PRANA BIOTECHNOLOGY

Clinical Development Update

David Stamler, M.D.

Annual General Meeting
16 November 2018

Highlights

PRANA BIOTECHNOLOGY

NOVEL DRUG CANDIDATE: PBT434

- Targets key proteins implicated in neurodegeneration of Parkinson's disease and atypical parkinsonism
- Prevents accumulation and aggregation of α-synuclein
- Phase 1 study in healthy volunteers ongoing

STRONG RESEARCH AND DEVELOPMENT

- Innovative discovery program
- Development team with proven track record
- Long standing collaborations with Harvard and Florey Institute of Neuroscience and Mental Health

MULTIPLE INDICATION OPPORTUNITY

- PBT434 active in several animal models of Parkinson's disease and atypical parkinsonism

U.S.-based clinical team with strong drug development experience and FDA approvals

David Stamler, M.D.
Chief Medical Officer & Senior VP, Clinical Development

Former VP, Clinical Development and Therapeutic Head, Movement Disorders, Teva Pharmaceuticals and Chief Medical Officer, Auspex Pharmaceuticals.

Part of Teva's US$3.5 billion acquisition of Auspex. Led development of AUSTEDO (deutetrabenazine), new drug for treatment of Huntington's disease (approved by FDA - April 2017) and tardive dyskinesia, also in 2017.

James Kerr
VP, Chemistry, Manufacturing and controls

Previously Executive Director CMC Teva/Auspex Pharmaceuticals. Senior member of leadership team responsible for budget managment and operational direction of CMC team. Prior to Auspex, was Senior Director, CovX Operations at Pfizer WRD.

Margaret Bradbury, Ph.D
VP, Nonclinical Development

Previously Senior Director, Teva Pharmaceuticals. At Teva, led non-clinical development of several neuroscience programs. As Executive Director at Auspex Pharmaceuticals, led strategic planning and program management in Huntington Disease-chorea from IND through NDA filing.

PBT434 - Strong Development Rationale

- Alpha (α)-synuclein is an intracellular protein critical for neurotransmission
- Alpha-synulein accumulates and aggregates in many neurodegenerative diseases, implicated in pathology
- PBT434 blocks α-synuclein accumulation and aggregation, preserves neurons and improves function in animal models of synucleinopathy
- Clear link between iron and the synucleinopathies
- Clear development path for symptomatic therapy in atypical parkinsonism
  - Current symptomatic therapy has limited benefit
- Potential path for disease modifying therapy for the synucleinopathies

Conclusion: PBT434 is an excellent drug candidate to treat neurodegenerative diseases

Alpha-Synuclein – An Established Disease Target

Strong Genetic and Pathological Link to Disease

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THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

ALPHA-SYNUCLEIN PRIORITY AREA

Therapeutic approaches to target alpha-synuclein pathology

Patrik Brundin[a,*], Kuldip D. Dave[b], Jeffrey H. Kordower[a,c]

*We conclude that alpha-synuclein remains **one of the most compelling therapeutic targets** for Parkinson's disease, and related synucleinopathies, and that the multitude of approaches being tested provides hope for the future.*

Exp. Neurology 2017 Dec;298(Pt B):225-235

Biogen *Phase 2 in Parkinson's disease (SPARK) ongoing*

Roche *Phase 2 in Parkinson's disease (PASADENA) ongoing*

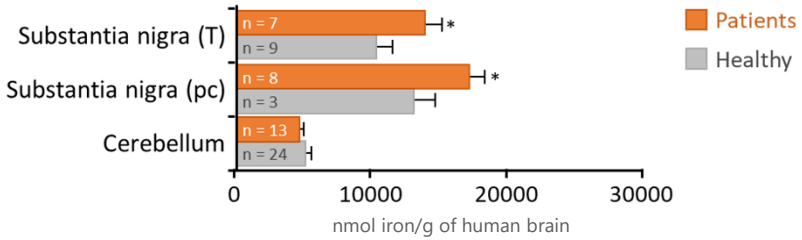
AstraZeneca Takeda *Phase 1 in Healthy volunteers ongoing*

https://www.michaeljfox.org/research/priority-area-detail.php?alpha-synuclei

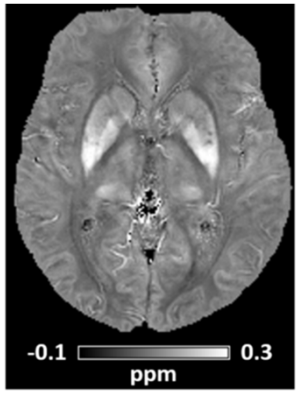
Prana's Phase 1 study of PBT434

- Single and multiple ascending dose study
- Healthy adult and elderly volunteers
- Goals include assessing the safety, tolerability and pharmacokinetics of PBT434
- Commenced in June '18 at Nucleus Network in Melbourne
  - Several single dose cohorts completed
  - Multiple dose cohorts have been dosed
- Expect to complete study as designed
- Plan to report results in 1H '19

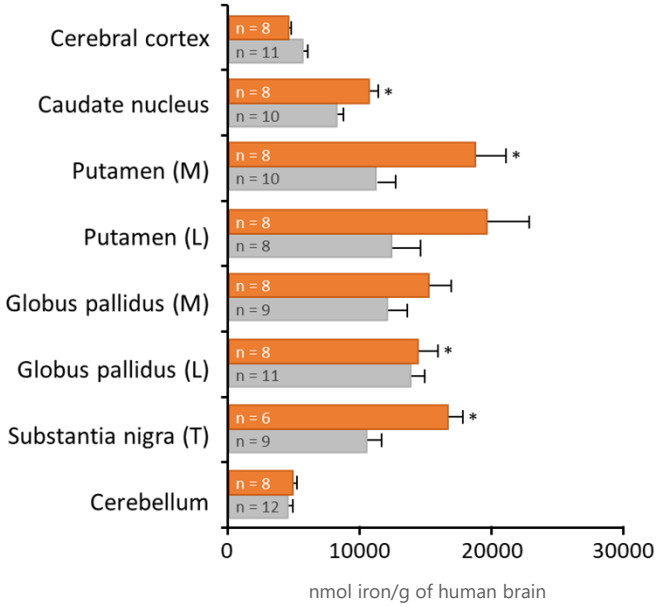
Brain Iron Increased in Parkinson's Disease Patients



Specialised MRI Technique (QSM) to Non-invasively Quantify Brain Iron (PD Patient)



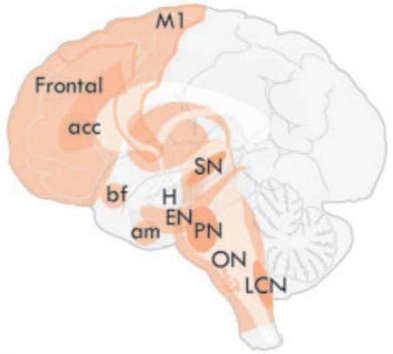
And In Multiple System Atrophy Patients



Dexter. Brain.1991;114
Langkammer. PLoS ONE 11(9): e0162460. 2016

Multiple System Atrophy
A form of Atypical Parkinsonism

- Rapidly progressive neurodegenerative disorder leading to severe disability and impairment in quality of life
- Sporadic, typically presents in 50s to 60s
- Orphan Indication: Prevalence ~5 per 100,000 in the U.S.
- Characterized by a variable combination of
  - Parkinsonism, which responds poorly to levodopa
  - Cerebellar impairments: impaired gait and speaking
  - Autonomic failure: Orthostatic hypotension, bladder dysfunction, erectile dysfunction, constipation
- MSA patients have neuron loss in multiple brain regions
- The hallmark of MSA is the accumulation of α-synuclein within neurons and glial support cells



Halliday 2015, based on
Brain 2015: 138; 2293–2309

PBT434 Reduces Alpha-synuclein and Glial Cell Inclusions, Preserves Neurons and Improves Motor Function

Transgenic Mouse Model (PLP)-α-SYN of MSA

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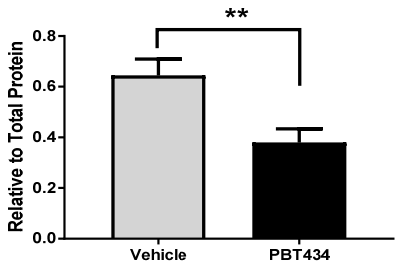
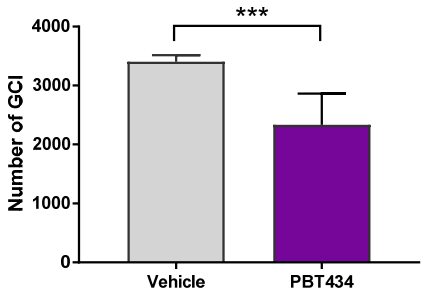
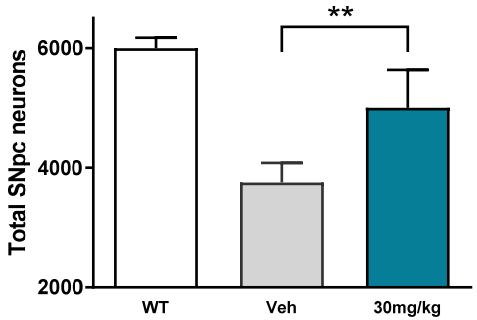
Alpha-Synuclein



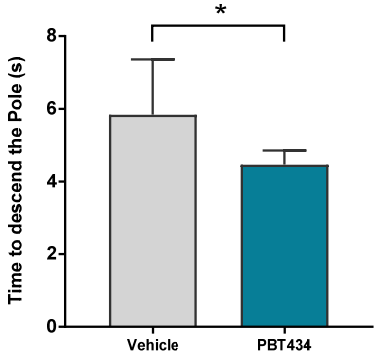
Glial Cell Inclusions



Neurons



Motor Function (Pole test)



Treatment: Randomly allocated, 4 months, ~30 mg/kg/day or Vehicle
Data presented are for animals at 16 mo age; substantia nigra

Summary

- PBT434 targets α-synuclein, a biologically important protein implicated in neurodegenerative diseases
- Iron is increased in the brain of patients with target diseases
- PBT434 restores iron balance and blocks the accumulation and aggregation of this protein
- PBT434 has shown clear efficacy in multiple animal models of disease
- Potential indications include the synucleinopathies such as Parkinson's disease and Multiple System Atrophy
- Phase 1 study commenced June '18 and progressing well
- Orphan Drug application for MSA filed with the U.S. FDA
- Key work to support Phase 2 is ongoing