

256 A Small Molecule that Blocks Alpha Synuclein Transmission in Neurodegenerative Disorders

► Asset Overview

Product Type	Small molecule
Indication	CNS Diseases
Current Stage	Lead Identification/optimization
Target(MoA)	alpha-synuclein (α -Syn)
Brief Description	<p>Researchers at UC San Diego have developed a novel strategy to treat PD by using small molecules interacting with native α-Syn that could protect and stabilize specific conformations present in the ensemble, which in turn could provide protective action. A compound has been identified that displayed protective activity in preventing the transmission of α-Syn from cell to cell thus supporting the notion that small molecules can target an intrinsically disordered protein such as α-Syn. This compound does not directly affect the process of α-Syn misfolding or aggregation and thus offers a novel mode-of-action beyond previously described aggregation blockers.</p>
Organization	University of California, San Diego

► Differentiation

Neurodegenerative Disorders

- A universal commonality among these diseases is the presence of misfolded aggregated proteins in the brain or with cells of the brain
- These aggregated proteins can take different forms and be used help diagnosis the specific neurodegenerative disease

Alpha-synuclein (α -Syn)

- A mutation in the gene encoding α -Syn (SNCA) or simple overexpression of wild-type α -Syn will lead to PD. The presence of misfolded α -Syn is also seen in other synucleinopathy diseases including Alzheimer's disease (AD) and Dementia with Lewy Bodies (DLB), the two most prevalent progressive dementia diseases and MSA

It has potential to block the spread and pathogenesis of α -Syn

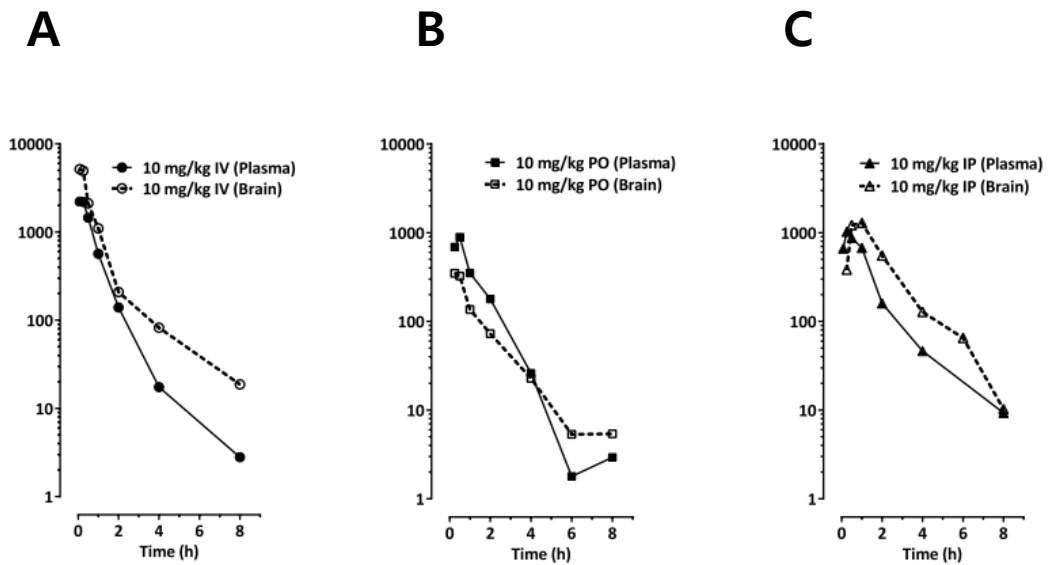
- The most common forms of symptomatic treatment for PD fail to show improvement over the course of 2-5+ years
- This compound does not directly affect the process of α -Syn misfolding or aggregation and thus offers a novel mode-of-action
- The compound blocks the cell-to-cell propagation of α -Syn and thus has potential to block the spread and pathogenesis of α -Syn in synucleinopathies such as PD, AD, DLB, and MSA

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► Key Data

Brain levels of small molecule parallel plasma levels

Indirect experiment data



Brain levels of small molecule parallel plasma levels following all routes of administration in C57BL/6 mice. Compound exposure data are presented as group means for specific time points for intravenous (A), oral (B), and intraperitoneal (C) administration.

Price, Diana L., et al. Scientific reports 8.1 (2018): 16165.

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► Intellectual Property

Patent No.	
Application Date	
Status	
Country	

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