Alterity THERAPEUTICS

Investor Presentation

April 2019

Mr Geoffrey Kempler
CEO and Chairman

Dr David Stamler
Chief Medical Officer & SVP Clinical Development

Alterity

AN ALTERNATE FUTURE

We exist to create an alternate future for people living with neurodegenerative diseases. An alternate, healthier life.

We’re here to disrupt the trajectory for people with these debilitating diseases.

Improving Lives

Alterity is developing first-in-class therapies to treat neurodegenerative diseases. Our lead drug candidate, PBT434, has demonstrated pre-clinical evidence as a first-in-class therapy for the treatment of Parkinsonian disorders and is well advanced in its Phase 1 clinical program.

INVESTMENT PROPOSITION

- **Well funded** clinical stage drug development company following up to $44M strategic investment led by **Life Biosciences LLC** allowing accelerated and focused clinical development
- **Strong and highly experienced board and management team** with significant R&D and commercialisation experience including **3 drug approvals by US FDA**
- PBT434 is a **novel drug candidate** targeting key proteins implicated in neurodegeneration of Parkinson's disease and atypical parkinsonism
- PBT434 is completing its **Phase 1 clinical trial program**
- **First therapeutic target selected** – Multiple System Atrophy (MSA), a form of atypical parkinsonism, is a devastating disease with no approved treatments
- **FDA Orphan Drug designation for PBT434** for the treatment of MSA received.
- **Significant market potential** for MSA alone – estimated peak sales of US$750M

STRATEGIC INVESTMENT

- Strategic lead investor in a capital raise up to of approx. A$44.5 million.
- The funding will accelerate the Company's drug development programs.
- Life Biosciences is a private US biopharmaceutical company focused on the development of novel therapies, technologies and drugs to address age-related decline.
- Provides funding through end of Phase 2

Alterity

Therapeutic Focus

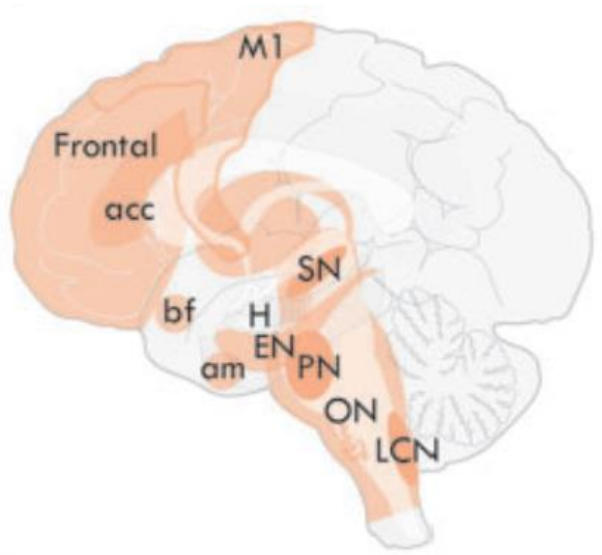
PARKINSONIAN DISORDERS REPRESENT A SUBSTANTIAL UNMET MEDICAL NEED

- Parkinsonism is a general term for a group of symptoms in Parkinson's disease such as slowness of movement, stiffness and tremor
- Parkinsonian disorders include idiopathic Parkinson disease (PD) and atypical forms such as progressive supranuclear palsy (PSP), multiple system atrophy (MSA), and corticobasal degeneration (CBD), among others
- The atypical forms have a limited response to current drugs that target the symptoms of PD such as levodopa
- The first target selected by Alterity is for the treatment of MSA, a highly debilitating disease with no approved treatments

MULTIPLE SYSTEM ATROPHY (MSA)

A form of Atypical Parkinsonism

- MSA is a rapidly progressive neurodegenerative disorder leading to severe disability and impairment in quality of life
- Sporadic (not inherited), typically presents in 50s to 60s
- Orphan disease: Prevalence ~5 per 100,000 in the U.S.
- Patients have a variable combination of
  - Parkinsonism, which responds poorly to levodopa
  - Autonomic failure: Orthostatic hypotension, bladder dysfunction, erectile dysfunction, constipation
  - Cerebellar impairments: impaired gait and speaking
- MSA patients have neuron loss in multiple brain regions
- Pathological hallmark of MSA is the accumulation of α-synuclein within neurons and glial support cells



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

PHASE 1 CLINICAL TRIAL PROGRAM ADVANCING

- Single- and Multiple-Ascending Dose study to be completed Q2’19
- Recruiting healthy adult and elderly volunteers
- Primary goal is to evaluate the safety and tolerability of PBT434
- Secondary goals include assessing pharmacokinetic measures to understand how PBT434 is absorbed and metabolized by the body

FDA ORPHAN DESIGNATION FOR MSA

- January 2019, US Food and Drug Administration (FDA) granted Orphan Drug Designation for PBT434 for the treatment of MSA.

- Orphan Drug designation entitles Alterity to seven years of market exclusivity for the use of PBT434 in the treatment of MSA and qualifies the sponsor of the drug for various development incentives of the Orphan Drug Act 1983, including tax credits for qualified clinical testing.

THERAPEUTIC STRATEGY

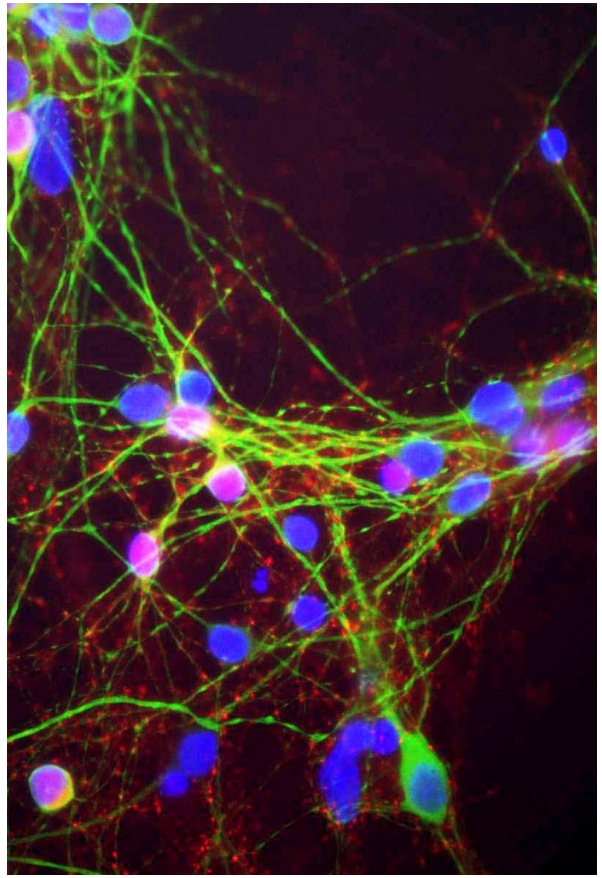
- Alpha (α)-synuclein is an intracellular protein critical for neurotransmission α-synuclein accumulates and aggregates in many neurodegenerative diseases and is implicated in pathology
- PBT434 blocks α-synuclein accumulation and aggregation, preserves neurons and improves function in animal models of synucleinopathy (Parkinson's disease, MSA)
  - PBT434 also prevents tau accumulation and improves function in animal models of tauopathy
- Link between increased brain iron and the synucleinopathies
- Phase 2 data in Parkinson's disease patients with a related compound supports proof of concept
- Clear development path for symptomatic therapy in atypical parkinsonism
  - Current symptomatic therapy has limited benefit
- Potential path for disease modifying therapy

PBT434 is an excellent drug candidate for treating neurodegenerative diseases

- Brain penetrant
- Established manufacturing process
- Strong preclinical evidence

IMPORTANCE OF α-SYNUCLEIN AS DISEASE TARGET

- α-Synuclein is an intracellular protein, abundantly expressed in the brain
- Critical for normal function of neurons
- Soluble, in highest concentration at presynaptic nerve endings
- Key regulatory protein involved in neurotransmission
- Enables neurotransmitter release by facilitating synaptic vesicle fusion to pre-synaptic membrane



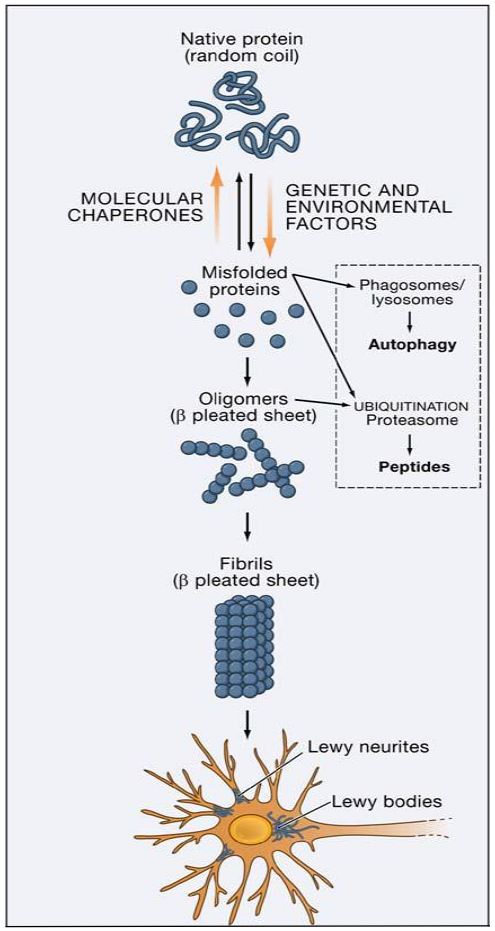
MAb to α-synuclein stains red

Increasing Industry & Research Prioritization

Alterity

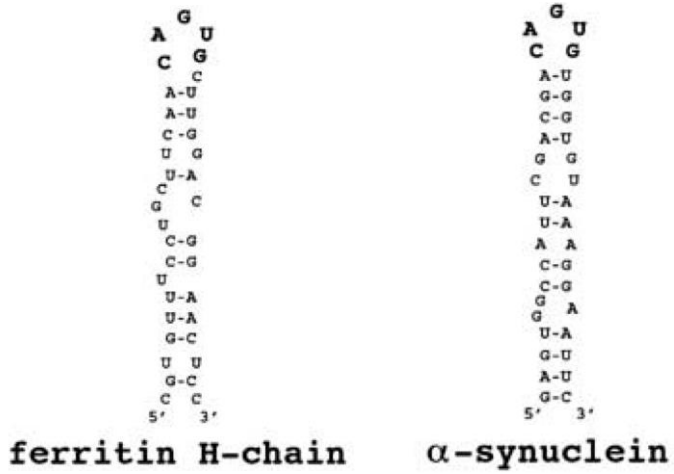
Science and Technology

α-SYNUCLEIN AS TARGET FOR PBT434



Lee and Trojanowski, 2006

- α-synuclein fibrillizes readily
- Factors regulating its production and conformation are relevant to disease pathogenesis and treatment
- Homeostasis of iron is disrupted in PD and atypical parkinsonism
- α-synuclein is highly conserved in vertebrates but only humans develop synucleinopathy
- Human α-synuclein mRNA contains an Iron responsive element

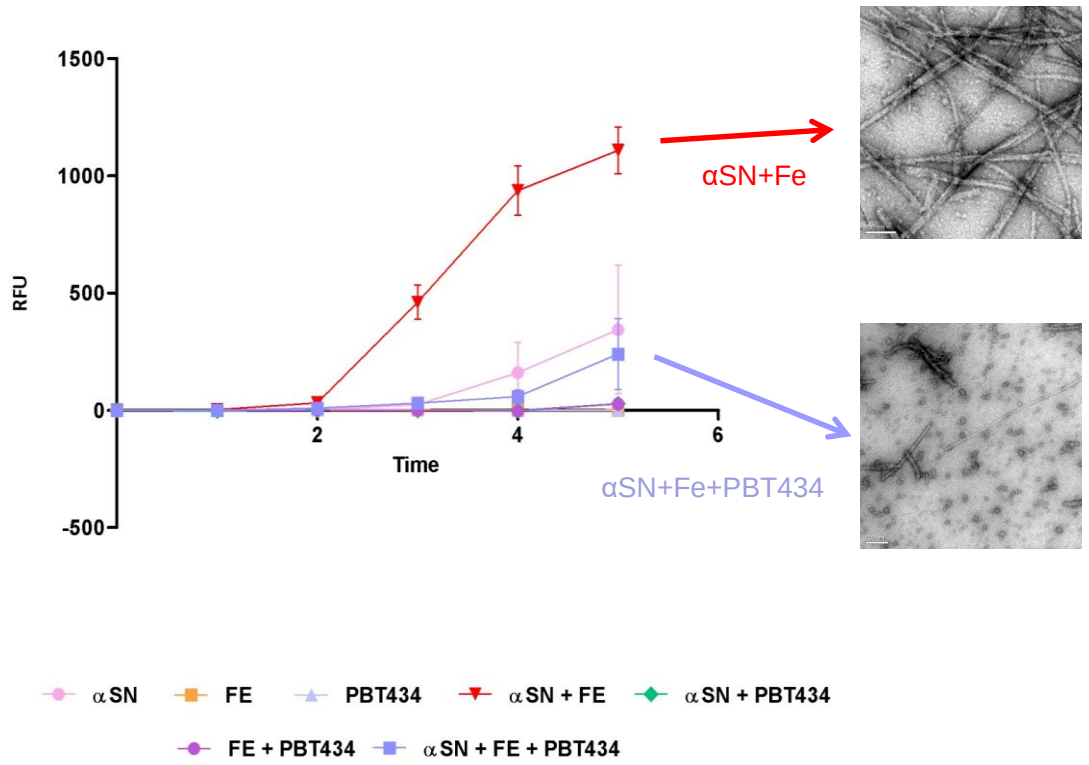


from Friedlich, Tanzi, et al. 2007

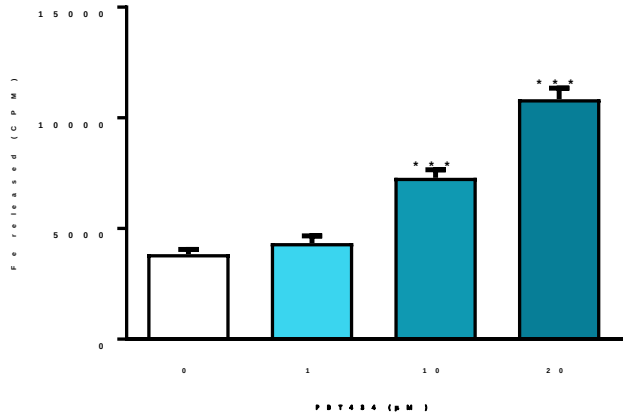
- The iron responsive element (IRE) of α-synuclein is a 5’-untranslated region of mRNA predicted to form a single RNA stem loop
- The stem loop shows striking similarity to the 5’-UTRs of mRNAs encoding ferritin and ferroportin

PBT434 INHIBITS α-SYNUCLEIN AGGREGATION BY RESTORING INTRACELLULAR IRON BALANCE

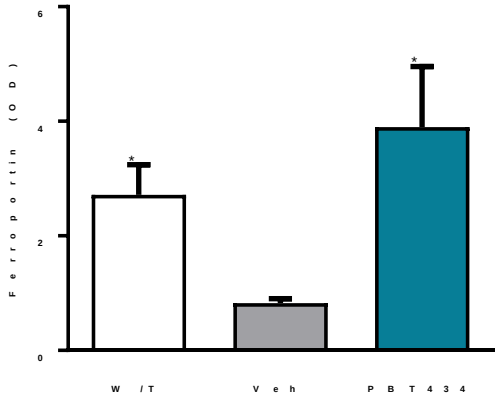
PBT434 blocks the aggregation of α-synuclein in vitro



Iron efflux from cultured M17 cells



PBT434 treatment preserves ferroportin levels in vivo

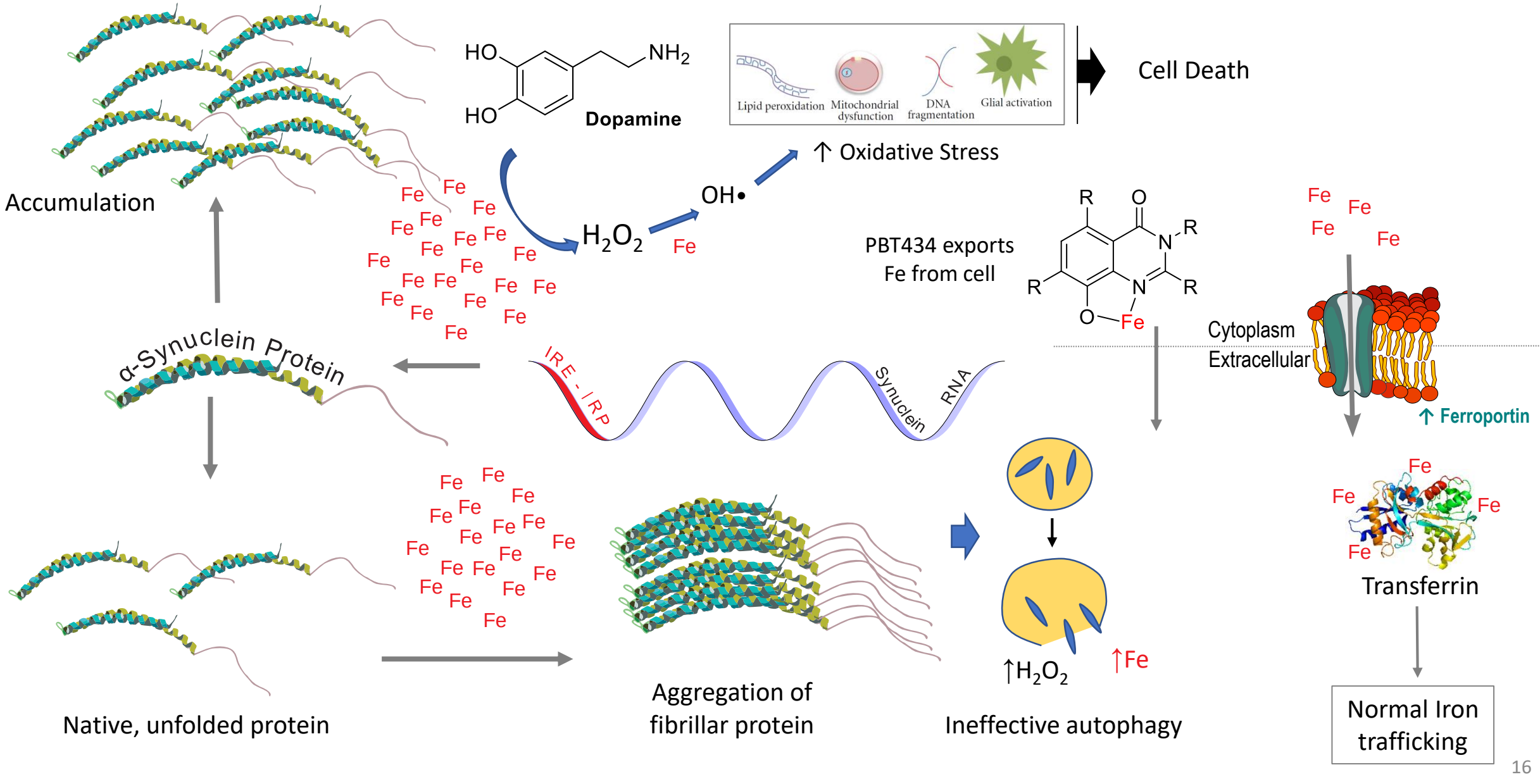


PBT434 Dose: 30 mg/kg

ALPHA-SYNUCLEIN PATHOLOGY AND PBT434 MECHANISM OF ACTION

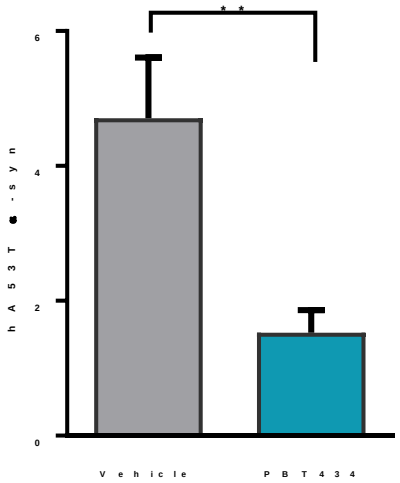
PBT434 reduces α-synuclein accumulation, aggregation and preserves neurons

Alterity THERAPEUTICS

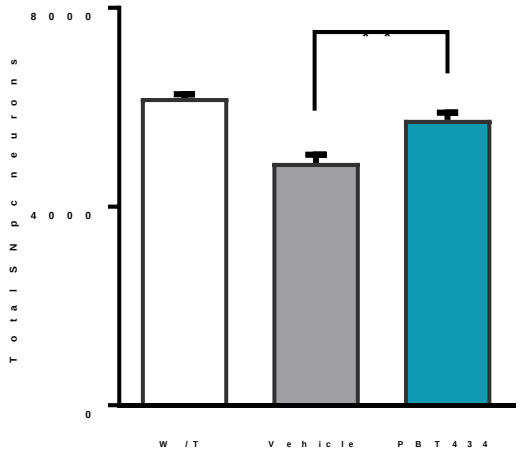


PBT434 LOWERS α-SYNUCLEIN, PREVENTS NEURONAL DEATH AND IMPROVES MOTOR FUNCTION TRANSGENIC ANIMAL MODEL OF PARKINSON'S DISEASE

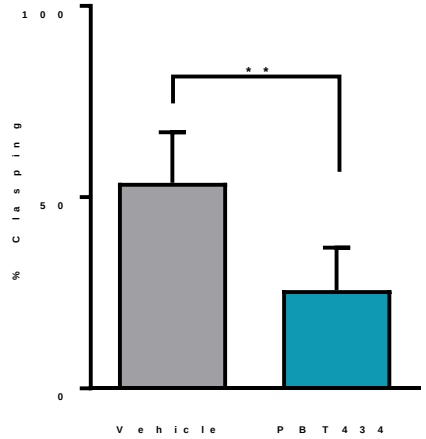
↓ α-Synuclein aggregation



Preserves neurons in S. nigra



Foot Clasping



Treatment randomly allocated
- 4-8 months of age
- ~30 mg/kg/day (via feed)

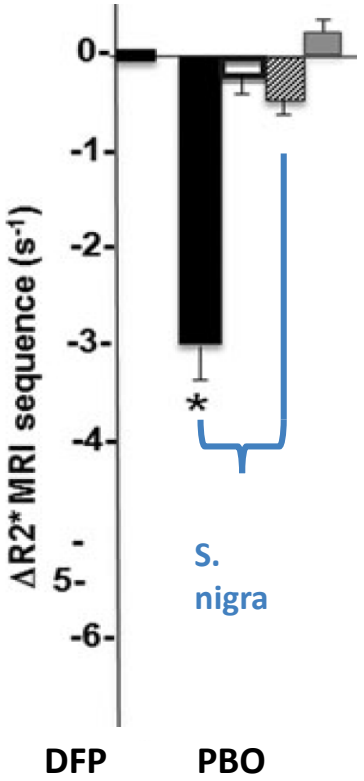
Assessments done in blinded manner

Finkelstein et al. Acta Neuropath Comm (2017) 5:53

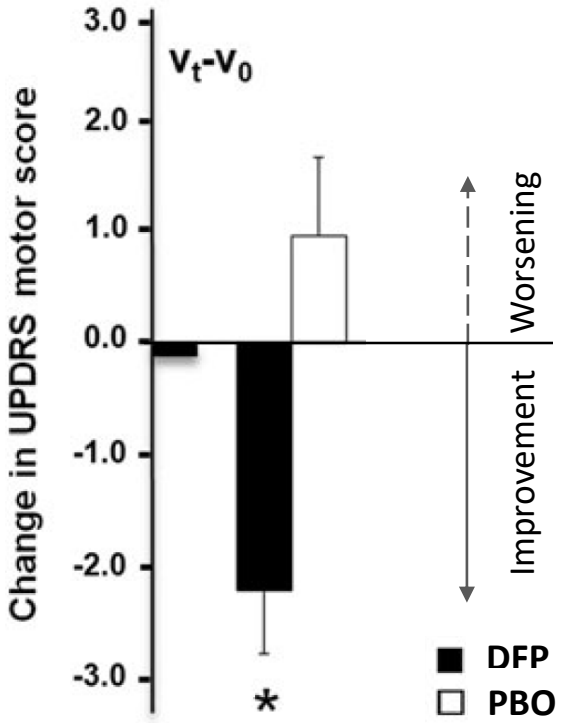
STRATEGY SUPPORTED BY PROOF OF CONCEPT WITH DEFERIPRONE

6 MONTH PLACEBO CONTROLLED DATA IN PARKINSON'S DISEASE PATIENTS

Brain Iron by MRI



Motor Function – UPDRS III



Reducing excess iron associated with improved motor function

Deferiprone

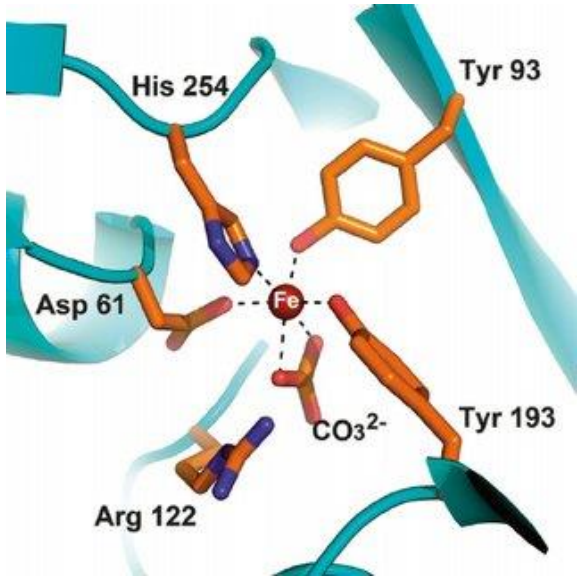
- Indicated for Treatment of Iron Overload
- Black Box for neutropenia and agranucloctyosis
- Iron Binding Affinity Kd=10^{-36}

Devos et al. Antiox. and Redox Signaling. 2014; 21: 195

PBT434 HAS OPTIMAL IRON BINDING AFFINITY FOR EFFICACY AND SAFETY

Agent/Protein	Kd for Fe^{3+}
α-Synuclein	10^{-5}
PBT434	10^{-10}
Ferritin	10^{-22}
Transferrin	10^{-23}
Deferiprone	10^{-36}

Stronger binding



Davies et al. PLoS ONE. 2011; 6; 1; e15814. doi.org/10.1371/journal.pone.0015814
Aisen P and Listowsky I. Ann Rev Biochem 1980 49: 357-393
Aisen P, Leibman A, Zweier J. J Biol Chem. 1978; 253:1930-1937
Kline MA and Orvig C. Clin Chem (1992); 38: 562-565

LINK BETWEEN IRON AND SEVERITY OF PD

The Relevance of Iron in the Pathogenesis of Parkinson's Disease

Gotz et al. Ann N.Y. Acad Sci. 2004

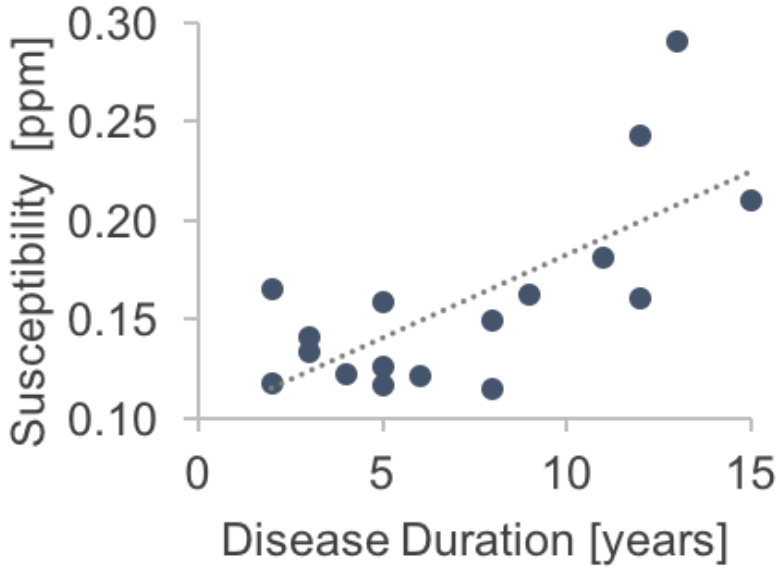
The nigral increase in iron levels identified biochemically in the postmortem brain from parkinsonian patients appears to be confirmed and is related to the severity of the disease in the living patient as assessed by magnetic resonance imaging (MRI).[53–56]

Midbrain iron content in early Parkinson disease

A potential biomarker of disease status

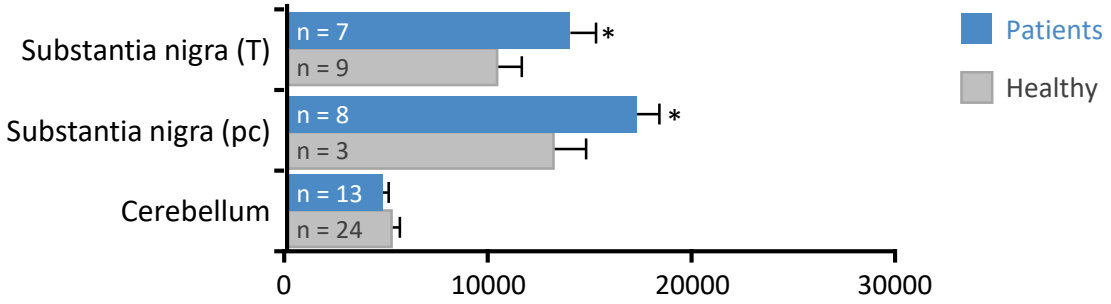
Martin, et al. Neurology 2008;70:1411–1417

Iron concentrations increase with disease severity



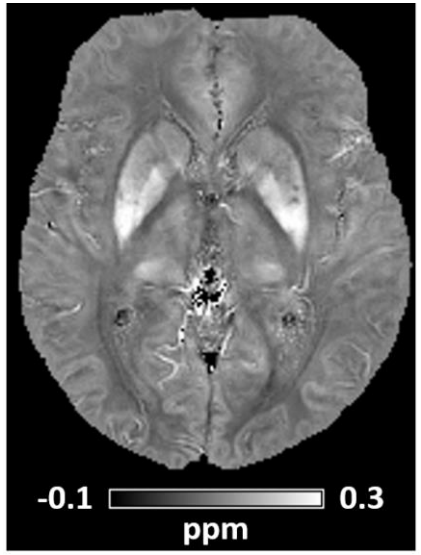
However, biochemical studies have reported increased iron content in the nigra in PD,[2-4] with the changes most marked in severe disease (PD)[5]

BRAIN IRON INCREASED IN PARKINSON'S DISEASE PATIENTS



nmol iron/g of human brain

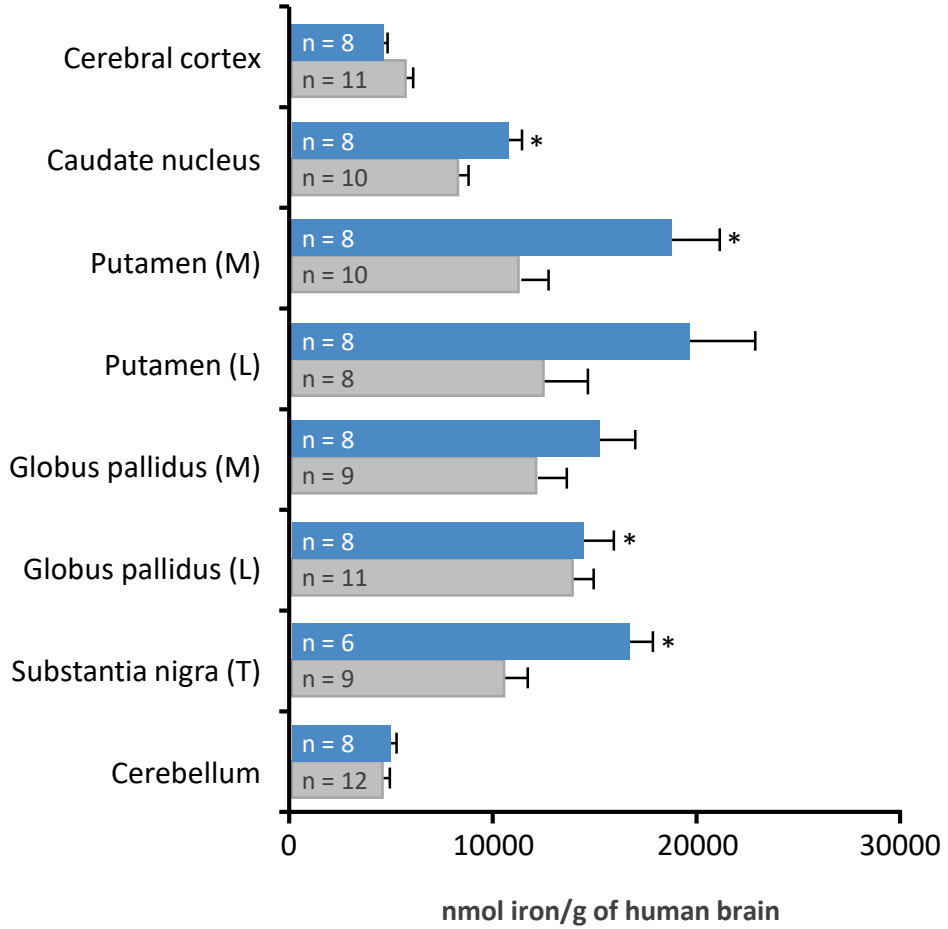
Specialized MRI Technique (QSM) to Non-invasively Quantify Brain Iron (PD Patient)



Dexter. Brain.1991;114

Langkammer. PLoS ONE 11(9): e0162460. 2016

AND IN MULTIPLE SYSTEM ATROPHY PATIENTS

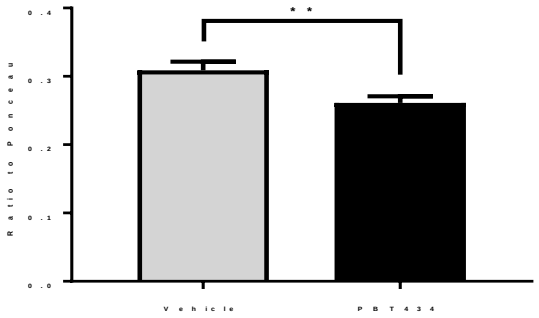


PBT434 REDUCES ALPHA-SYNUCLEIN AND LOWERS GLIAL CELL INCLUSIONS

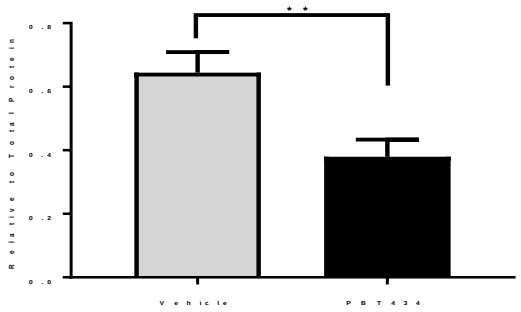
Transgenic Mouse Model (PLP)-α-SYN of MSA

↓ α-Synuclein

Oligomeric

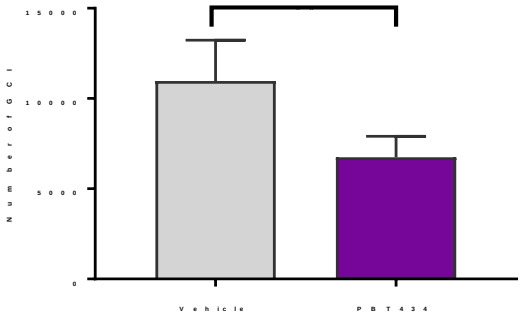


Aggregated

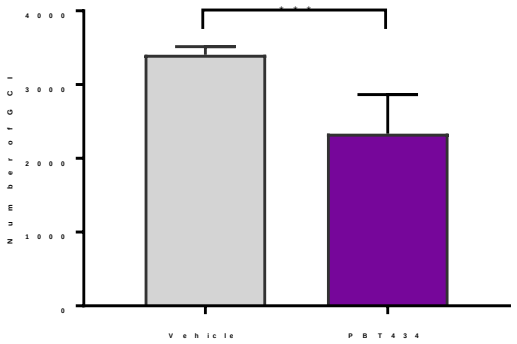


↓ Glial Cell Inclusions

Pontine Nucleus



SNpc

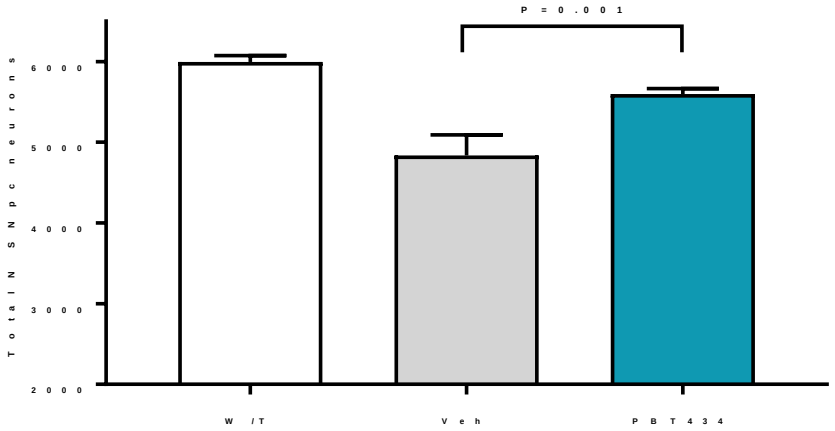


Treatment: Randomly allocated, 4 months, ~30 mg/kg/day or Vehicle (Veh)
Data presented are for animals at 16 mo age

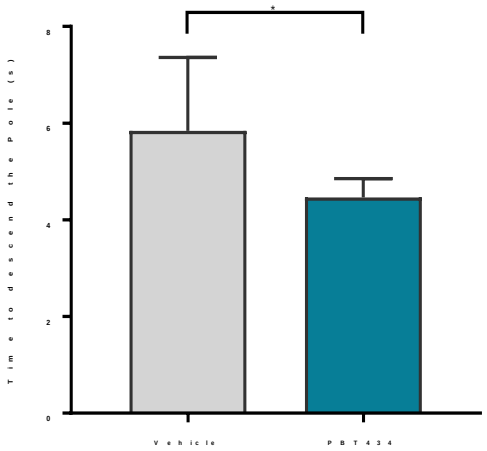
PBT434 PRESERVES NEURONS AND IMPROVES MOTOR FUNCTION

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

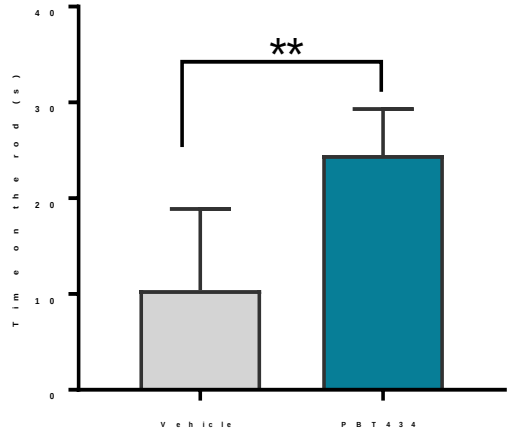
S. Nigra Neurons at 16 months



Pole Test after 4 months treatment 30 mg/kg at 16 months



Rotarod after 4 months treatment 30 mg/kg/day at 20 months

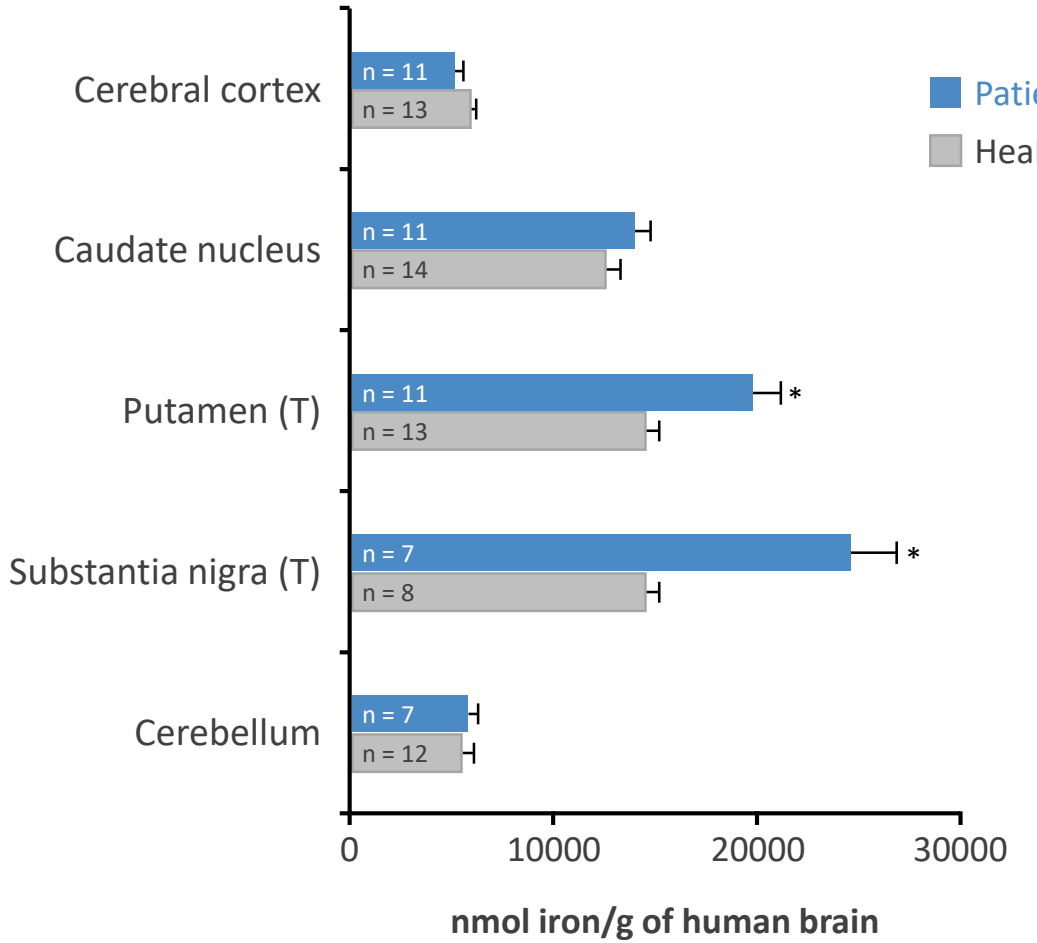


Treatment: Randomly allocated, 4 months, ~30 mg/kg/day or Vehicle

Brain Iron is also Increased in Tauopathies

PROGRESSIVE SUPRANUCLEAR PALSY (PSP)

A form of Atypical Parkinsonism



Brain Iron increased compared to Healthy controls

Dexter et al. *Brain. 1*991;114:1953.

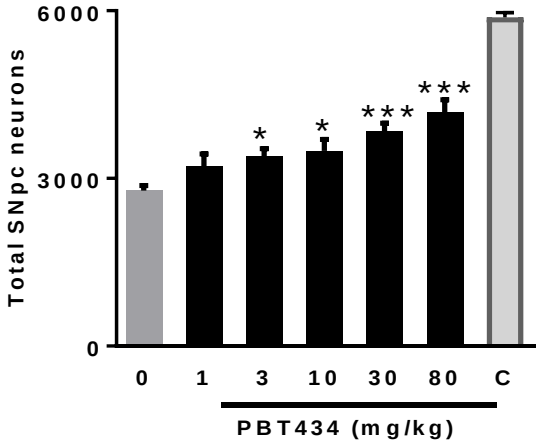
PBT434 IN AN ANIMAL MODEL OF ACUTE OXIDATIVE STRESS

MPTP mouse model

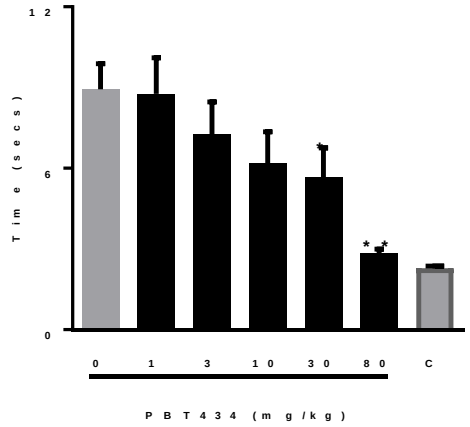
- MPTP is a potent inhibitor of complex 1 of the mitochondrial electron transport chain
- Significant neuron loss in SNpc and motor impairment

- Rapid and sustained elevation of iron in the SNpc causes acute elevation in ROS and oxidative damage
- PBT434 or vehicle treatment† started 1 day after toxin administration

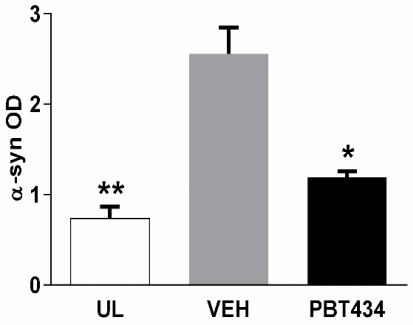
Total SNpc neurons



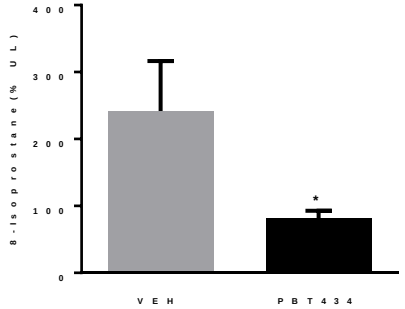
Pole test



α-Synuclein



Lipid peroxidation



For α-synuclein, lipid peroxidation: PBT434 dose 30 mg/kg/d
†Treatment randomly allocated, assessors blinded
*P<0.05, **P<0.01, ***P<0.001

PBT434 preserves neurons, improves motor function and reduces α-Synuclein accumulation and oxidative stress in the MPTP mouse

Market Opportunity and Company Information

COMMERCIAL OPPORTUNITY

SUBSTANTIAL UNMET NEED

Severely debilitating, fatal illnesses with no current treatments are ripe for new entrants targeting what may be the actual cause of the disease.

STRONG INTENT TO PRESCRIBE

Motivated by efficacy in treating the disease and not just the symptoms, clinicians intend to offer PT434 to most of their patients with MSA.

UNIQUE MOA

Inhibition of iron-mediated protein accumulation and aggregation is a novel mechanism of action that may ultimately prove in clinical practice to impact more than motor symptoms.

EASE OF USE

Given similar efficacy, clinicians will likely prefer PBT434's once or twice daily oral administration vs. the monthly IV infusions or injections required for alpha-synuclein antibodies that come to market.

*Does not include spontaneous use in PD.

CORPORATE OVERVIEW

Capital Structure

Ordinary Shares on issue	860,837,432
Share price (9/04/19)	$0.049
Market Capitalization	$AUD 42 million
Net Cash (31/12/18)	$8.4M
Additional Funds (Life Bio)	$11.4M

Board

Name	Position
Geoffrey Kempler	CEO & Chairman
Lawrence Gozlan	Non-Executive Director
Peter Marks	Non-Executive Director
Dr David Sinclair	Non-Executive Director
Tristan Edwards	Non-Executive Director
Brian Meltzer	Non-Executive Director

Management Team

Geoffrey Kempler CEO & Chairman	Founded Prana Biotechnology in 1997 , Mr Kempler has extensive experience in investment and business development and has been responsible for the implementation of Alterity's strategic plan and technology commercialisation. Mr Kempler is a qualified psychologist.
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) for treatment of Huntington disease (approved by FDA - April 2017) and tardive dyskinesia, also in 2017.
James Kerr VP, Chemistry, Manufacturing and controls	Previously CMC leadership at Auspex/Teva. Senior member of leadership team responsible for budget management 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 Non-Clinical leadership at Auspex/Teva. At Teva, led non-clinical development of several neuroscience programs. At Auspex Pharmaceuticals, led strategic planning and program management in Huntington Disease chorea from IND through NDA filing.
Kathryn Andrews CFO	Highly experienced biotechnology CFO and CPA. Joined Prana in 2014

INVESTMENT SUMMARY

- Proven track record in taking new drugs through to market. Team responsible for 3 new drugs approved by FDA
- Lead drug candidate PBT434 has the potential as a disease modifying treatment and is currently completing a phase 1 clinical trial program
- First disease target selected – MSA, a highly debilitating disease with no treatment options. Orphan Drug designation received from the US FDA.
- Well funded and backed by major life science investors

Contact

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Alterity