David Stamler, MD
CEO

June 2024

Alterity THERAPEUTICS

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.”

Alterity is dedicated to creating an alternate future for people living with neurodegenerative diseases

Alterity means **the state of being different**

Our goal is to **modify the course of disease**

We aim to **disrupt the trajectory** of illness and improve quality of life

Investment Highlights

- Developing disease modifying therapies
- ATH434: Novel drug candidate targeting proteins implicated in neurodegeneration of Parkinson's disease and related disorders
- First indication: Multiple System Atrophy (MSA)
  - Parkinsonian disorder with no approved treatment
  - Orphan Drug designation for ATH434 in MSA, US and EU
  - Two Phase 2 clinical trials ongoing:
    - Randomized, double blind study in early-stage MSA
    - Biomarker trial in more advanced MSA
  - Natural history study to optimize endpoints and de-risk Phase 2 program
- Strong patent portfolio
- Significant R&D experience including 3 neurology drug approvals by FDA

Experienced Clinical Leadership Team with Multiple FDA Approvals in Neurology

David Stamler, M.D.

Chief Executive Officer

Auspex/Teva | Abbott | Prestwick Xenoport | Fujisawa

- **3 FDA Approvals in Neurology**
- Former CMO, Auspex
- VP, Clinical Development & Therapeutic Head, Movement Disorders, Teva Pharmaceuticals
- Part of Teva's US$3.5 billion acquisition of Auspex in 2015
- Led development of AUSTEDO® (deutetrabenazine) for treatment of Huntington disease and Tardive dyskinesia, both approved in 2017

Margaret Bradbury, Ph.D.

VP, Nonclinical Development

Auspex/Teva | Neurocrine | Merck

- Auspex - led strategic planning and program management in Huntington Disease chorea from IND through NDA filing
- Teva - led non-clinical development of several neuroscience programs

Cynthia Wong, M.P.H.

Senior Director, Clinical Operations

Auspex/Teva | Nextwave | Astex | Intermune | Impax Labs

- Clinical Operations leadership at Auspex/Teva.
- Led clinical trial activities for the registration study of AUSTEDO® in Huntington Disease chorea.
- Prior, led Phase 1-3 studies, including registration studies for marketing approval for Quillichew ER, Esbriet and Infergen.

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

Promising Portfolio in Neurodegenerative Diseases

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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*				*Enrollment Complete*		
ATH434	Parkinson's Disease						THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH
bioMUSE	Multiple System Atrophy *Natural History Study*						VANDERBILT UNIVERSITY MEDICAL CENTER
Drug Discovery	Neurodegenerative Diseases						

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.

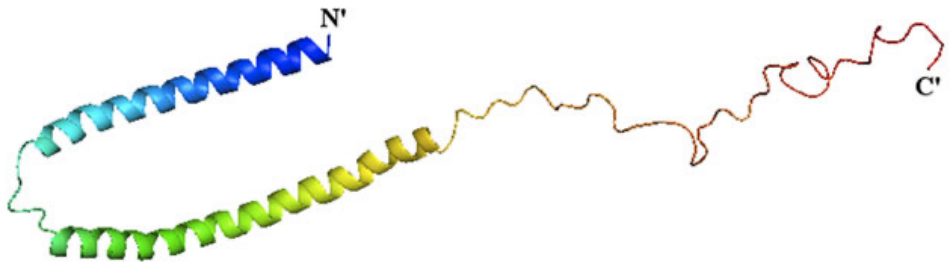
Ease of Use

Twice daily oral administration of ATH434 preferred by physicians

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

The Role of Alpha-Synuclein and Iron in Parkinsonian Disorders

Alpha-Synuclein: Critical for Normal Neuron Function

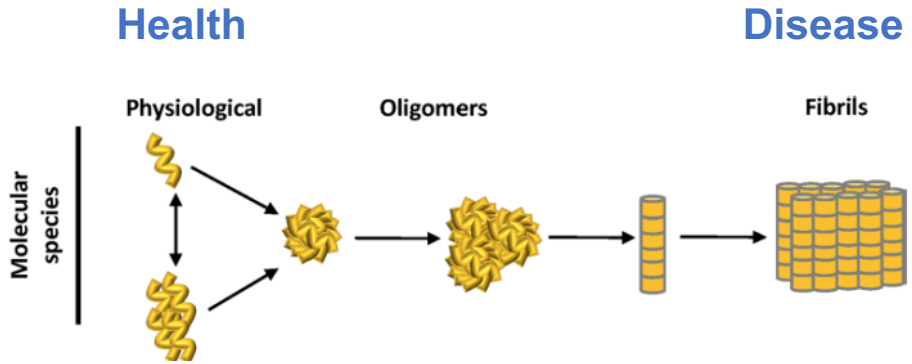


Our Strategy

- Inhibit misfolding and aggregation of intracellular α-synuclein
- Target misfolding α-synuclein by redistributing loosely bound excess iron in areas of pathology
- Address underlying pathology of disease

α-Synuclein

- An intracellular protein critical for normal function of neurons
- Native, unfolded protein enables neurotransmission
- α-synuclein *aggregates* in Parkinson's Disease and Multiple System Atrophy

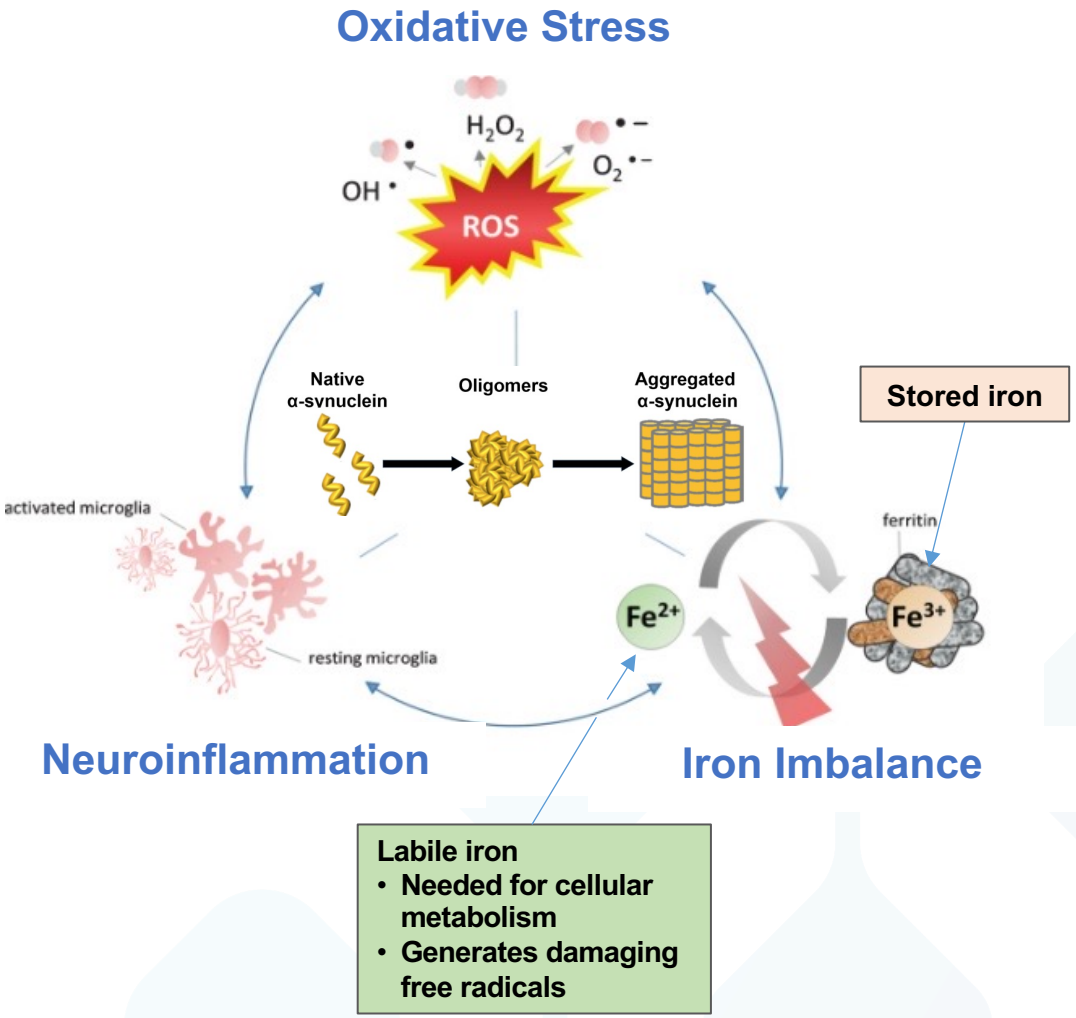


Sources: Ritchie et al, 2012; DOI:10.4236/health.2012.431175; Bengoa-Vergniory et al, 2017.DOI 10.1007/s00401-017-1755-1

Iron is Critical in Disease Pathogenesis

Iron and α-Synuclein are important contributors to MSA pathology

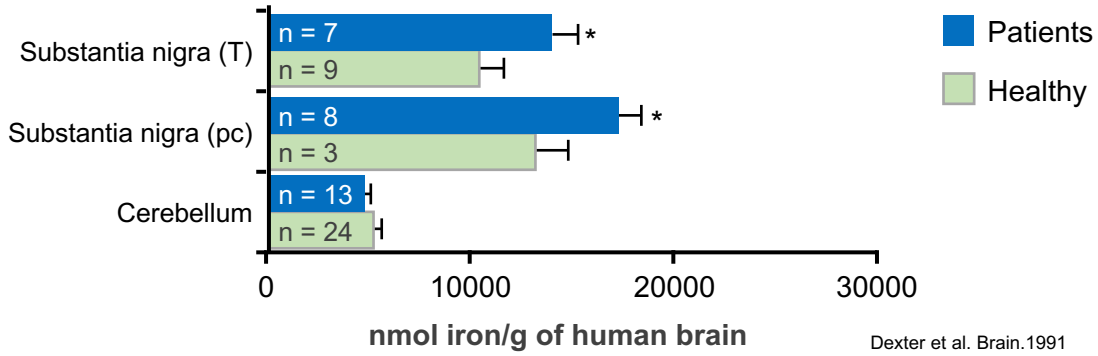
- Adverse impact of excess labile iron
  - Leads to *α-synuclein aggregation* → neuronal dysfunction
  - Oxidative stress with intracellular damage
  - Cell death
- Hallmark of MSA pathology
  - α-synuclein aggregates in neurons and glial (support) cells
  - Neuron and glial cells loss
  - Atrophy in multiple brain regions



Sources: Kaindlstorfer, J. Alzheimers Dis. 2018; Bengoa-Vergniory N, Acta Neuropathol. 2017

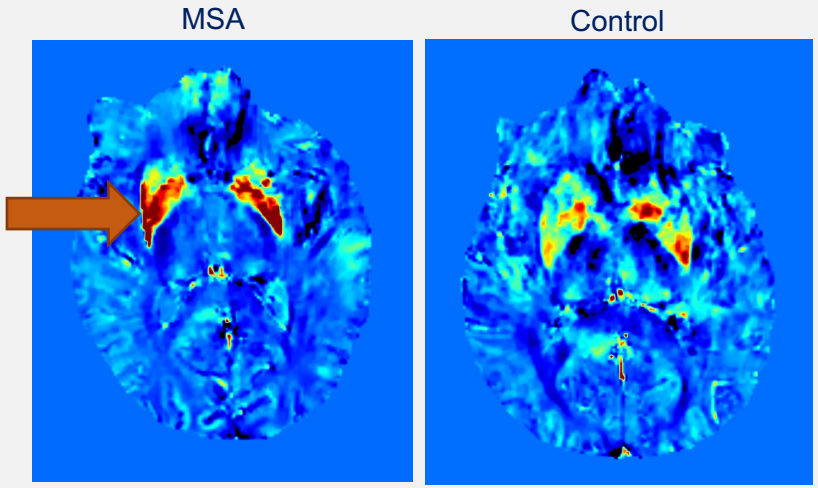
Increased Brain Iron in Synuclein-related Diseases

Parkinson's disease



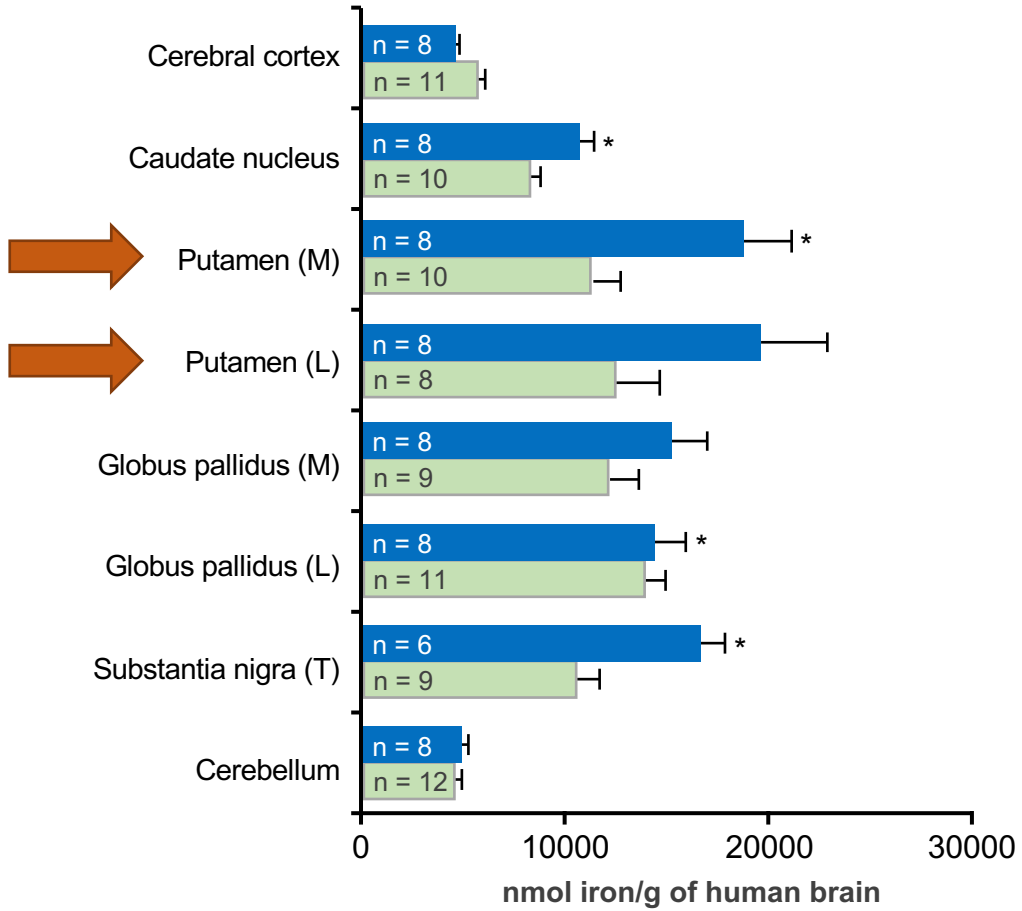
Dexter et al. Brain.1991

Advanced Quantitative MRI to measure brain iron

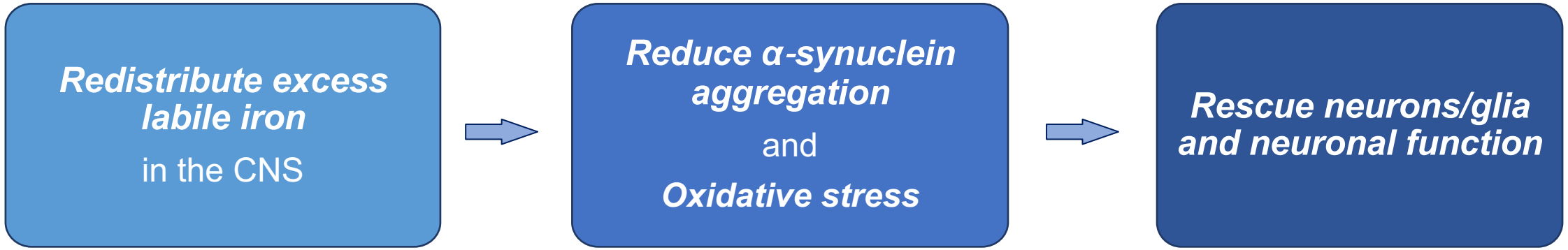


Courtesy of P. Trujillo, D. Claassen

Multiple System Atrophy



Approach: Address Underlying Pathology of Disease

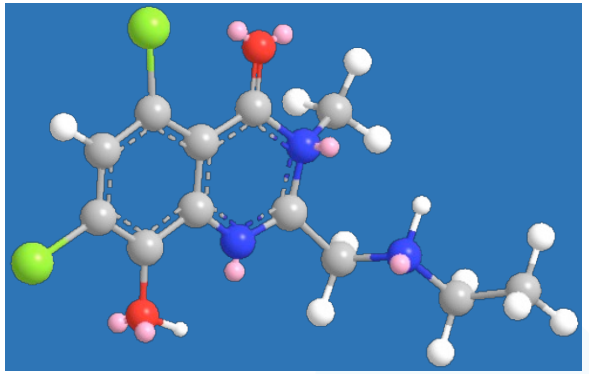


Potential Disease Modifying Therapy for MSA

ATH434: Disease Modifying Drug Candidate

ATH434: Potential Use in Multiple Indications

- Small molecule drug candidate ↓ α-synuclein aggregation
  - Iron chaperone, redistributes excess labile iron in CNS
  - 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 MSA treatment
- Development pathway endorsed by FDA and EMA



ATH434

Pharmacologic Actions of ATH434

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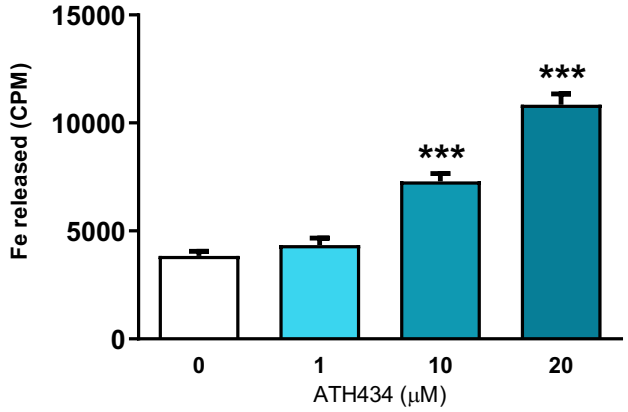
Redistributes loosely bound excess iron

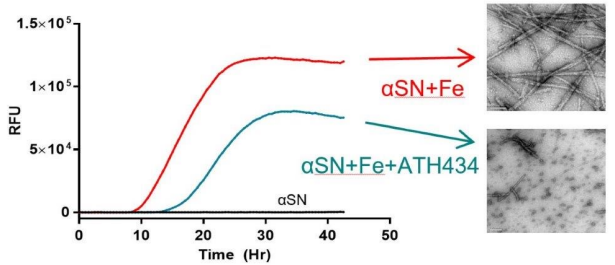


Ligand	Kd for Fe^{3+}
α-synuclein	10^{-5}
ATH434	10^{-10}
Transferrin	10^{-23}

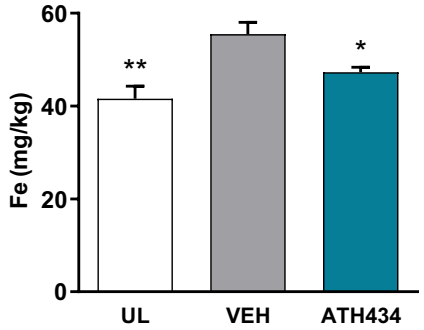
Stronger binding

ATH434 does not interfere with normal iron trafficking proteins

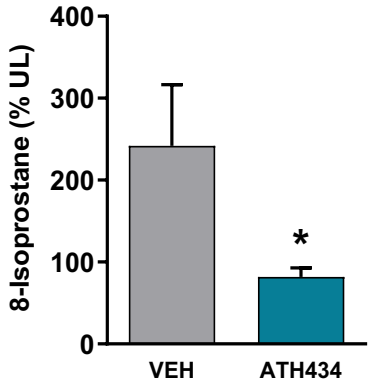
Reduces α-synuclein aggregation



Blocks increase in brain iron



Inhibits oxidative stress in vivo



Sources: Davies et al, 2011; Finkelstein, et al, 2017; Harris WR, 2002.
* P < 0.05, ** P < 0.01, *** P < 0.001

ATH434 Reduces Neuropathology and Improves Motor Function in Parkinson's Disease and MSA Animal Models

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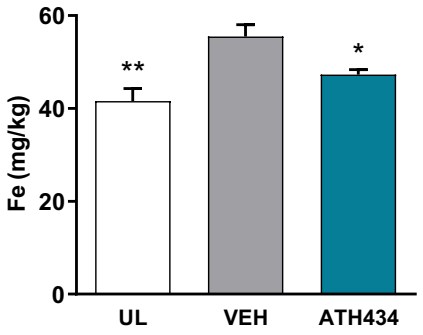
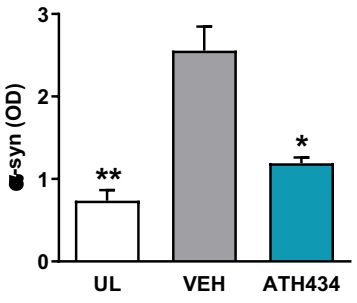
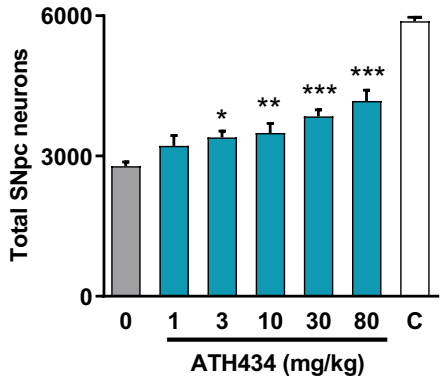
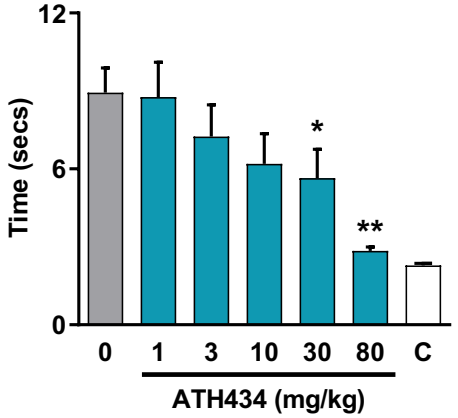
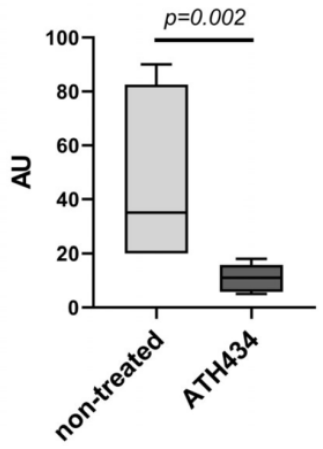
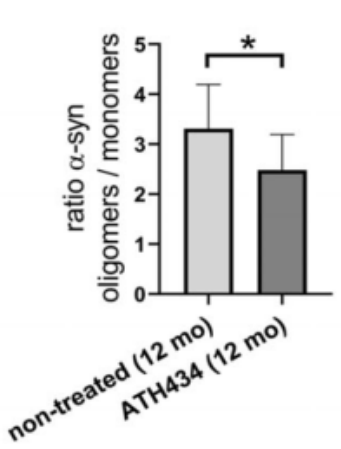
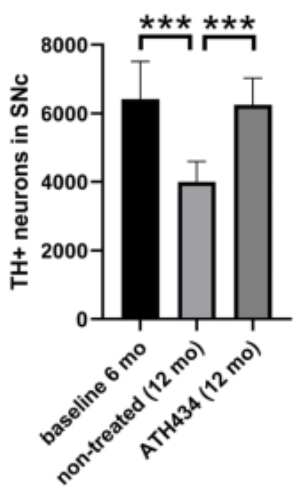
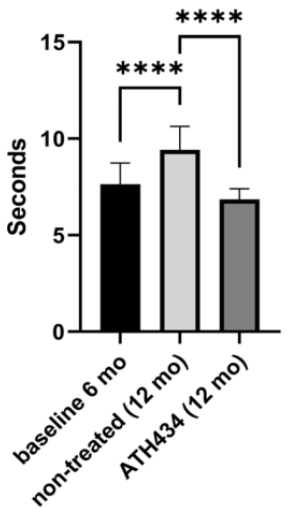
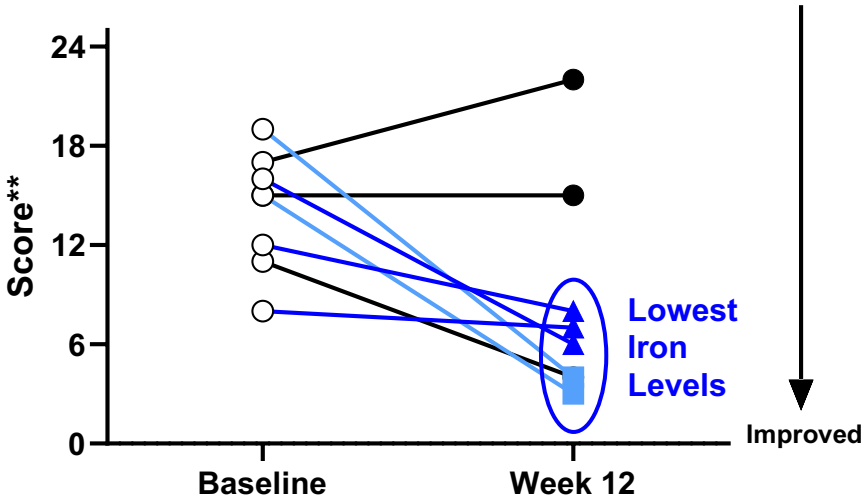
	↓ Iron	↓ α-Synuclein	Preserves Neurons	Improves Motor Function
Parkinson's Disease Mouse Model				
MSA Mouse Model				

Sources: Finkelstein, et al. Acta Neuropath Comm. 2017; Heras Garvin, et al. Mov. Disord. 2021. UL: unlesioned, C: control |* P < 0.05, ** P < 0.01, *** P < 0.001, ****P < 0.0001

Primate Parkinson's Disease Study

ATH434 Improved Behavior/Function and Increased Neuronal Connectivity

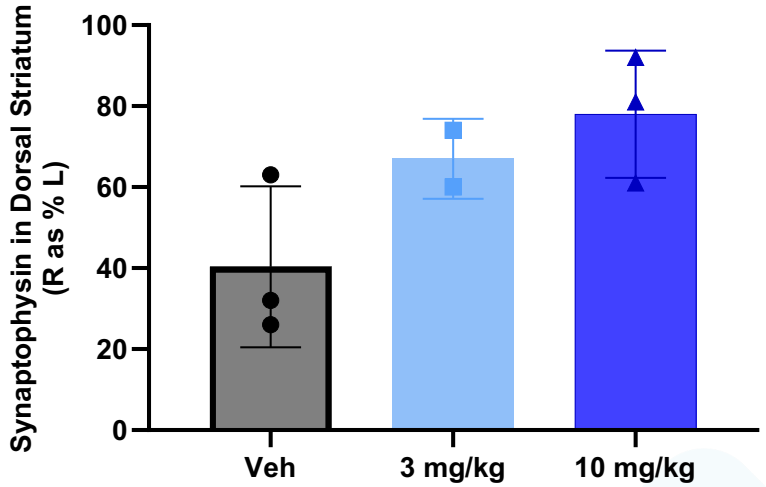
Behavior/Function



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

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

Neuronal Connectivity



ATH434: All (N=5) had Improved Behavior Function Scores

Placebo: 2 of 3 had Stable or Worsening Scores

Source: Bradbury, et al, "Effects of ATH434, a Clinical-Phase Small Molecule with Moderate Affinity for Iron, in Hemiparkinsonian Macaques", AAN 2024

Primate Study Validates ATH434 Clinical Approach

- Monkey closer to humans in neuroanatomy and behavior
- ATH434 treatment **improved behavior/function** in monkeys with experimentally induced Parkinson's disease
- Dose dependent increase in synaptophysin, marker of **functional connection between neurons**
- Favorable impact on Parkinson's symptoms in animals with redistributed brain iron
- New data increase overall confidence in ongoing Phase 2 trials

Accumulated Evidence of ATH434 Efficacy

Target Disease	Model	Midbrain* Iron	α-Synuclein	Preserve Neurons/ Function	Clinical Observations
Parkinson's disease	Mouse MPTP	↓	↓	↑	Improved motor performance
Parkinson's disease	Mouse A53T	↓	↓	↑	Improved motor performance
Parkinson's disease	Mouse tau knockout	↓	↓	↑	Improved motor performance
MSA	PLP-α-syn	↓	↓	↑	Improved motor performance
MSA	PLP-α-syn	↓	↓	↑	Improved motor performance
Parkinson's disease	Monkey MPTP	↓	n/a	↑	Improved motor performance

* includes s. nigra

ATH434 consistently improved motor performance across diverse animal models of disease by redistributing iron and preserving neurons

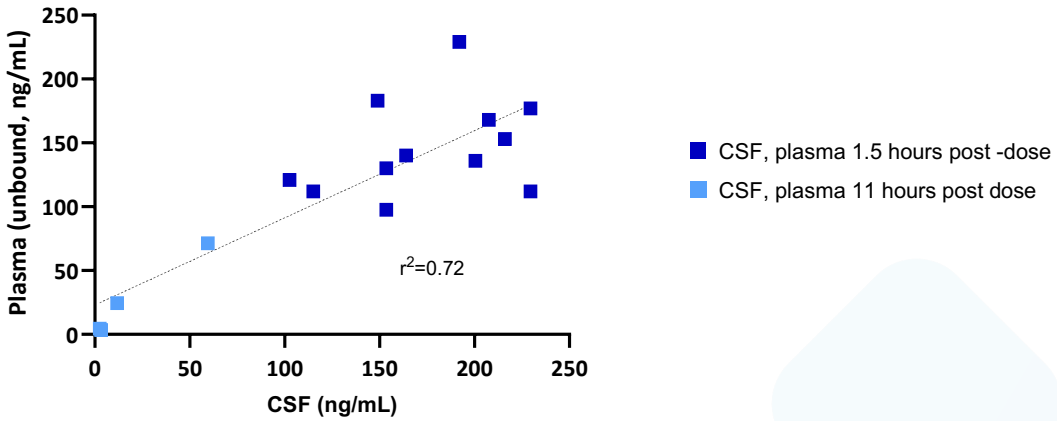
Source: Finkelstein, Acta Neuropath Comm 2017; Beauchamp et al, Neurotherapeutics 2022; Heras-Garvin et al, Mov Disord. 2021; Finkelstein et al, J Park Dis 2022; Bradbury et al, Am Acad. Neurol 2024

Multiple System Atrophy Clinical Development Program

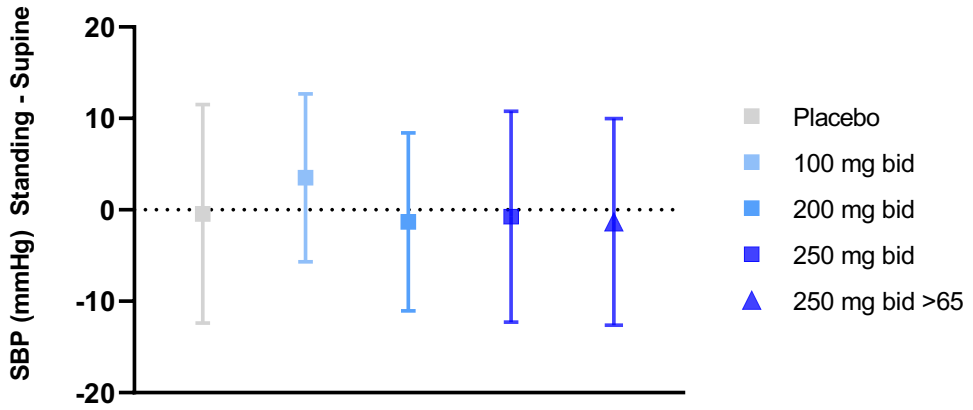
Completed Phase 1: Favorable Safety Profile

- Achieved drug concentrations associated with efficacy in animal models
- Favorable safety profile
  - All Adverse Events (AEs) were mild to moderate in severity
  - No SAEs or AEs leading to withdrawal
- No significant findings observed in vital signs, clinical labs or 12-lead ECGs
- Favorable cardiovascular safety profile

ATH434 Levels at Steady-State



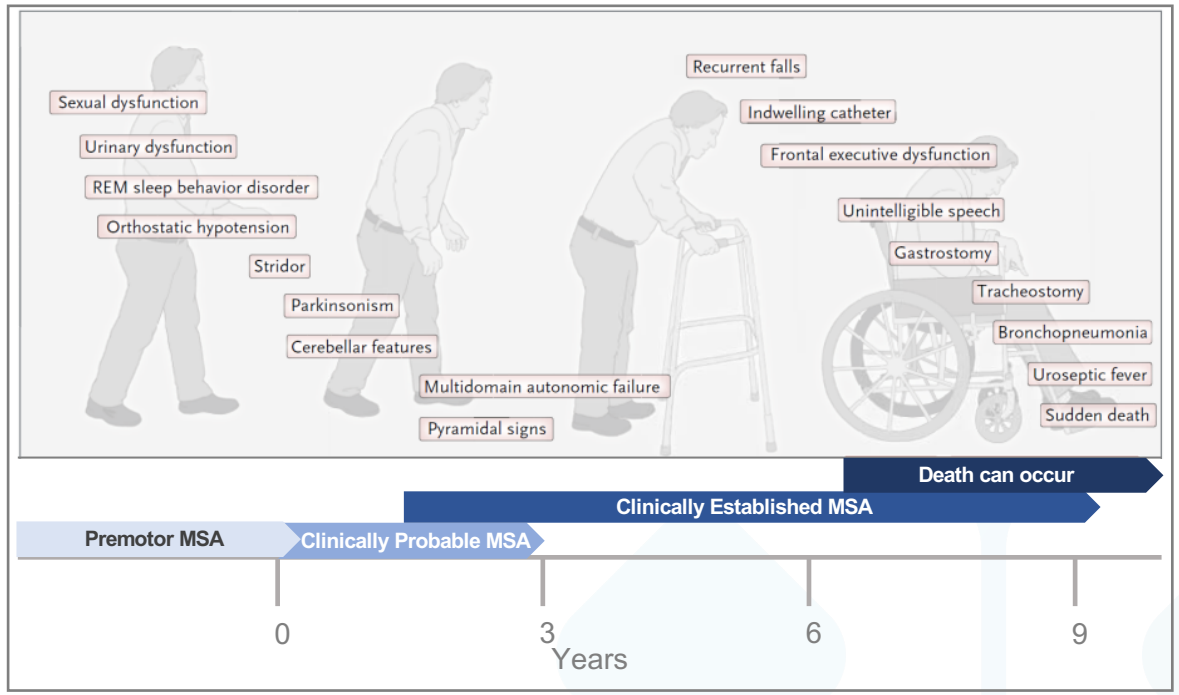
No effect on BP with Standing



Source: Phase 1 clinical trial; Alterity data on file

Multiple System Atrophy (MSA): Rare, Highly Debilitating and Rapidly Progressive Neurodegenerative Disease

- Parkinsonian disorder with no approved treatment
- Orphan disease
- Disease characteristics
  - Motor: Parkinsonism, uncoordinated movements, balance problems/falls
  - Autonomic dysfunction: blood pressure maintenance, bladder control, bowel function
  - Brain atrophy in multiple regions
- Median survival 7.5 years after symptom onset



Sources: Fanciulli, Wenning. NEJM 2015 | Wenning, et al. Mov Disorders 2022 | Coon, et al. Brain 2015 | Claassen,et al. Mov Disorders 2021

Clinical Studies in MSA: Natural History Study

Study	bioMUSE
Design	Observational
Objectives	Characterize early-stage MSA
Population	Clinically Probable MSA
Sample Size	N = 21 enrolled
Observation period	12 months
Brain MRI Biomarkers	Iron, volume, glial pathology
Fluid Biomarkers	NfL, Aggregated α-synuclein
Other Biomarkers	Wearable movement sensors
Clinical Measures	Motor exam, autonomic function, activities of daily living, global/functional measures

BioMUSE Natural History Study
Learnings to Date

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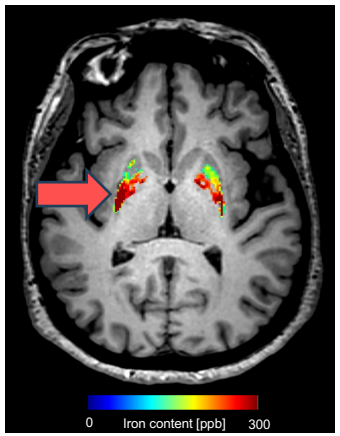
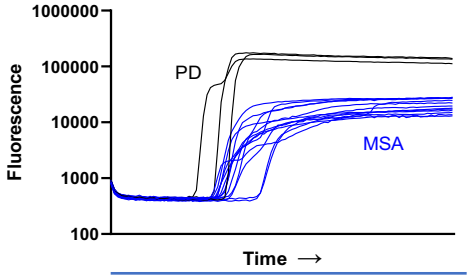
Optimize Patient Selection

Advanced MRI methods



Identify "iron signature" of early MSA

α-synuclein in CSF

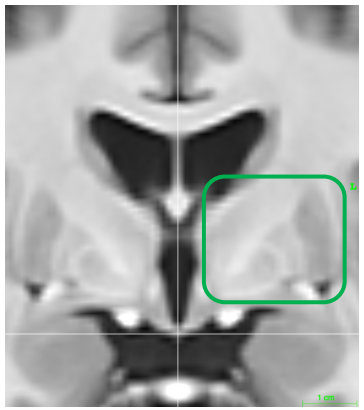


Differentiate MSA from PD

Revised selection criteria in ATH434-201 and ATH434-202 protocols to exclude PD patients

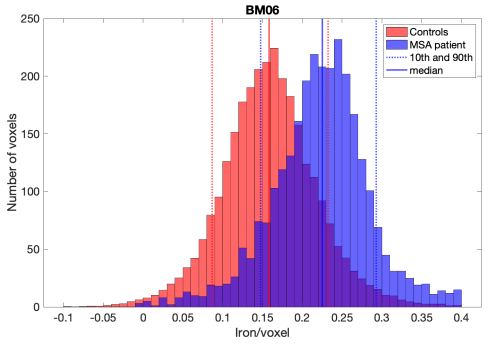
Precision Endpoint Assessment

New MRI Template



Improve precision of structural MRI

Iron distribution in MSA

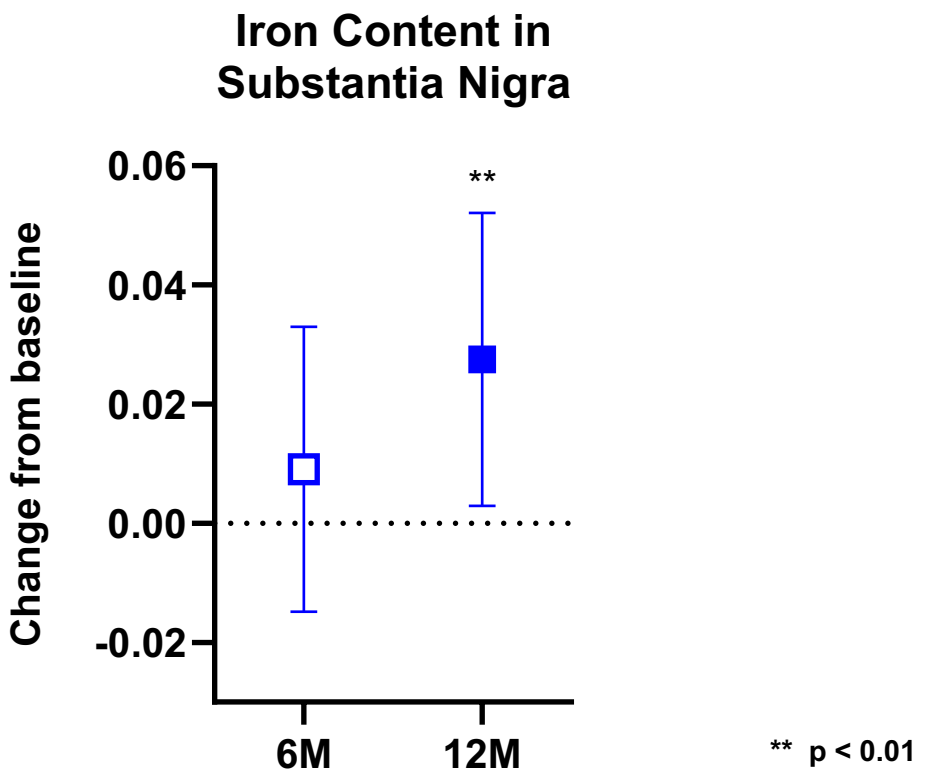


Novel strategies for measuring brain iron in individual regions

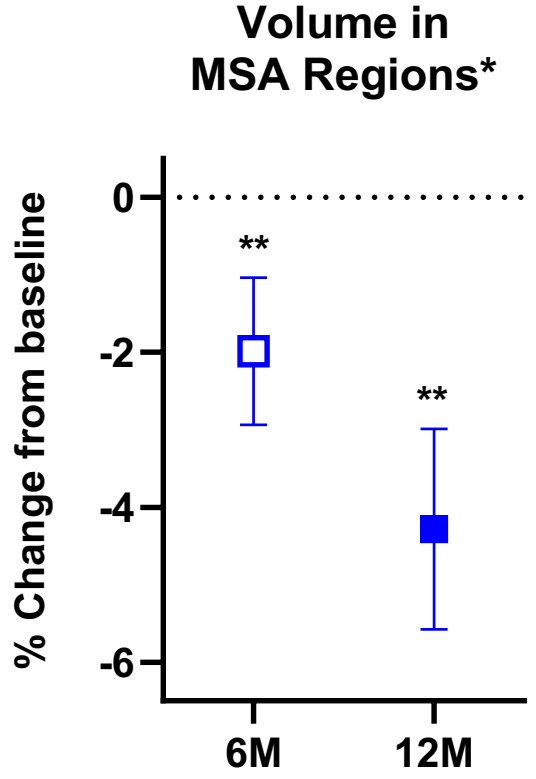
State of the art methods enabled precise measurements of iron and brain volume with MRI

Sources: Presentations/Posters on file, including Claassen et al, MDS Conference 2021 and 2022.

BioMUSE: Longitudinal MRI Data



** p < 0.01



Iron significantly increased at 12 months in the substantia nigra
Volume significantly decreased at 6 and 12 months in four key MSA regions

* Cerebellum, brainstem, Putamen, Globus pallidus

BioMUSE Summary

- Observational Study in MSA
- Goals: improve patient selection and choose endpoints for Phase 2
- Iron content: **Significant increase in iron** observed at 12 months in one brain region (s. nigra)
- Brain volume: **Significant decrease in volume** observed over 12 months in all four MSA regions
  - ❖ Novel Imaging Biomarker: **MSA Volume Index**

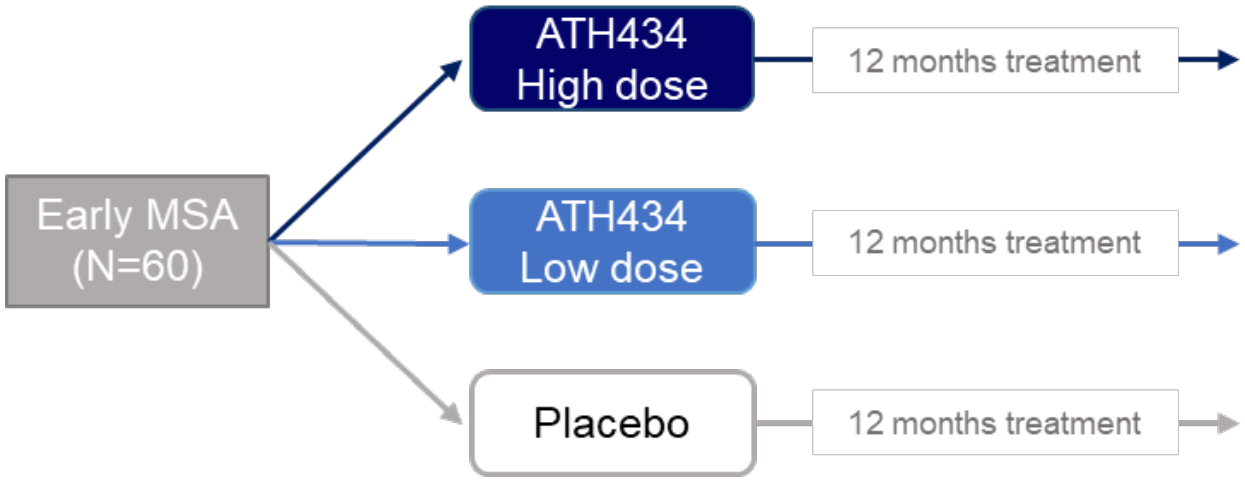
Clinical Studies in MSA: Phase 2

Study	bioMUSE – Natural History	ATH434-202 – Phase 2	ATH434-201 – Phase 2
Design	Observational	Single arm, open-label	Randomized, double-blind
Objectives	Characterize early-stage MSA	Efficacy and safety of ATH434	Efficacy and safety of ATH434
Population	Clinically Probable MSA	Clinically Established MSA	Clinically Probable MSA
Sample Size	N = 21 enrolled	N = 10	N = 77
Observation/Treatment	12 months	12 months treatment: ATH434	12 months treatment: ATH434 high dose, low dose, placebo
Brain MRI Biomarkers	Iron, volume, glial pathology	Same as bioMUSE	Same as bioMUSE
Fluid Biomarkers	NfL, Aggregated α-synuclein	Same as bioMUSE	Same as bioMUSE
Other Biomarkers	Wearable movement sensors	—	Same as bioMUSE
Clinical Measures	Motor exam, autonomic function, activities of daily living, global/fxnal measures	Same as bioMUSE	Same as bioMUSE

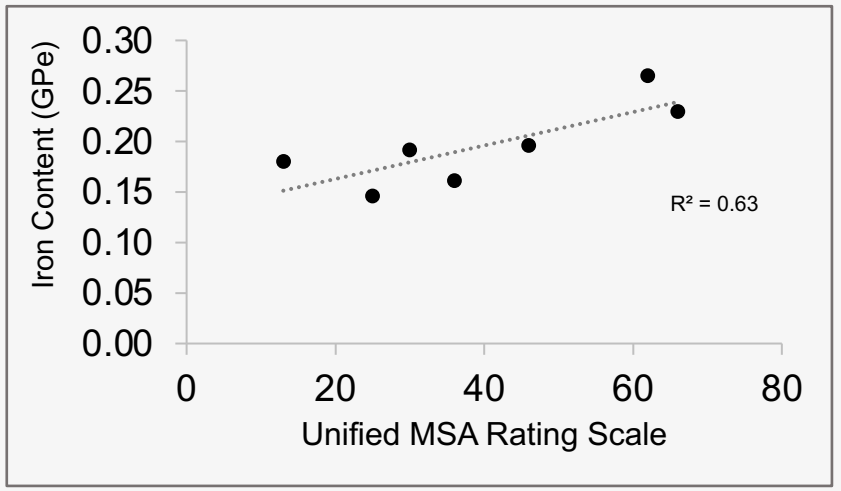
ATH434-202 Key Study Endpoints
Based on bioMUSE Findings

Primary Endpoint	**Change in *MSA Volume Index* by MRI at 12 months** • Based on the significant decrease in volume in relevant brain regions in MSA
Secondary Endpoint	**Change in *Iron content* in the substantia nigra by MRI at 12 months** • Based on the significant increase in iron in relevant brain region in MSA

ATH434-201 Phase 2 Design



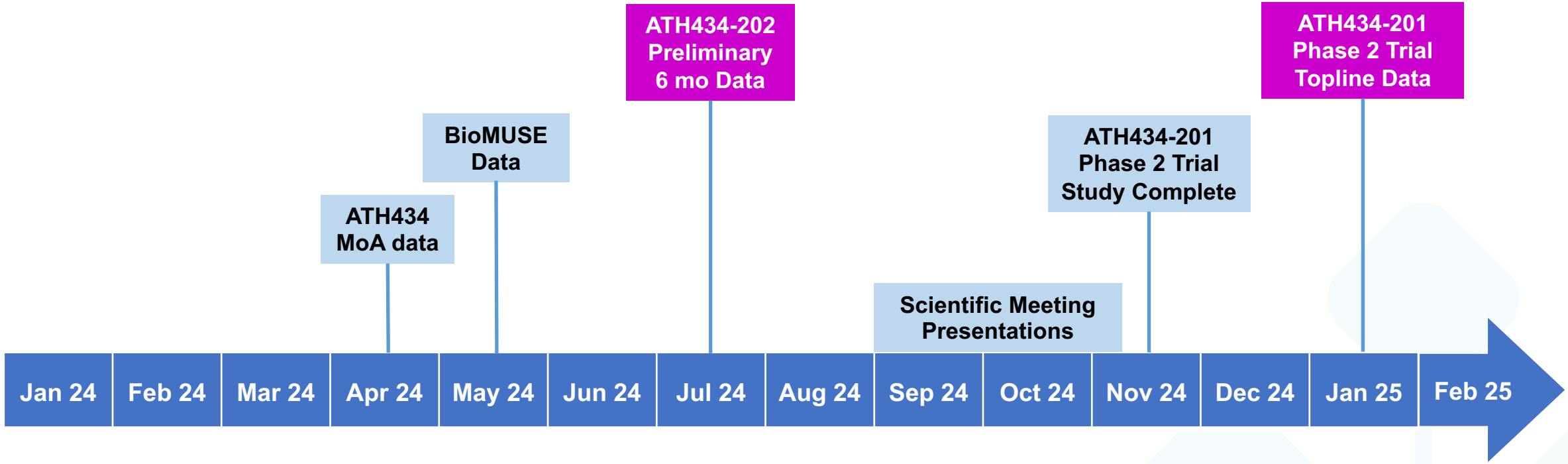
Brain iron correlates with disease severity



BioMUSE Natural History Study

Source: Claassen, et al. Mov Disorders 2021

Key Milestones



Alterity: Poised for Progress

- Targeting Orphan disease with no approved treatments
- Two Phase 2 clinical trials ongoing
  - Global double-blind trial enrollment completed
  - Biomarker trial enrollment completed
- bioMUSE Natural History Study de-risked Phase 2
- Development team with multiple FDA approvals
- Drug discovery generating patentable compounds as next generation therapies
- Cash balance of AU$18.3M as of 31 March 2024

Catalysts

MSA Natural History Study

- ✓ H1 2024: Present new biomarker data

ATH434-201 Phase 2 Double-Blind Trial

- ✓ Nov 2023: Enrollment Complete
- Nov 2024: Study Complete
- Jan 2025: Topline Data

ATH434-202 Phase 2 Biomarker Trial

- Jul 2024: Preliminary 6-mo Data
- Q4'24/Q1'25: 12-month Data

Alterity THERAPEUTICS

ASX:ATH | NASDAQ:ATHE