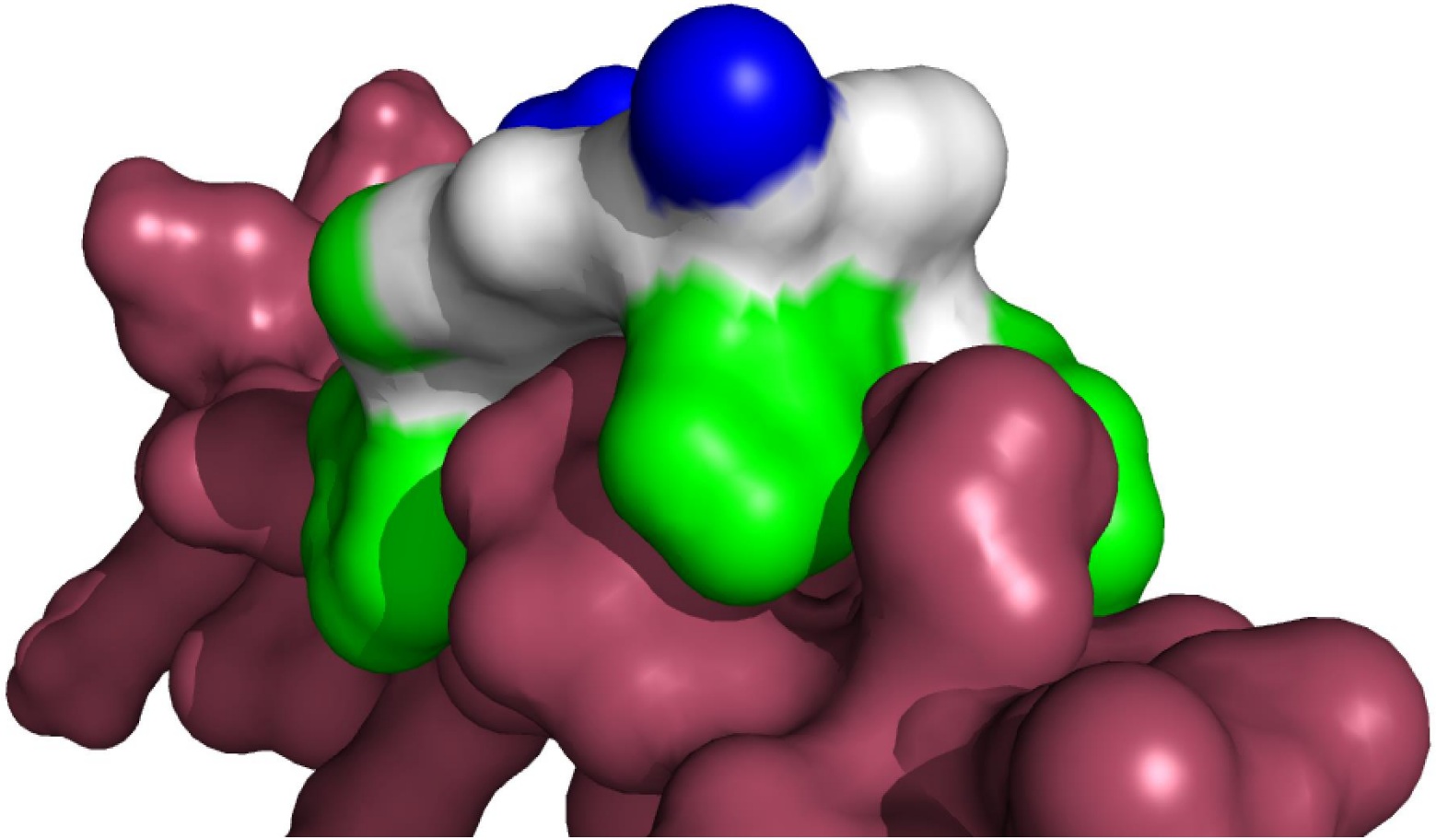
2019 Blavatnik Achievements



Designed Pangomer ™ Analogue Shown Docked to MSA Target

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Funding requested to advance MSA-specific analogues to animal testing

- Translational diabetes work:
  $100K, Jun 2017, Blavatnik Fund for Innovation at Yale
  $500K, Jan 2018, State of CT Biosciences Innovation Fund

- Multiple System Atrophy (MSA):
  $100K, Jun 2019, Blavatnik Fund for Innovation at Yale

- **Seeking $300K** for chemistry and *in vitro* proof-of-concept

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Enrique Alvarez	(860) 304-6030	enrique@pangolintherapeutics.com
Susan Froshauer	(203) 606-0081	sfroshauer@pangolintherapeutics.com
Andrew Miranker	(203) 215-9083	amiranker@pangolintherapeutics.com