



## **Alterity CEO Dr David Stamler presents to US investors at the HC Wainwright Global Life Science Conference**

**MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 10<sup>th</sup> March 2021:** Alterity Therapeutics (ASX: ATH, NASDAQ: ATHE) (“Alterity” or “the Company”) CEO Dr David Stamler is presenting to US investors this week as part of the HC Wainwright Global Life Science Conference.

The conference held virtually, attracts specialist life science and healthcare investors and features leading companies from around the world.

Dr Stamler’s presentation is appended and includes:

- The progress of the company’s lead compound ATH434 for the treatment of Multiple System Atrophy (MSA);
- Expanded safety data on ATH434;
- Update on a Natural History Study in MSA at Vanderbilt University Medical Center in the US which is providing important data to inform and de-risk the phase 2 clinical study;
- The expected commercialisation pathway for ATH434 including the initiation of the Phase 2 clinical trial; and
- The underlying science.

Dr Stamler said: “Alterity has made significant progress over this last 6-12 months and we are pleased with the growing interest from investors, scientists and clinicians.”

**END**

### **Authorization & Additional information**

This announcement was authorized by David Stamler, CEO of Alterity Therapeutics Limited.

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**About Alterity Therapeutics Limited and ATH434**

Alterity's lead candidate, ATH434 (formerly PBT434), is the first of a new generation of small molecules designed to inhibit the aggregation of pathological proteins implicated in neurodegeneration. ATH434 has been shown to reduce abnormal accumulation of  $\alpha$ -synuclein and tau proteins in animal models of disease by redistributing labile iron in the brain. In this way, it has potential to treat Parkinson's disease and atypical forms of Parkinsonism such as Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP).

ATH434 has been granted Orphan designation for the treatment of MSA by the US FDA and the European Commission.

For further information please visit the Company's website at [www.alteritytherapeutics.com](http://www.alteritytherapeutics.com).

**About Multiple System Atrophy**

Multiple System Atrophy (MSA) is a rare and rapidly progressive neurological disorder affecting adults. It has no known cause. In addition to presenting with motor symptoms like those in Parkinson's disease, individuals with MSA may also experience loss of ability to coordinate voluntary movements and impaired regulation of involuntary body functions such as blood pressure, bowel and bladder control. Most of these symptoms are not addressed by available drugs for patients with Parkinson's disease. As the condition progresses, daily activities become increasingly difficult and complications such as increased difficulty swallowing, vocal cord paralysis, progressive immobility, and poor balance become more prominent. Symptoms tend to appear after age 50 and rapidly advance, leading to profound disability.

**Forward Looking Statements**

*This press release contains "forward-looking statements" within the meaning of section 27A of the Securities Act of 1933 and section 21E of the Securities Exchange Act of 1934. The Company has tried to identify such forward-looking statements by use of such words as "expects," "intends," "hopes," "anticipates," "believes," "could," "may," "evidences" and "estimates," and other similar expressions, but these words are not the exclusive means of identifying such statements.*

*Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements are described in the sections titled "Risk Factors" in the Company's filings with the SEC, including its most recent Annual Report on Form 20-F as well as reports on Form 6-K, including, but not limited to the following: statements relating to the Company's drug development program, including, but not limited to the initiation, progress and outcomes of clinical trials of the Company's drug development program, including, but not limited to, ATH434 (formerly PBT434), and any other statements that are not historical facts. Such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to the difficulties or delays in financing, development, testing, regulatory approval, production and marketing of the Company's drug components, including, but not limited to, ATH434, uncertainties relating to the impact of the novel coronavirus (COVID-19) pandemic on the company's business, operations and employees, the ability of the Company to procure additional future sources of financing, unexpected adverse side effects or inadequate therapeutic efficacy of the Company's drug compounds, including, but not limited to, ATH434, that could slow or prevent products coming to market, the uncertainty of patent protection for the Company's intellectual property or trade secrets, including, but not limited to, the intellectual property relating to ATH434.*

*Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.*



**Alterity**  
THERAPEUTICS

# Alterity Therapeutics (NASDAQ:ATHE, ASX:ATH)

David Stamler, MD  
CEO  
March 2021



## Forward Looking Statements



This presentation may contain some statements that may be considered “Forward-Looking Statements”, within the meaning of the US Securities Laws. Thus, any forward-looking statement relating to financial projections or other statements relating to the Company’s plans, objectives, expectations or intentions involve risks and uncertainties that may cause actual results to differ materially. For a discussion of such risks and uncertainties as they relate to us, please refer to our 2020 Form 20-F, filed with US Securities and Exchange Commission, in particular Item 3, Section D, titled “Risk Factors.”

## Our Purpose



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 diseases.

## H1 Progress and Financials

- Cash balance of \$35M
- Cash burn in line with expectations of \$7.3M
- Significant progress:
  - bioMUSE Natural History study for MSA patients progressing well
  - New patent to support new compound development across neurodegenerative diseases
  - Michael J Fox grant of US\$500K to explore Parkinson's disease
  - New opportunities for our legacy product PBT2 to address antibiotic resistant superbugs

# Review of Progress



Cardiovascular data which strengthens the safety profile of ATH434



Commence enrolling Multiple System Atrophy patients in bioMUSE Study



Michael J. Fox Foundation grant for ~US\$500K for Parkinson's disease



ATH434 reduces  $\alpha$ -synuclein pathology, preserves neurons, and improves motor performance



Potential application of PBT2 for antibiotic resistance in superbugs



US FDA provides development pathway for ATH434



Allowance of US patent for next generation compounds for neurodegenerative diseases



ATH434 crosses blood brain barrier in humans; clinically tested doses achieved concentrations in the brain



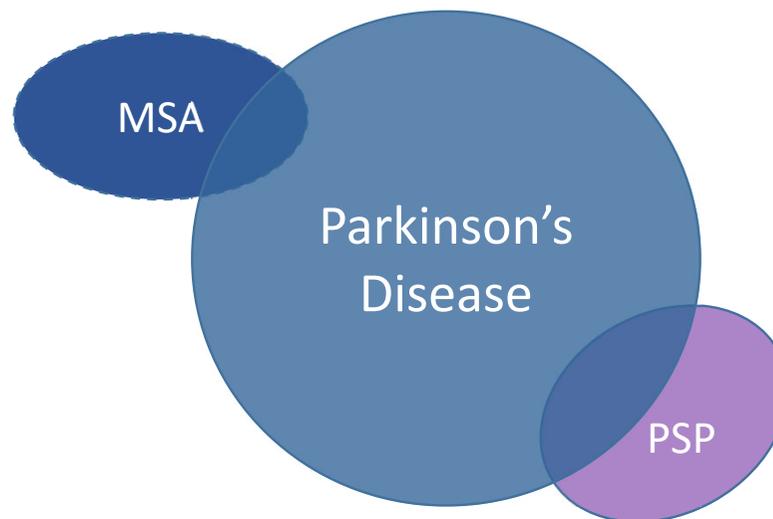
\$35M Placement to international and Australian institutions and sophisticated investors

# Parkinsonian Disorders – A Significant Unmet Need



Lees et al. Lancet 2009

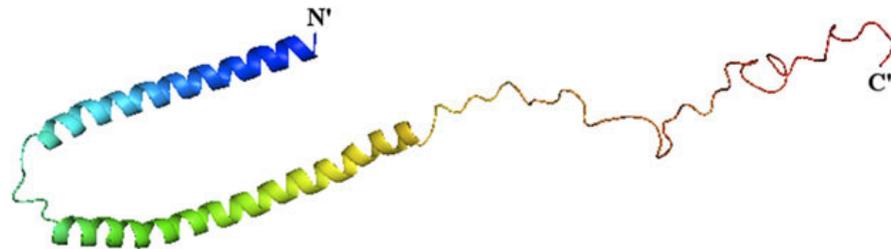
- Parkinsonism is a syndrome of motor symptoms that includes slowness of movement, stiffness and tremor
  - Major source of disability



- Parkinsonian disorders also include atypical variants such as Multiple system atrophy (MSA) and Progressive supranuclear palsy (PSP)
  - Atypical forms have prominent non-motor symptoms and a limited response to available treatments
  - Lead indication is MSA, a highly debilitating disease with no approved treatments

# Our Target is Alpha-Synuclein

## A Major Focus of Treating Parkinsonian Disorders



Structure of  $\alpha$ -synuclein

- $\alpha$ -synuclein is an intracellular protein, abundantly expressed in nerve terminals
- Critical for normal function of neurons
- Native, unfolded protein enables neurotransmission
- $\alpha$ -Synuclein *aggregates* in certain Parkinsonian conditions such as PD and MSA

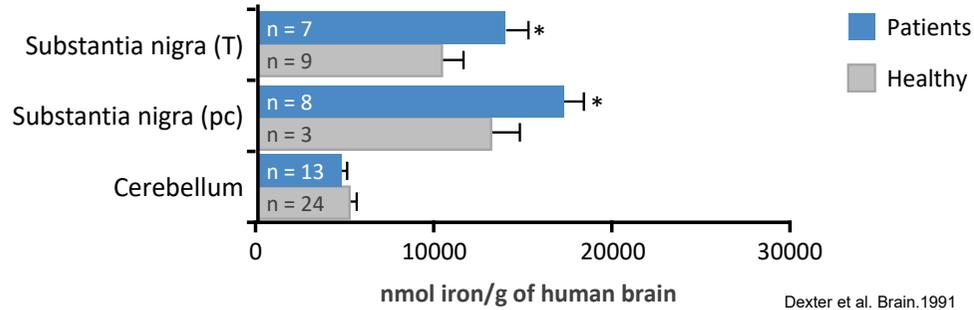


*"We conclude that alpha-synuclein remains one of the most compelling therapeutic targets for Parkinson's disease and related synucleinopathies, and that the multitude of approaches being tested provides hope for the future."*

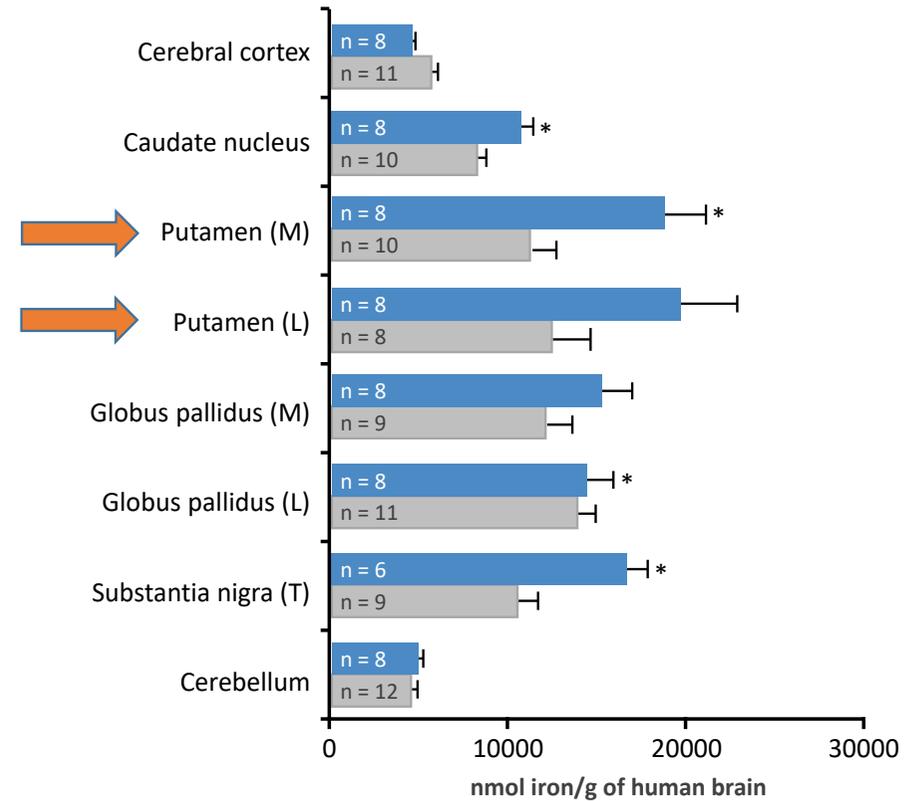
Exp. Neurol. 298,225-235, 2017.

# Increased Brain Iron in Synuclein-related Diseases

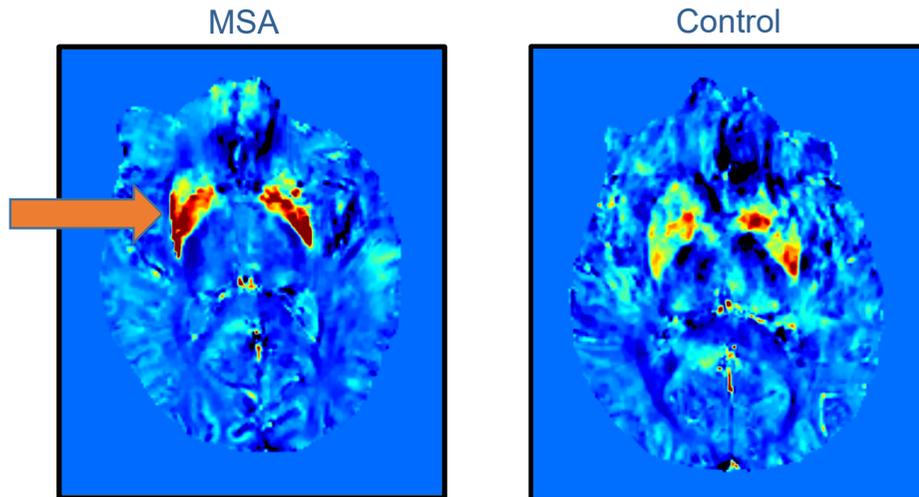
## Parkinson's disease



## Multiple System Atrophy



## Quantitative Susceptibility Mapping (MRI) to assess brain iron



Courtesy of P. Trujillo, D. Claassen

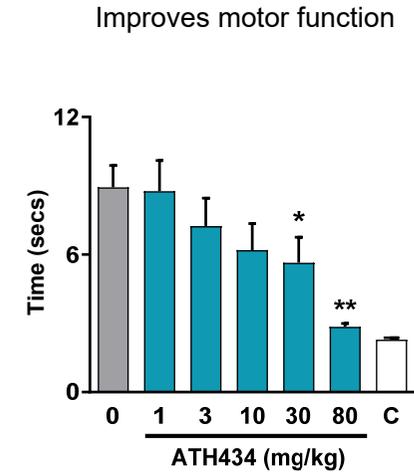
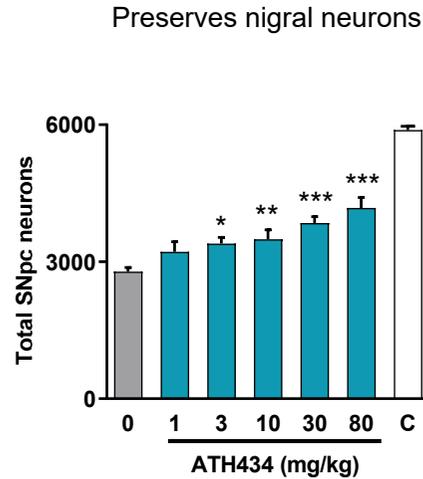
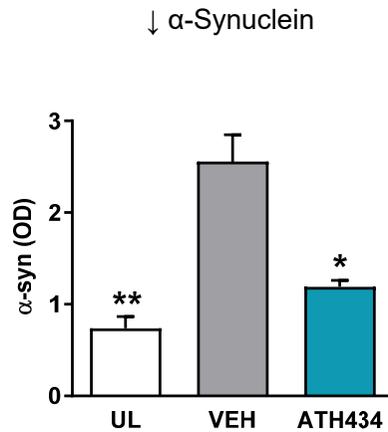
**ATH434 inhibits  $\alpha$ -synuclein pathology  
by redistributing brain iron**

# ATH434 Reduces Alpha-Synuclein-related Neuropathology

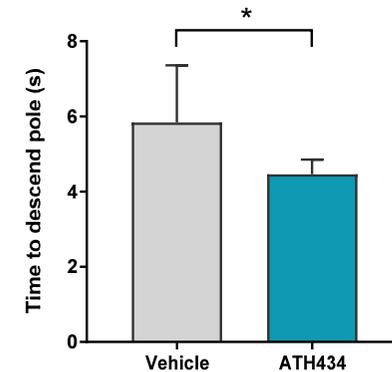
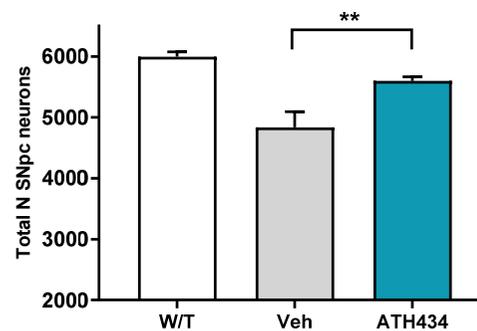
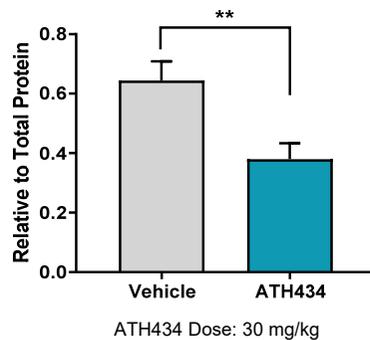
## Preserves Neurons and Improves Function in Parkinson's and MSA Animal Models



**Parkinson's disease model**



**MSA model**



Finkelstein, et al. Acta Neuropath Comm. 2017  
Finkelstein et al. Mov. Disorders. 2018

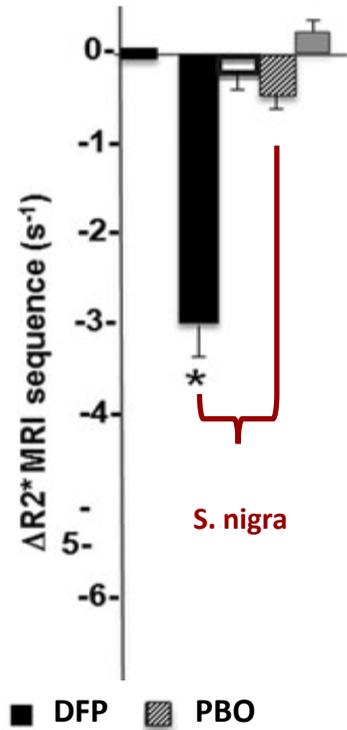
\* P < 0.05, \*\* P < 0.01, \*\*\* P < 0.001  
W/T: wild type, UL: unlesioned, C: control

# Strategy Supported by Proof of Concept in Parkinson's

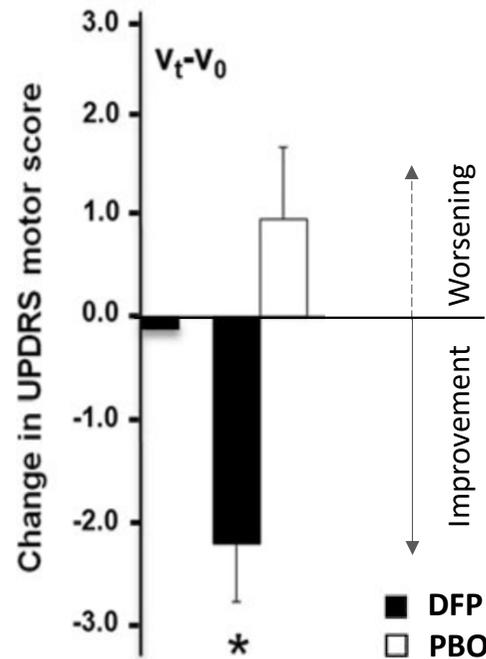
6 month placebo-controlled data from study of Deferiprone – a drug for treating iron overload



Brain Iron by MRI



Motor Symptom Severity



Reducing excess iron led to improved motor function

## Deferiprone

- Binds iron with very high affinity
- Boxed Warning for hematological toxicity

Ligand	K <sub>d</sub> for Fe <sup>3+</sup>
α-Synuclein	10 <sup>-5</sup>
ATH434	10 <sup>-10</sup>
Ferritin	10 <sup>-22</sup>
Transferrin	10 <sup>-23</sup>
Deferiprone	10 <sup>-36</sup>

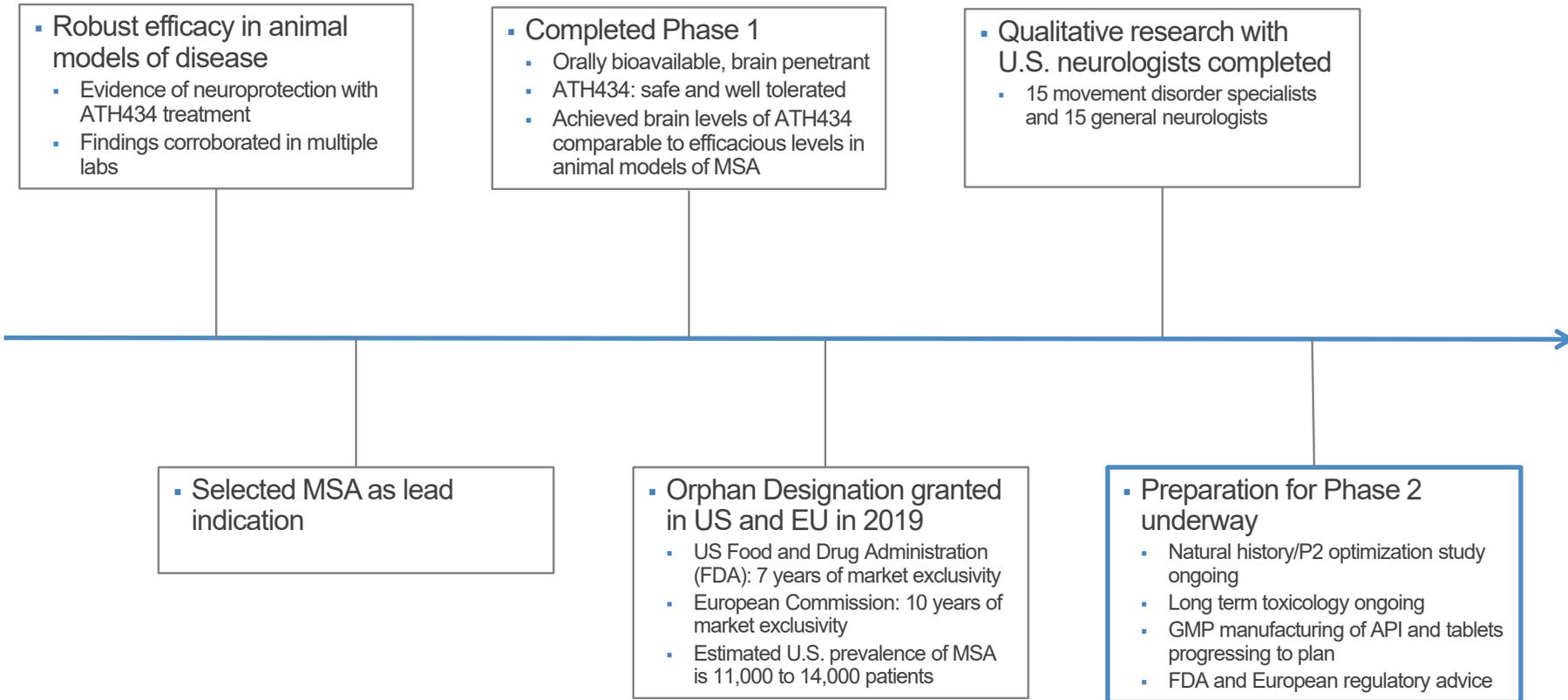
↓ Stronger binding

FERRIPROX® (deferiprone) tablets, for oral use  
Initial U.S. Approval: 2011

**WARNING: AGRANULOCYTOSIS/NEUTROPENIA**  
See full prescribing information for complete boxed warning.

- Ferriprox can cause agranulocytosis that can lead to serious infections and death. Neutropenia may precede the development of agranulocytosis. (5.1)
- Measure the absolute neutrophil count (ANC) before starting Ferriprox and monitor the ANC weekly on therapy. (5.1)
- Interrupt Ferriprox if infection develops and monitor the ANC more frequently. (5.1)
- Advise patients taking Ferriprox to report immediately any symptoms indicative of infection. (5.1)

# Excellent Progress with Lead Drug Candidate ATH434



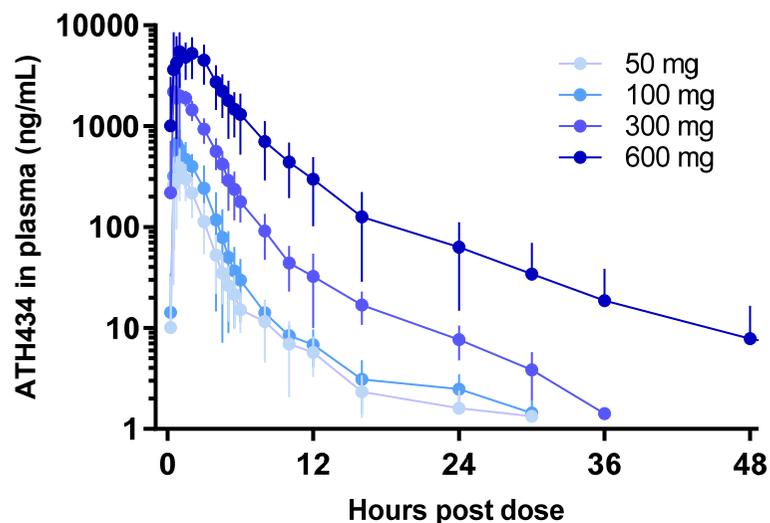
# Clinical Development

# Phase 1 Completed

## Clinical Pharmacokinetics of ATH434

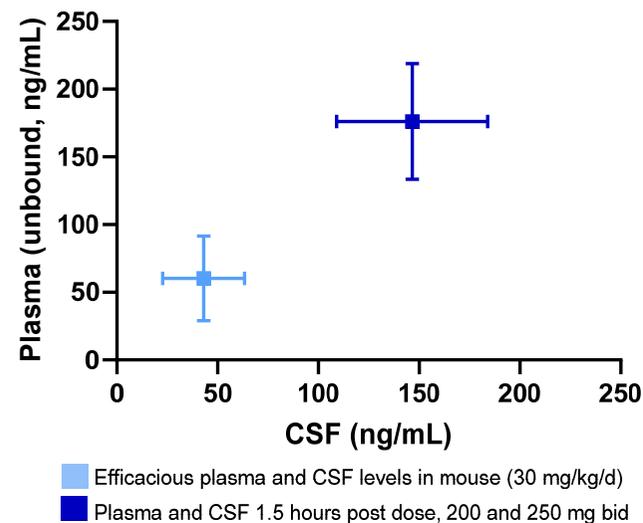


Plasma Profile after Single Dose Administration



- Rapid absorption after oral administration
- Dose dependent PK after single doses up to 600 mg and multiple doses up to 250 mg bid
- Mean elimination half-life up to 9.3 hrs

CSF and Plasma Concentrations 1-2 hrs after dosing



- CSF concentrations at well-tolerated doses exceeded those associated with efficacy in animal models of PD and MSA

## Adverse Event Summary

<i>Single Ascending Doses</i>	Placebo (N=8)	50 mg (N=6)	100 mg (N=6)	300 mg (N=6)	600 mg (N=6)
Patients with ≥ 1 AE	3 (38%)	0	0	1 (17%)	1 (17%)
Patients with AEs leading to Withdrawal	0	0	0	0	0
Patients with Serious AEs	0	0	0	0	0

<i>Multiple Ascending Doses</i>	Placebo (N=8)	100 mg BID (N=8)	200 mg BID (N=8)	250 mg BID (N=8)	250 mg BID ≥65 (N=8)
Patients with ≥ 1 AE	5 (63%)	3 (38%)	6 (75%)	4 (50%)	5 (63%)
Patients with AEs leading to Withdrawal	0	0	0	0	0
Patients with Serious AEs	0	0	0	0	0

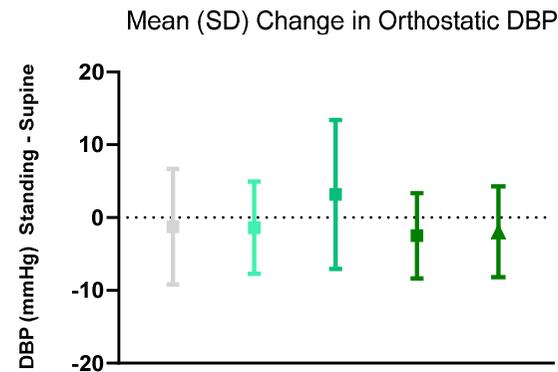
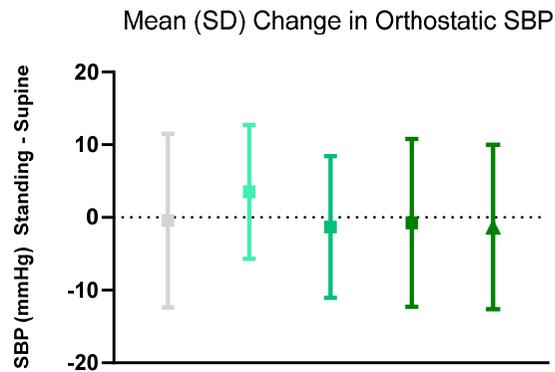
ATH434 was well tolerated with similar rates of AEs compared to placebo  
 No serious AEs or AEs leading to withdrawal

# Cardiovascular Data from 7<sup>th</sup> International MSA Conference

ATH434 had no significant effect on Blood pressure or QT interval

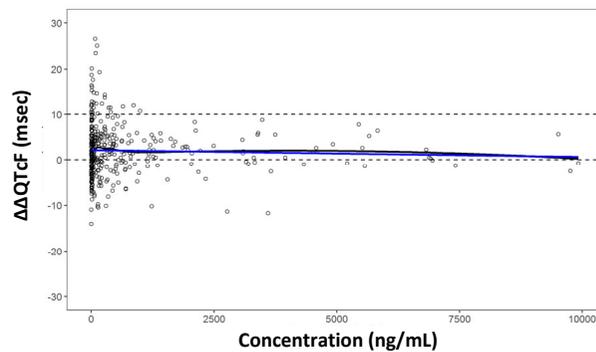


Steady state  
(2 hr post-dose)



- Placebo
- 100 mg bid
- 200 mg bid
- 250 mg bid
- 250 mg bid >65

$\Delta\Delta\text{QTcF}$  vs.  
ATH434 plasma  
concentration



Baseline-adjusted, placebo-corrected change in QTcF  
( $\Delta\Delta\text{QTcF}$ ) = 1.68 ms (90% CI: 0.386 to 3.75 ms),  
well below the threshold of regulatory concern

## Excellent Safety Profile

- No clinically significant AEs
- Similar AE profile for adults and older adults ( $\geq 65$  years)
- All AEs with ATH434 were mild to moderate in severity
- Most common AEs reported in ATH434 subjects was headache
- No significant findings observed in vital signs, clinical laboratory parameters or 12-lead ECGs
- No evidence of QT prolongation at projected clinical doses

## bioMUSE Natural History Study



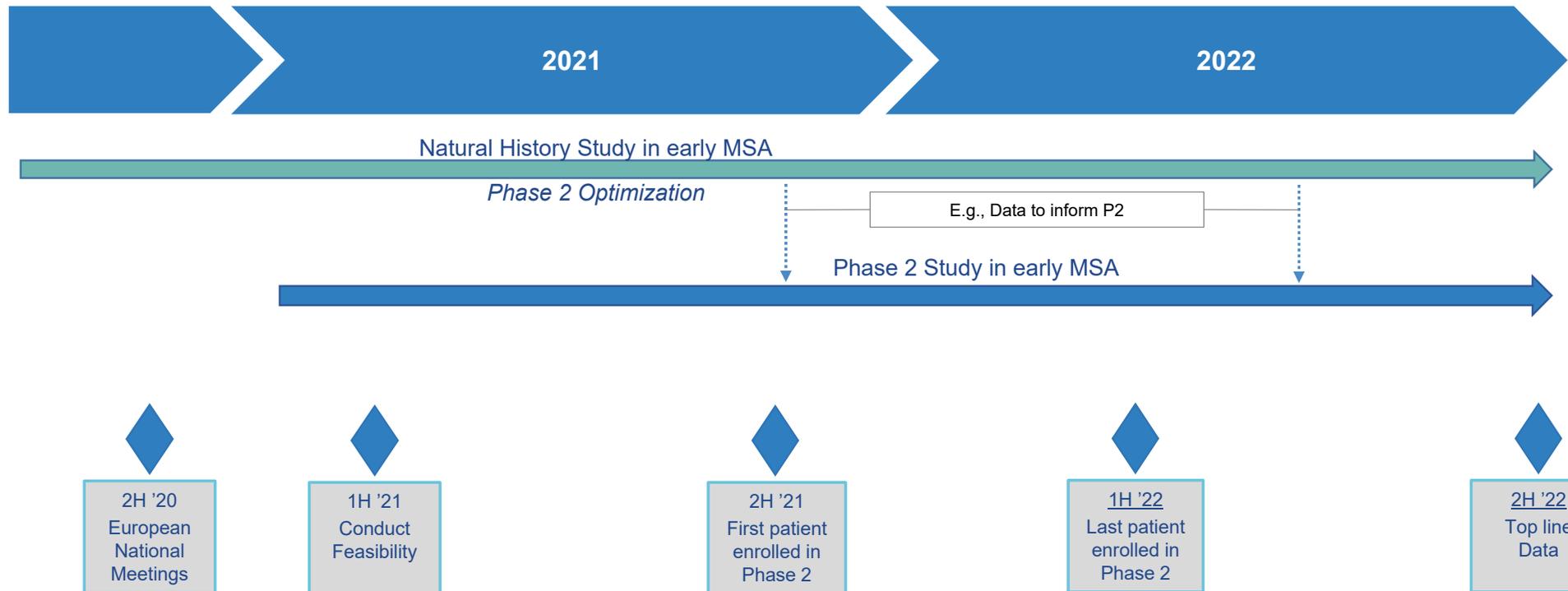
- Design: Observational (no treatment)
- Objective: De-risk Phase 2 study
  - Identify biomarker(s) suitable for endpoint in treatment study
  - Evaluate the change in biomarkers and clinical manifestations in patients with early MSA to track disease progression
- Population: Early MSA patients similar to Phase 2 population
- Observation period: 12 months
- No. participants: 10-20
- Biomarkers
  - MRI: Iron content, neuromelanin, oxidative stress, regional blood flow/metabolism
  - Protein: neurofilament light protein (CSF, plasma), Aggregating  $\alpha$ -synuclein (CSF), phos- $\alpha$ -synuclein (skin)
  - Wearable movement sensors
- Clinical Endpoints
  - Clinical: Motor exam, function/ADL inventory, global assessments of severity and change (clinician, patient)
  - Functional: Timed Up and Go, 2 min Walk Test

## Phase 2 Study Design

- Design: Randomized, double-blind, placebo controlled
- Objectives
  - Assess target engagement and preliminary efficacy of ATH434
  - Evaluate safety and tolerability of ATH434
- Population: Early MSA patients with motor symptoms  $\leq$  3 years
- Sample size: 60
- Treatment: 6 months duration
  - ATH434 high dose
  - ATH434 low dose
  - Placebo
- Biomarkers
  - MRI: Iron content, neuromelanin, oxidative stress, regional blood flow/metabolism
  - Protein: neurofilament light protein (CSF, plasma), Aggregating  $\alpha$ -synuclein (CSF), phos- $\alpha$ -synuclein (skin)
  - Wearable movement sensors
- Clinical Endpoints
  - Clinical: Motor exam, function/ADL inventory, global assessments of severity and change (clinician, patient)
  - Functional: Timed Up and Go, 2 min Walk Test
- Safety Endpoints: AEs, clinical laboratory parameters, 12-lead ECGs

# Clinical Development Timeline

ATH434 in Multiple System Atrophy



Commercial

# Commercial Opportunity – Multiple System Atrophy *Independent Analysis*

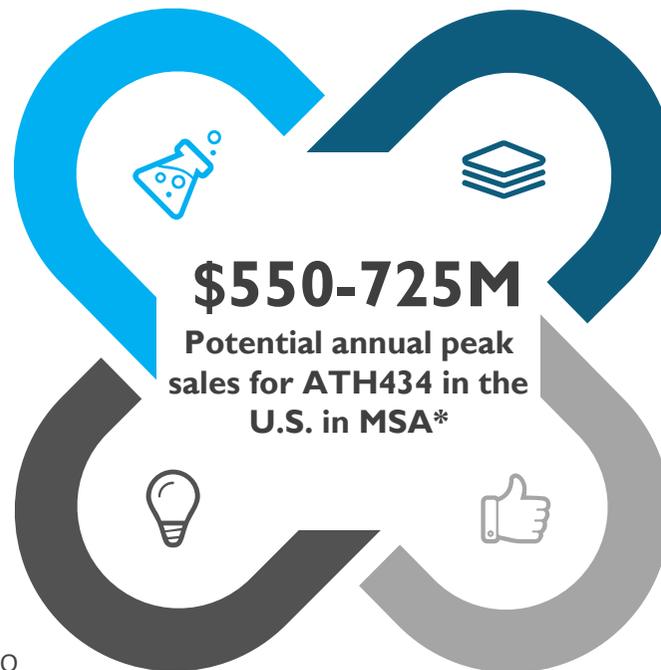


## SUBSTANTIAL UNMET NEED

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

## UNIQUE MOA

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



## STRONG INTENT TO PRESCRIBE

Motivated by efficacy in treating the underlying disease and not just the symptoms, clinicians intend to offer ATH434 to most of their patients with MSA.

## EASE OF USE

Given similar efficacy, clinicians will likely prefer ATH434'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

# Deal Landscape



Target / Therapeutic area	Neuro including AD, PD	AD & PD	AD	Neuro including AD, PD	PD
Development phase	Preclinical	Phase 1	Phase 1	Preclinical	Preclinical
Royalties (% on net sales)	High-single to low double-digit	Sub-teens to High single-digit	Undisclosed	Undisclosed	Double-digit
Upfront & equity	\$125m payment + \$225m in equity purchase	\$75m	\$205m payment + \$20m in equity purchase	\$150m	\$45m
Milestones	Up to \$2.37b \$925m pre-commercial, \$1.445b for sales thresholds	Up to \$635m Development, commercial	Up to \$986m	Up to \$90m	Up to \$600m Development, commercial

# Investment Summary



- ✓ Targeting Orphan disease with no approved treatments
  - ATH434 has potential U.S. peak sales up to US\$ 725 million
- ✓ Development team with proven track record at FDA
- ✓ Lead drug candidate ATH434
  - Completed Phase 1 with excellent safety profile
  - Achieved CSF concentrations associated with robust efficacy in MSA animal model
  - Novel mechanism targets  $\alpha$ -synuclein aggregation and root cause of oxidative stress
- ✓ Phase 2 program
  - Commenced Natural History study to de-risk P2 study
  - Topline data 2H '22
- ✓ Strong pipeline potential with new patent family supporting next generation therapies
- ✓ Opportunities to extract value from legacy PBT2 program with new indications
- ✓ Strong balance sheet



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