Alterity Therapeutics

(NASDAQ:ATHE, ASX:ATH)

David Stamler, MD
CEO

EGM – 29 December 2023

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 2023 Form 20-F, filed with US Securities and Exchange Commission, in particular Item 3, Section D, titled “Risk Factors.’’

Overview of Today's Presentation

- New Primate data with ATH434
- Update on our clinical programs
- Looking forward to 2024

Parkinsonian Disorders: A Significant Unmet Need

- Parkinsonism is a syndrome of motor symptoms that includes slowed movement, stiffness and tremor
  - Parkinson's disease most common cause
  - Major source of disability

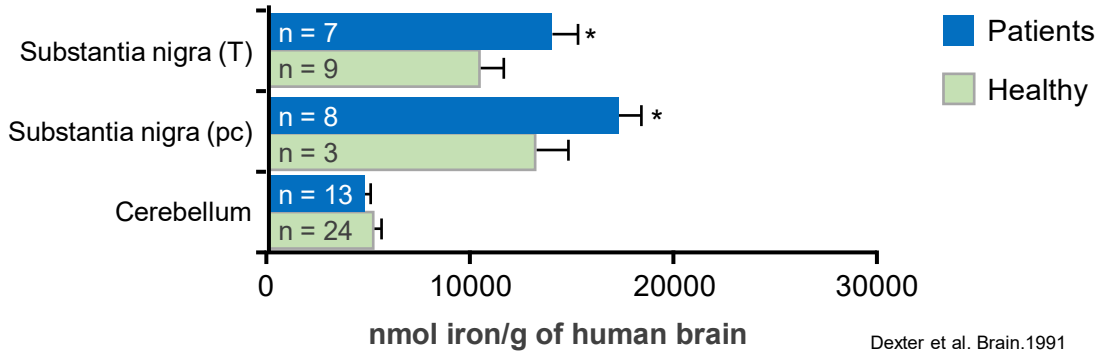
Parkinsonian Disorders: A Significant Unmet Need

- Parkinsonism is a syndrome of motor symptoms that includes slowed movement, stiffness and tremor
  - Parkinson's disease most common cause
  - Major source of disability
- Parkinsonian disorders include Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP)
  - MSA is a rare disease without approved therapy
  - Orphan Drug designation in US and EU

Parkinson's disease and MSA have similar underlying pathology

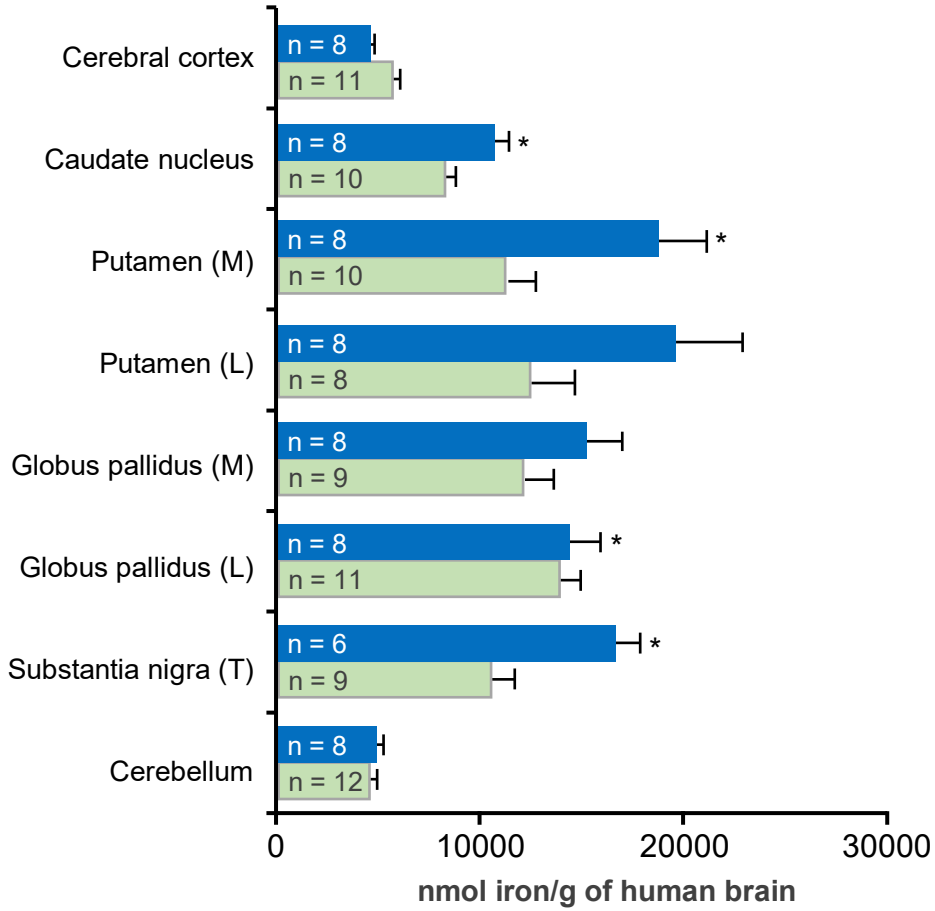
Increased Brain Iron in Parkinson's Disease and Related Disorders

Parkinson's disease



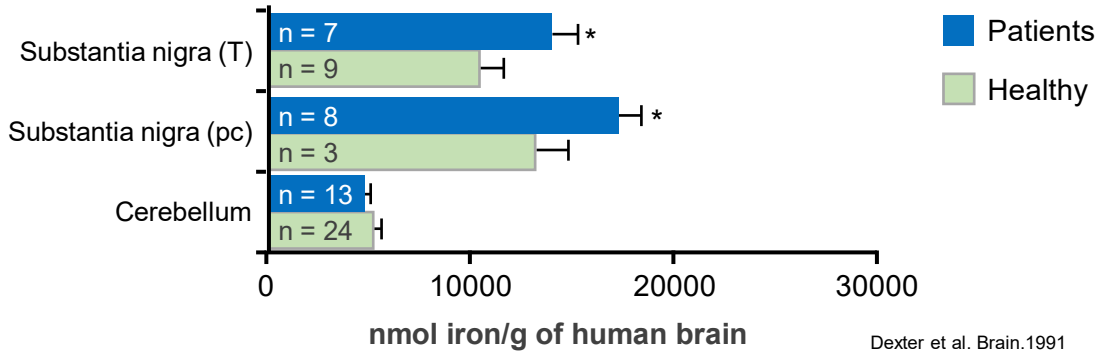
Dexter et al. Brain.1991

Multiple System Atrophy



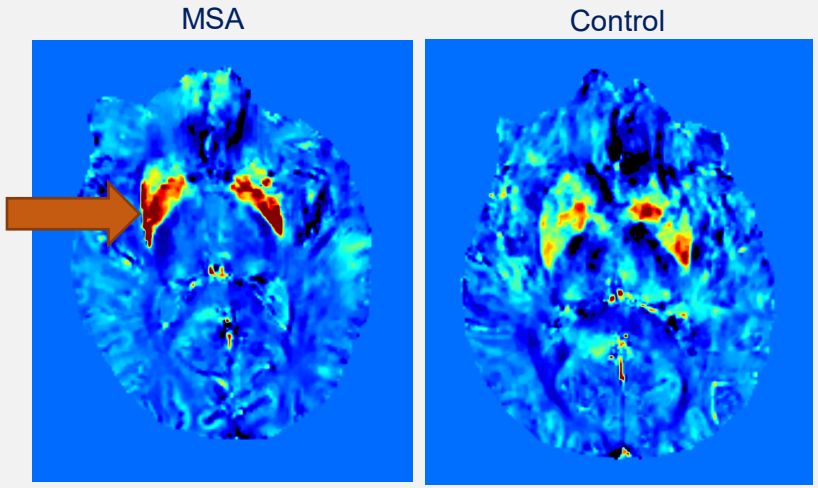
Increased Brain Iron in Parkinson's Disease and Related Disorders

Parkinson's disease



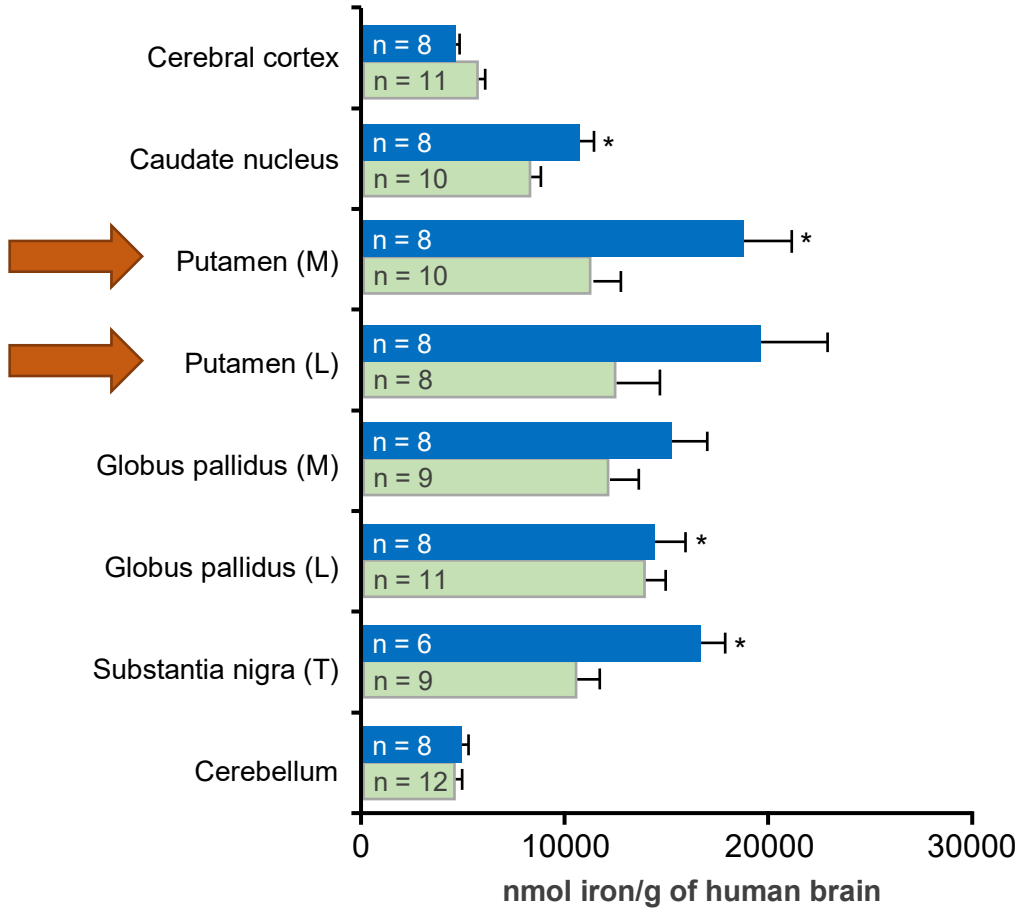
Dexter et al. Brain.1991

Advanced Quantitative MRI to measure brain iron

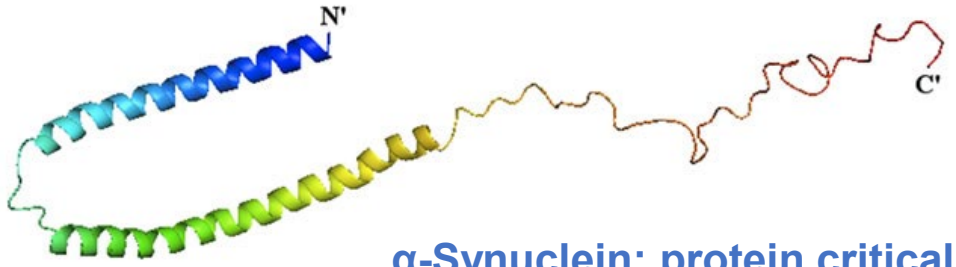


Courtesy of P. Trujillo, D. Claassen

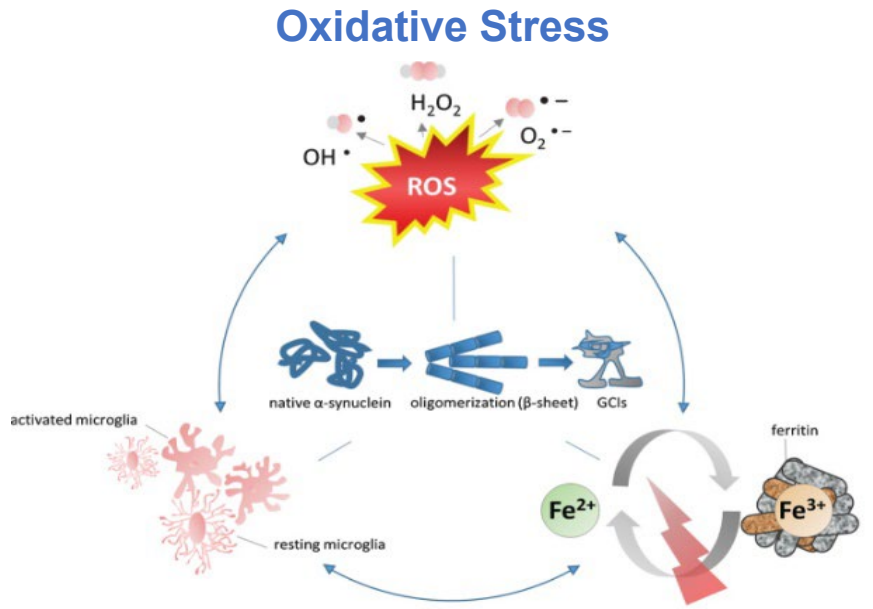
Multiple System Atrophy



Excess Iron and Alpha-Synuclein are Strong Contributors to Disease Pathology



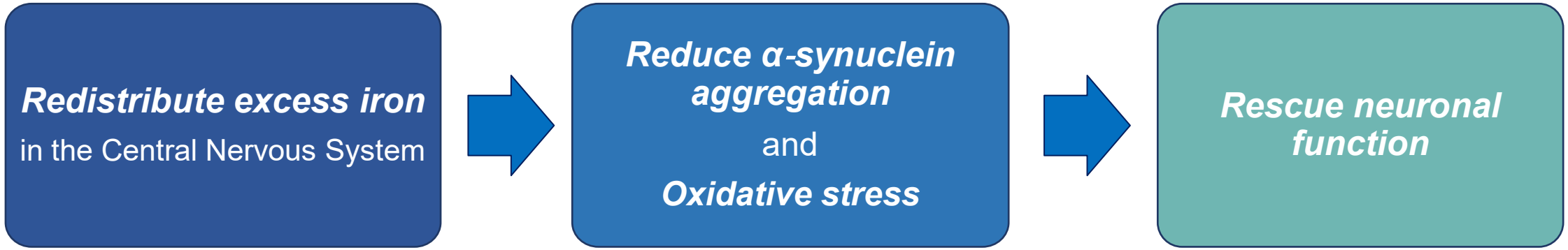
α-Synuclein: protein critical for normal function of neurons



- Adverse impact of excess iron
  - Promotes α-synuclein aggregation/clumping
  - Root cause of oxidative stress which damages intracellular structures and leads to neuroinflammation

Sources: Kaindlstorfer, J. Alzheimers Dis. 2018; Rodgers, J Neural Transm (Vienna). 2011

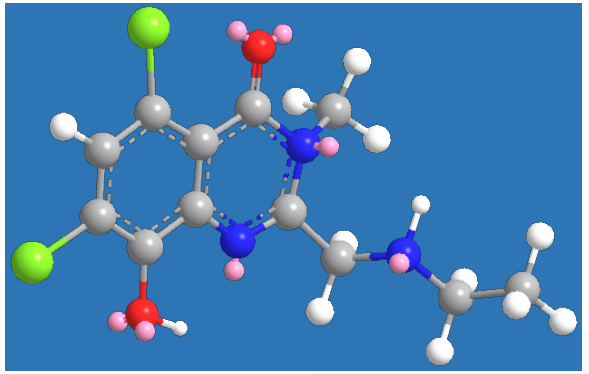
Approach: Address Underlying Pathology of Disease



Potential Disease Modifying Therapy

ATH434: Disease Modifying Drug Candidate

- ATH434 redistributes excess iron and reduces α-synuclein clumping in brain
  - Oral agent (tablet) for ease of use
  - Readily absorbed, shown to reach site of action in man
- Potential to treat various Parkinsonian disorders
- Orphan Drug Designation in the US and EU for treatment of MSA
- Development pathway endorsed by FDA and EMA

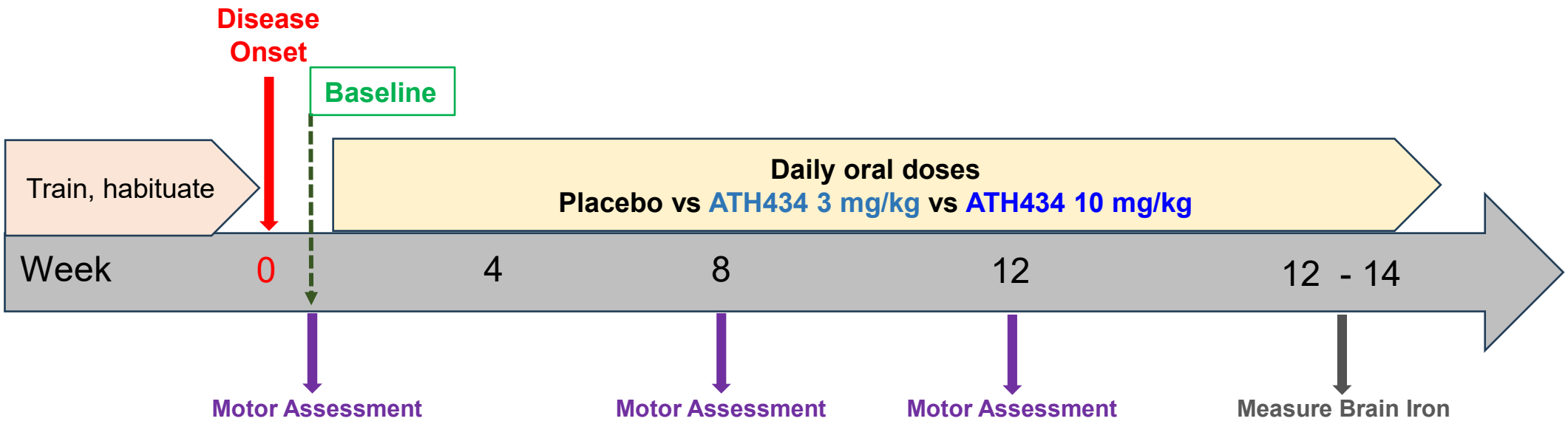


ATH434

Primate Study Validates ATH434 Clinical Approach
Promising New Data

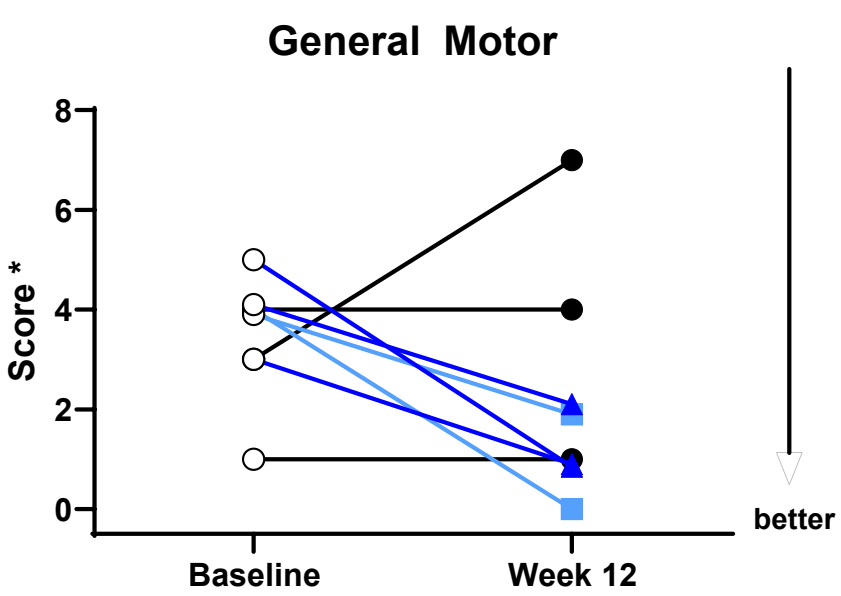
- Well established model of Parkinson's, primate closer to humans
- ATH434 treatment **improved motor skills and general behavior** in monkeys with experimentally induced Parkinson's disease
- Favorable impact on Parkinson's symptoms in animals with lower brain iron *in the area of pathology*
- ATH434 treatment increased levels of synaptophysin, a protein marker that reflects functional connections between neurons
- Increases our confidence level in ongoing Phase 2 trials

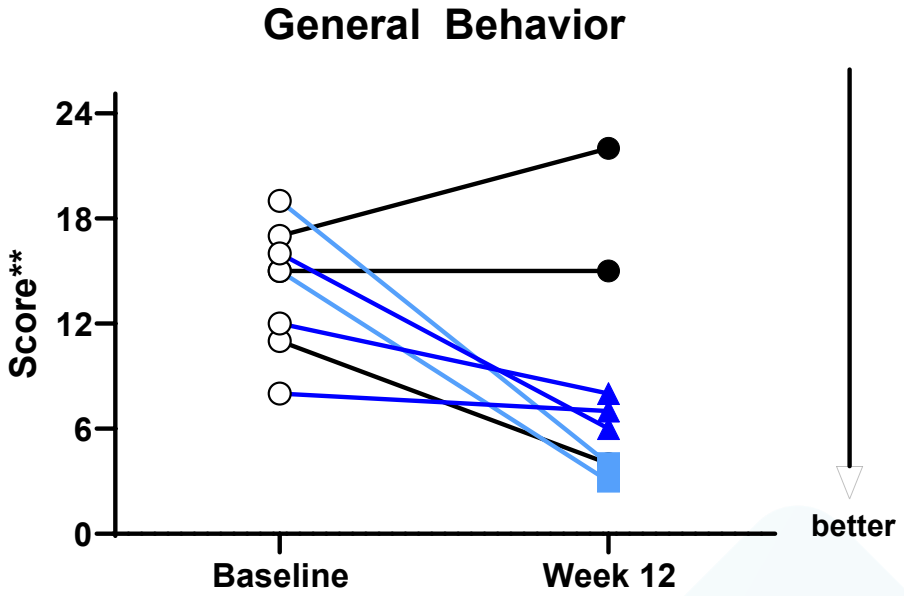
Monkey Parkinson's Disease Study



Source: Bradbury, et al, "Effects of ATH434, a Clinical-Phase Small Molecule with Moderate Affinity for Iron, in Hemiparkinsonian Macaques", Future of Parkinsons Disease, 2023

ATH434 Improved Motor and Behavior Scores
Improvement Associated with Reduced Iron



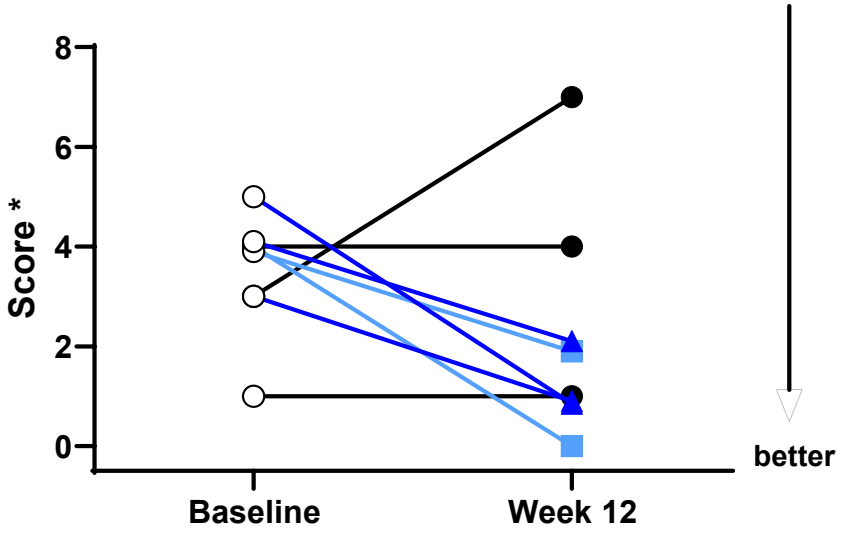


* Fine motor skills, eating, eyeblink

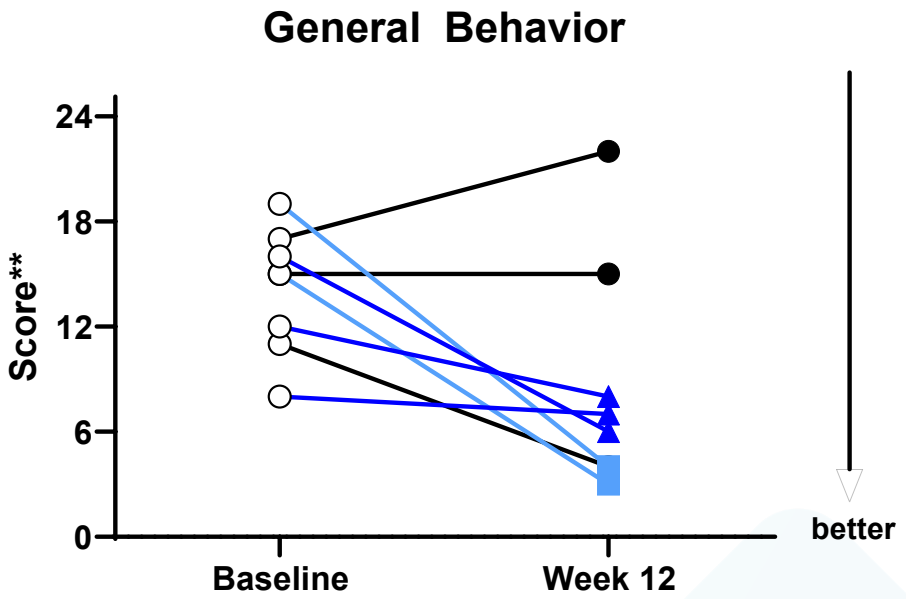
Placebo (veh)
3 mg/kg
10 mg/kg

** Appetite, response to food, activity, appearance, posture, balance, climbing, tremor, freezing, facial expression, defensive reactions

ATH434 Improved Motor and Behavior Scores
Improvement Associated with Reduced Iron



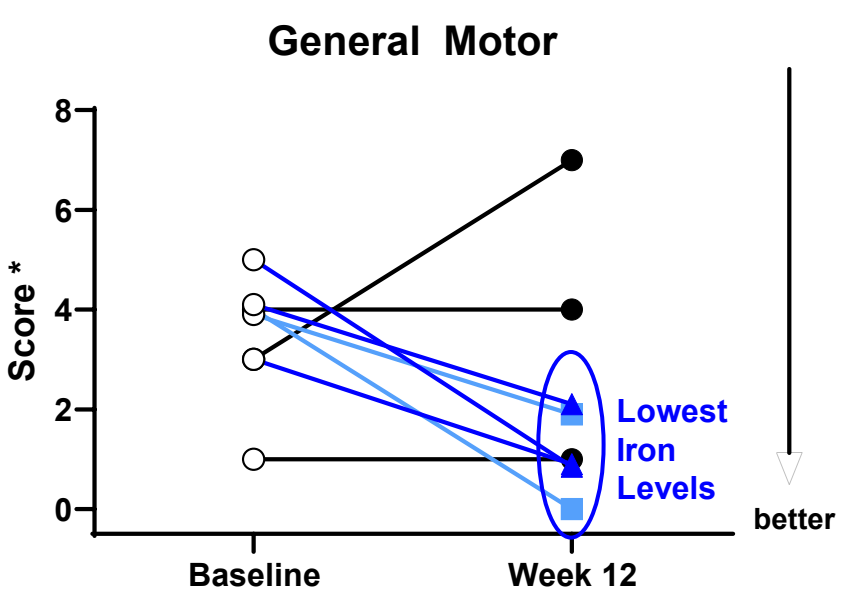
* Fine motor skills, eating, eyeblink



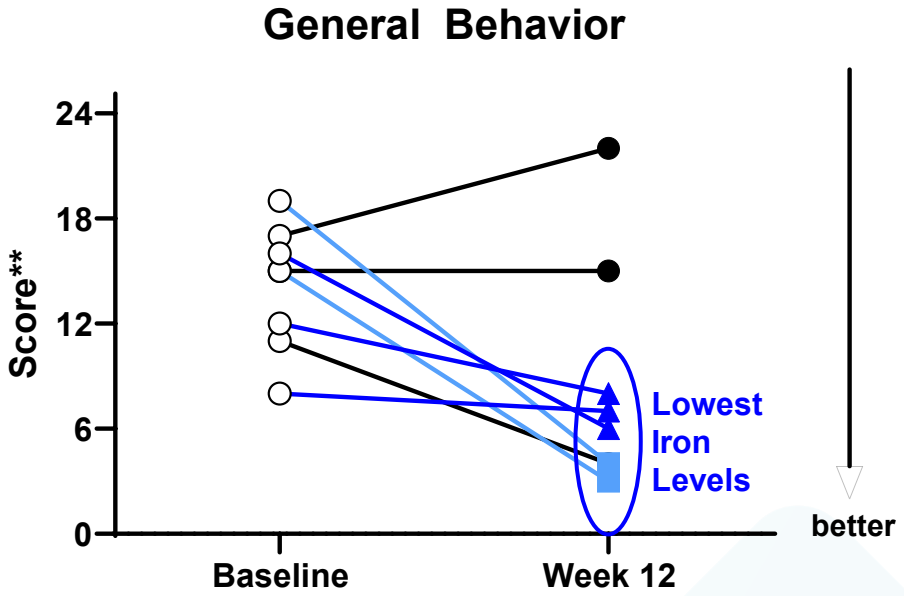
Placebo (veh)
3 mg/kg
10 mg/kg

** Appetite, response to food, activity, appearance, posture, balance, climbing, tremor, freezing, facial expression, defensive reactions

ATH434 Improved Motor and Behavior Scores
Improvement Associated with Reduced Iron



* Fine motor skills, eating, eyeblink



Placebo (veh)
3 mg/kg
10 mg/kg

** Appetite, response to food, activity, appearance, posture, balance, climbing, tremor, freezing, facial expression, defensive reactions

All ATH434 treated monkeys had improved Motor and Behavior scores and Lowest Iron Levels

Accumulated Data Supports ATH434 Efficacy

Target Disease	Model	Brain Iron	α-Synuclein	Neurons/ Connectivity	Clinical Observations	Author
Parkinson's disease	Mouse MPTP	↓	↓	↑	Improved motor performance	Finkelstein
Parkinson's disease	Mouse A53T	↓	↓	↑	Improved motor performance	Finkelstein
Parkinson's disease	Mouse tau knockout	↓	↓	↑	Improved motor performance	Beauchamp
MSA	PLP-α-syn	↓	↓	↑	Improved motor performance	Heras-Garvin
MSA	PLP-α-syn	↓	↓	↑	Improved motor performance	Finkelstein
Parkinson's disease	**Monkey MPTP**	**↓**	**n/a**	**↑**	**Improved motor performance**	**Bradbury**

ATH434 consistently **improved motor performance** across diverse animal models of disease with reduced brain iron and α-synuclein

Source: Finkelstein, Acta Neuropath Comm 2017; Beauchamp et al, Neurotherapeutics 2022; Heras-Garvin et al, Mov Disord. 2021; Finkelstein et al, J Park Dis 2022; Bradbury et al, Future of PD, 2023

Clinical Development Progress in Multiple System Atrophy

Promising Portfolio in Neurodegenerative Diseases

Alterity THERAPEUTICS

ASSET		PHASE					PARTNER
PROGRAM	**INDICATION**	**DISCOVERY**	**PRE-CLINICAL**	**NATURAL HISTORY**	**PHASE 1**	**PHASE 2**	**PARTNER / COLLABORATOR**
ATH434-201	Multiple System Atrophy *Early Stage*				*Enrollment Complete*		
ATH434-202	Multiple System Atrophy *Advanced*						
bioMUSE	Multiple System Atrophy *Natural History Study*						VANDERBILT UNIVERSITY MEDICAL CENTER
ATH434	Parkinson's Disease						THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH
Drug Discovery	Neurodegenerative Diseases						

Clinical Development in MSA

Study	ATH434-201 – Phase 2	ATH434-202 – Phase 2	bioMUSE – Natural History
Design	Randomized, double-blind, placebo controlled	Single arm, open-label	Observational
Objectives	Efficacy and safety of ATH434 Assess target engagement with biomarkers	Efficacy and safety of ATH434 Assess target engagement with biomarkers	Design and de-risk Phase 2 Identify biomarker endpoints for treatment study
Population	Early-stage MSA	Advanced MSA	Early-stage MSA (~ATH434-201 population)
Sample Size	N=77; 23 global sites	N=15	~20 participants
Treatment	12 months: 2 dose levels of ATH434 or placebo	12 months	—
Primary Endpoint	Change in iron content as measured by brain MRI	Change in iron content as measured by brain MRI	Evaluate Clinical (motor, autonomic) and Functional (walk)
Secondary Endpoints	Clinical (daily living, motor, autonomic); Wearable Sensors, Biomarkers	Clinical (daily living, motor, autonomic); Wearable Sensors, Biomarkers	Evaluate Imaging and fluid biomarker; Wearable sensors

Significant Commercial Opportunity in Treating Multiple System Atrophy

Substantial Unmet Need

Severely debilitating illnesses with no current treatments are ripe for new entrants targeting underlying pathology of the disease.

Unique MOA

Inhibition of protein aggregation is a novel mechanism of action that may prove to impact more than motor symptoms.

Strong Intent to Prescribe

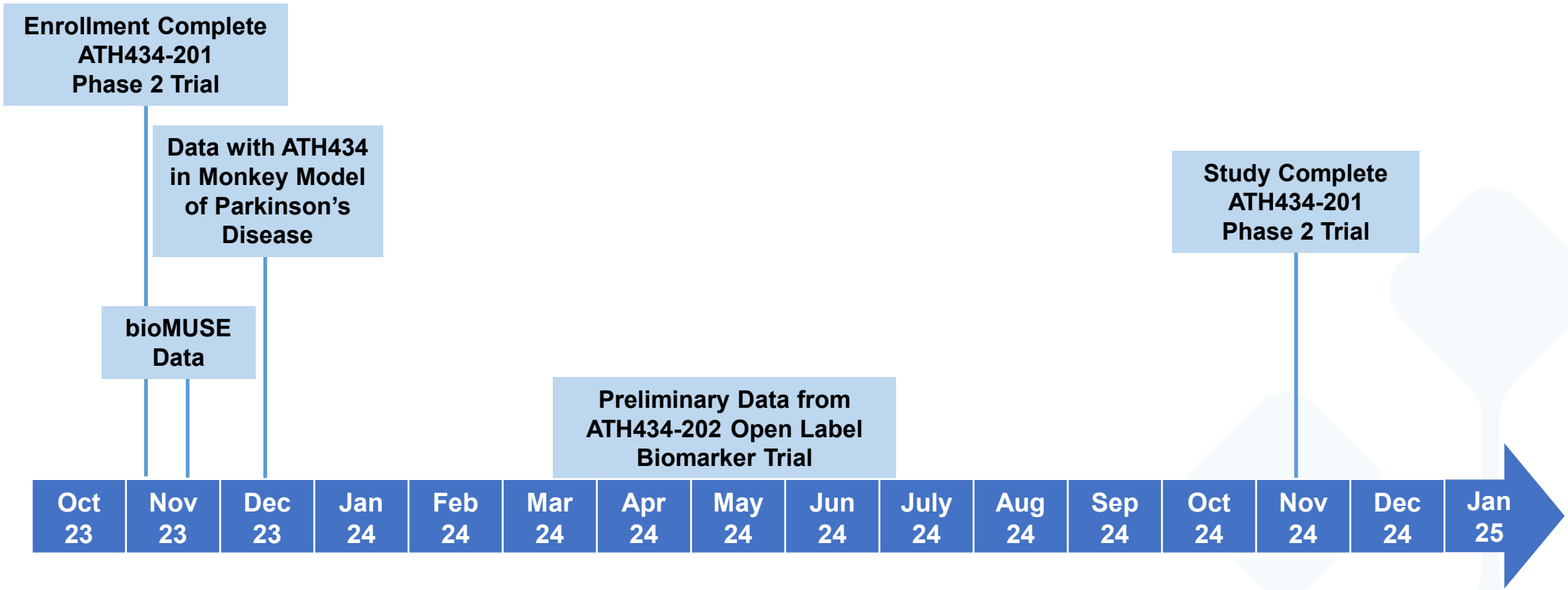
Motivated by efficacy of treating the underlying disease and not just the symptoms, clinicians intend to offer ATH434 to most of their patients with MSA.

Ease of Use

Twice daily oral administration of ATH434 preferred by physicians

Source: Survey of U.S. neurologists, updated 2023

Key Milestones



Poised for Progress in 2024

- New primate data validates our clinical strategy
- Achieved all clinical and corporate milestones in 2023
- ATH434: Novel drug candidate for various parkinsonian disorders
- First indication: Multiple System Atrophy (MSA)
  - ATH434-201 (early-stage MSA): Fully enrolled
  - ATH434-202 (advanced MSA): Phase 2 preliminary data 1H 2024
- Development team with 3 FDA approvals in neurology area
- Securities purchase plan (SPP) expected to commence January 2024


Alterity
THERAPEUTICS