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 \( \alpha \)-synuclein (\( \alpha S \))
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
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
Many diseases are caused by the missassembly of multiple copies of unstructured proteins.

<table>
<thead>
<tr>
<th>Key Examples</th>
<th>Unstructured Target</th>
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<tbody>
<tr>
<td>Multiple System Atrophy (MSA)</td>
<td>αS</td>
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<tr>
<td>Type II diabetes</td>
<td>IAPP</td>
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<tr>
<td>Alzheimer’s</td>
<td>Aβ</td>
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<tr>
<td>Amyotrophic lateral sclerosis (ALS)</td>
<td>SOD</td>
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<tr>
<td>Traumatic Brain Injury (TBI)</td>
<td>Tau</td>
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</tbody>
</table>
Human islets challenged with high glucose for seven days stained for Death Receptor and Nuclei
*In vivo* rescue of insulin secretion function in transgenic, diabetic mice treated with disease-specific Pangomer analogue ADM-116
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.
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
Pangolin in Unique Position to Address MSA

MOA: toxic oligomers of $\alpha$-Synuclein propagate through the brain

Our discovery: neuron specific glycans are required
Pangomer™ Design Step 1
Identify a Disease-Relevant Region
Pangomer™ Design Step 2
Computer impose an α-helix conformation
2019 Blavatnik Achievements

Designed Pangomer ™ Analogue Shown Docked to MSA Target
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