David Stamler, MD
CEO

November 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

- Clinical stage biopharmaceutical company developing disease modifying treatments for Parkinson's disease and related disorders
- Phase 2 topline results expected in January 2025
  - Parkinsonian disorder without approved treatment
  - Orphan Drug Designation in U.S. in Multiple System Atrophy (MSA)
  - Positive data from open label study confirms clinical approach
- Strong patent portfolio
- Significant leadership in movement disorders including 3 FDA approvals in neurology

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.

What Are Movement Disorders?

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Movement disorders are a group of neurological conditions that involve abnormal or involuntary movements. They affect the way a person moves and can cause significant disability, from social isolation to unstable gait and falls.

Causes of Movement Disorders

Causes vary widely and can include:

- **Genetic factors** (e.g., Huntington's disease)
- **Neurodegenerative conditions** (e.g., Parkinson's disease)
- **Autoimmune diseases**
- **Infections** (e.g., encephalitis or viral infections)
- **Traumatic brain injuries** or stroke
- **Toxins or medications** (e.g., drug-induced movement disorders like tardive dyskinesia)
- **Metabolic disorders** (e.g., Wilson's disease, which affects copper metabolism)

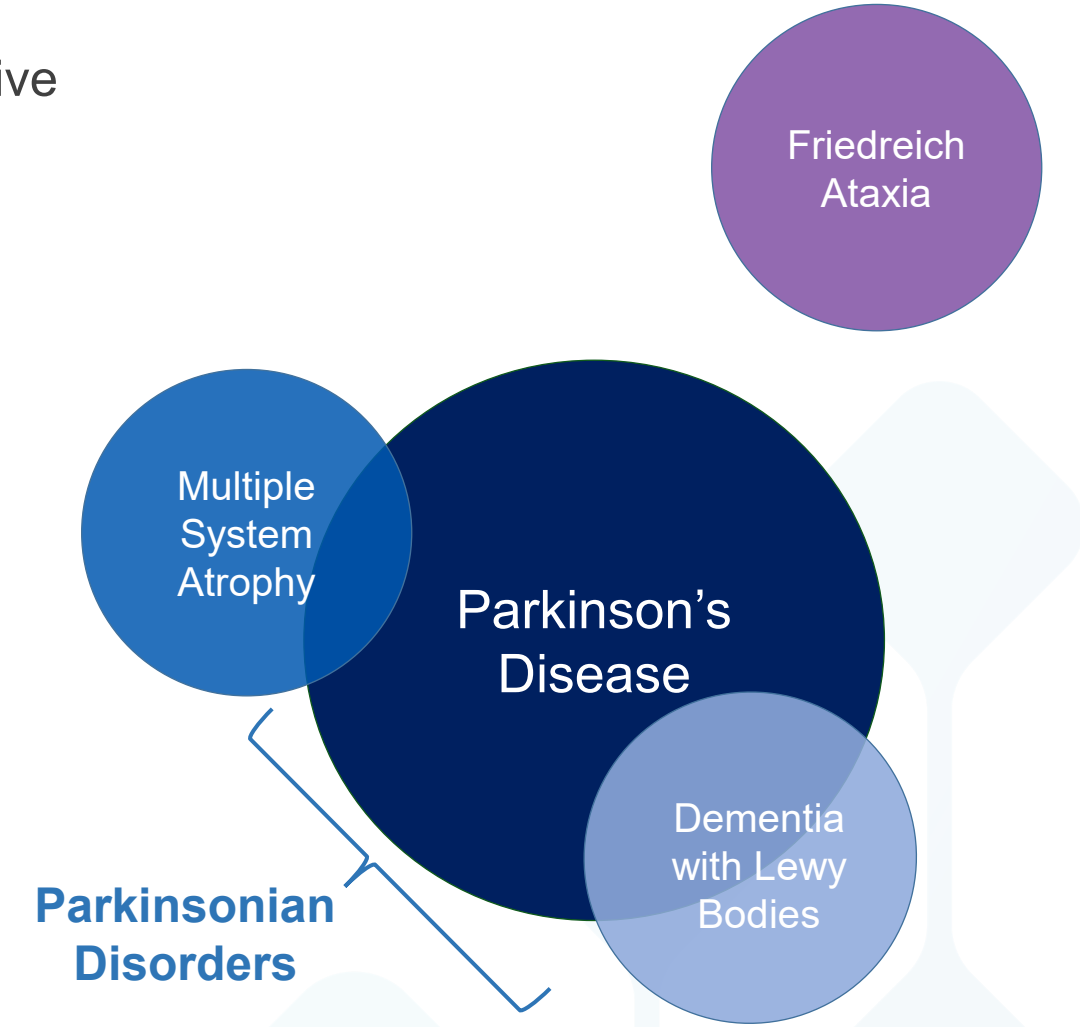
Symptoms

Symptoms can range widely depending on the type of movement disorder and its severity, but common signs include:

- Tics
- Tremors or shaking
- Stiffness or rigidity in the muscles
- Uncontrolled movements or spasms
- Difficulty with balance and coordination
- Slowed or abnormal walking (gait problems)
- Difficulty maintaining posture

Targeting Iron-Related Neurodegenerative Diseases

- Iron: central to pathology of many neurodegenerative diseases
- Parkinsonian disorders include
  - Parkinson's disease (PD)
  - Rare diseases with similar motor symptoms
    - Multiple System Atrophy (MSA)
    - Dementia with Lewy Bodies (DLB)
  - Similar underlying pathology
- Friedreich's Ataxia
  - Rare disease with uncoordinated movements
  - Genetic disorder that appears in childhood



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
ATH434	Friedreich's Ataxia						
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

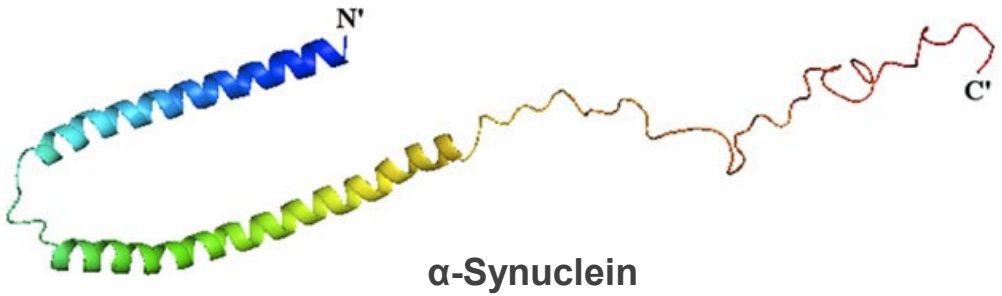
Source: Survey of U.S. neurologists, updated 2023

ATH434: Disease Modifying Drug Candidate Targeting Alpha-Synuclein and Iron in Parkinsonian Disorders

Alpha-Synuclein and Iron in Health

α-Synuclein protein

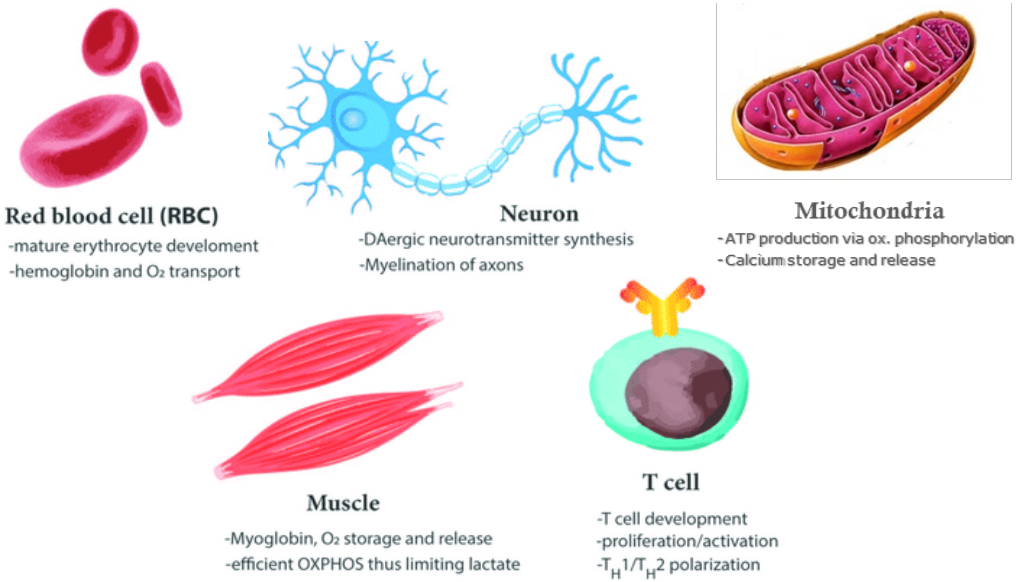
- Critical for normal function of neurons
- Enables nerves to communicate with each other via neurotransmitters



α-Synuclein

Iron is Essential for Life

- Red blood cell production, oxygen transport
- Neurotransmitter synthesis in neurons
- Energy production via ATP and activity of many enzymes

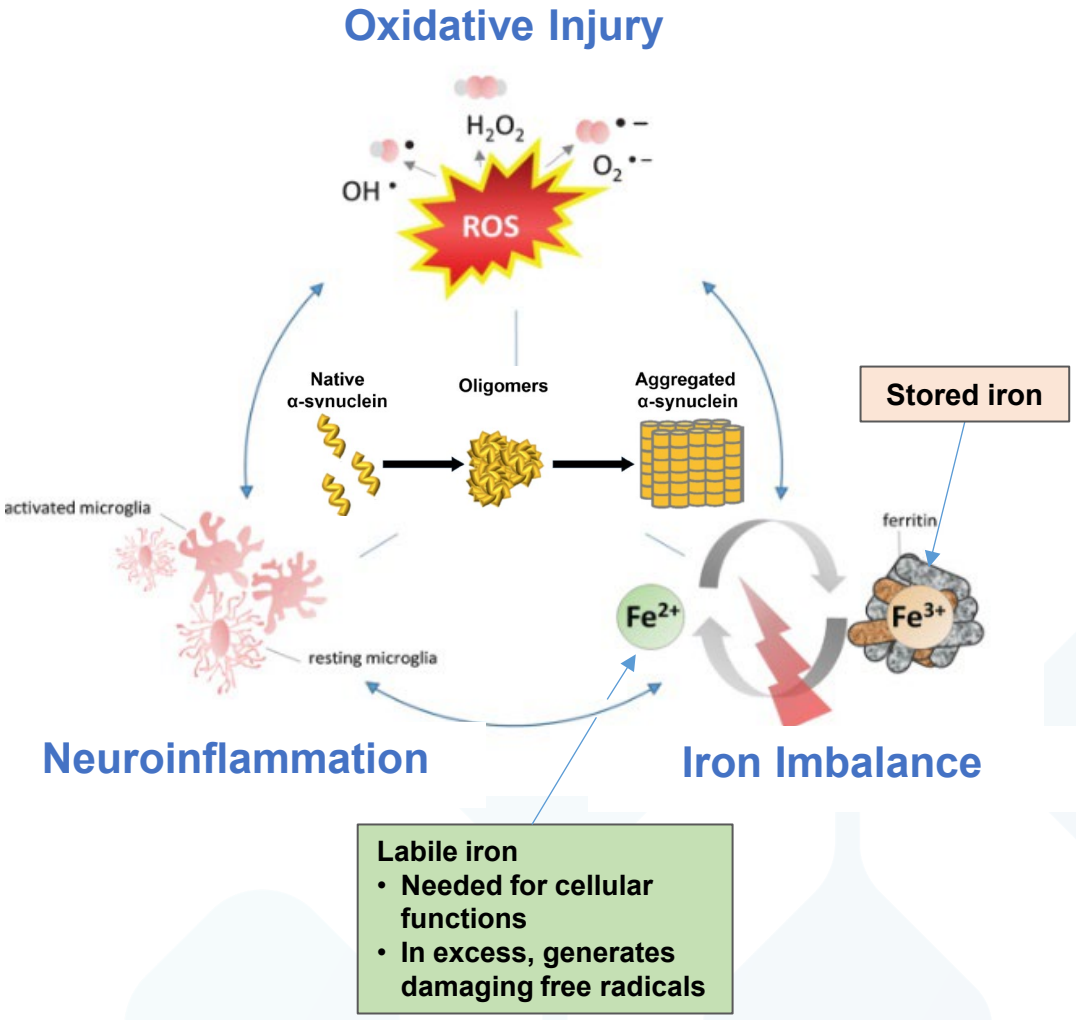


Sources: Ritchie et al, 2012; DOI:10.4236/health.2012.431175; Cronin et al, 2019, doi.org/10.3389/fmolb.2019.00116

Iron and α-Synuclein are Important Contributors to Pathology in Parkinsonian Disorders

Vicious cycle of cellular injury

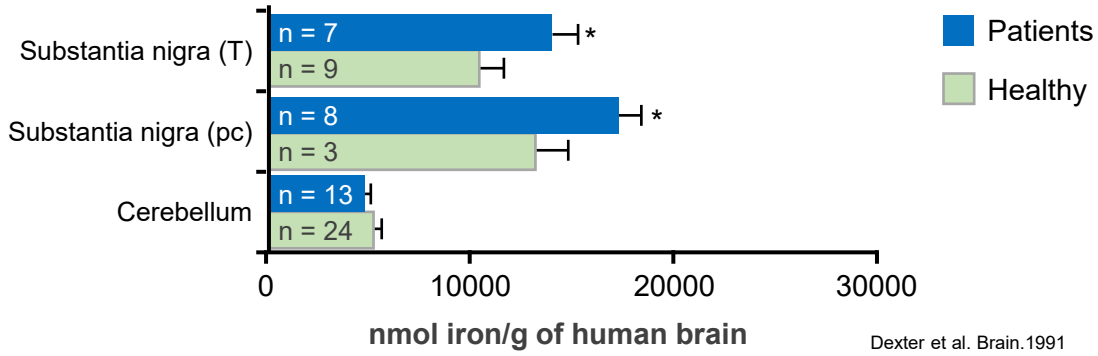
- Adverse impact of excess labile iron
  - Alpha-synuclein aggregation
  - Oxidative stress with intracellular damage
  - Cell death
- Adverse impact of aggregating α-synuclein
  - Neuronal dysfunction
  - Loss of trophic support to neurons
  - Increases oxidative stress
  - Cell death



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

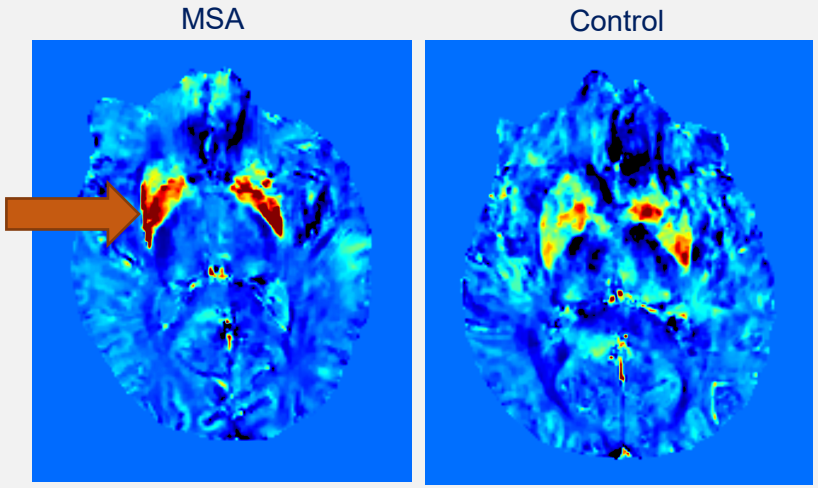
Increased Brain Iron in Parkinson's Disease and Multiple System Atrophy

Parkinson's disease



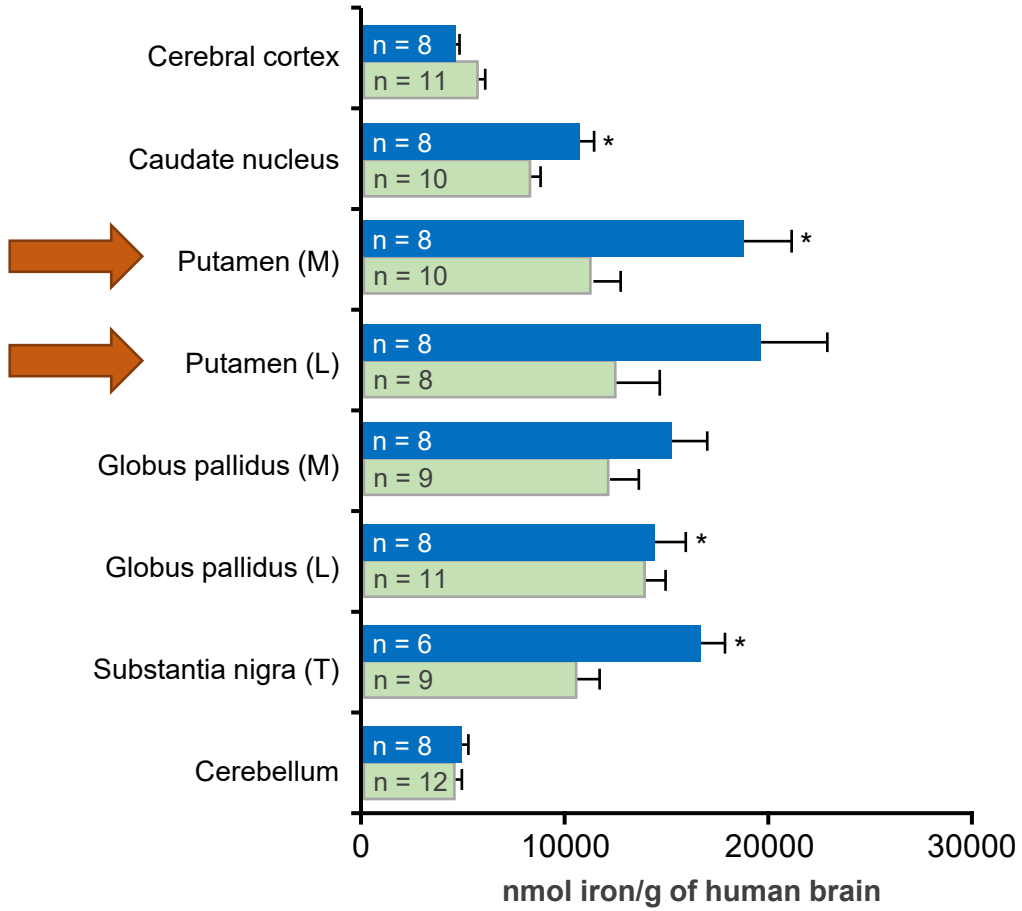
Dexter et al. Brain.1991

Advanced Quantitative MRI to measure brain iron

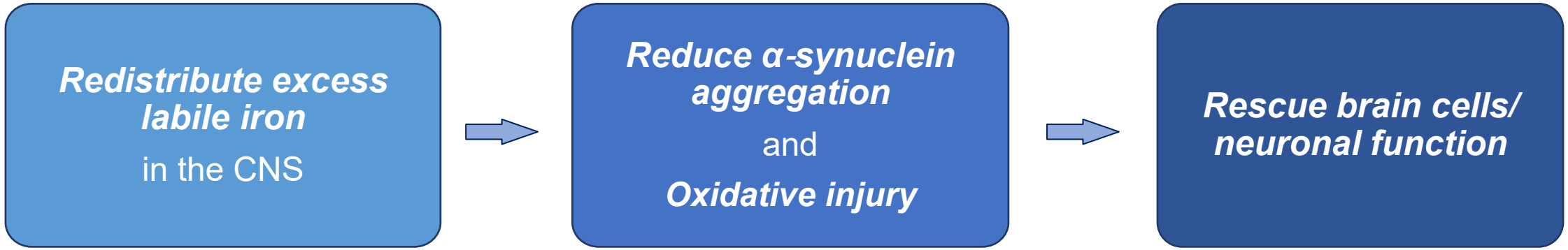


Courtesy of P. Trujillo, D. Claassen

Multiple System Atrophy



Treatment Approach: Address Underlying Pathology

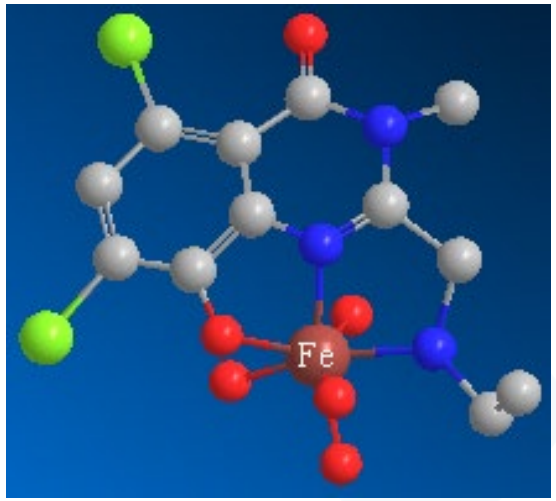


Potential Disease Modifying Therapy for MSA

ATH434: Potential Disease Modifying Therapy

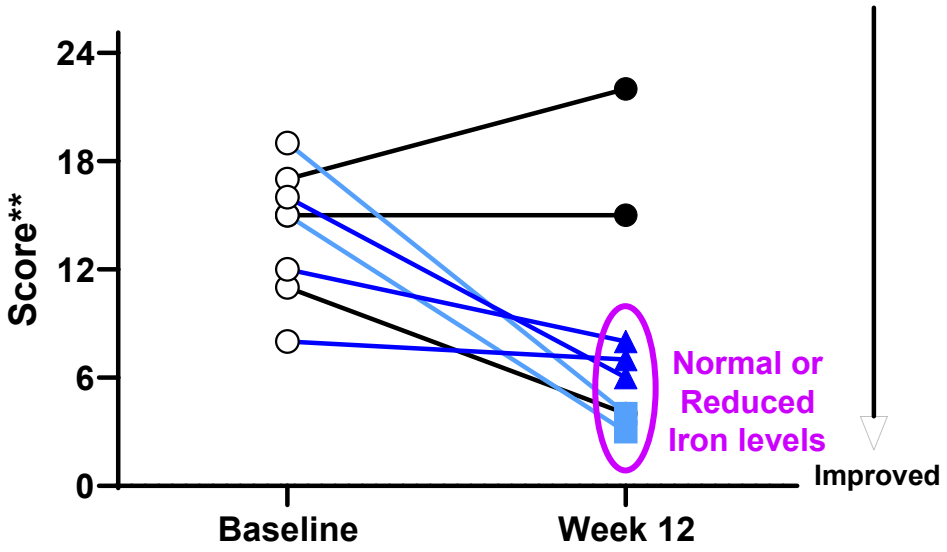
- Small molecule drug candidate
  - Decreases pathologic protein aggregation (α-synuclein) in CNS
  - Iron chaperone: redistributes excess labile iron in CNS
- Oral medication
  - Preferred over infusions and injections
- Potential to treat iron-related neurodegenerative disease
- Orphan Drug Designation in the US and EU for MSA treatment
- Development pathway endorsed by FDA and EMA

ATH434 binding to iron



Efficacy Demonstrated in Primate Model of Parkinson's Disease

ATH434-treated: All Monkeys Improved (n=5)
Placebo: 2 of 3 had Stable or Worsening Scores



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

Placebo
3 mg/kg
10 mg/kg

- Monkey closely related to humans in neuroanatomy and behavior
- ATH434 improved behavior and function in monkeys with experimental Parkinson's disease
- Favorable impact on Parkinson's symptoms in animals with redistributed brain iron
- Data validate clinical approach and increase overall confidence in ongoing Phase 2 trials

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Accumulated Evidence of ATH434 Efficacy

Target Disease	Model	Midbrain* Iron	α-Synuclein	Preserve Neurons/ Function	Clinical Observations
Parkinson's disease	Monkey MPTP	↔ or ↓	n/a	↑	Improved motor performance
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[1]	PLP-α-syn	↓	↓	↑	Improved motor performance
MSA[2]	PLP-α-syn	↔ or ↓	↓	↑	Improved motor performance

* includes s. nigra

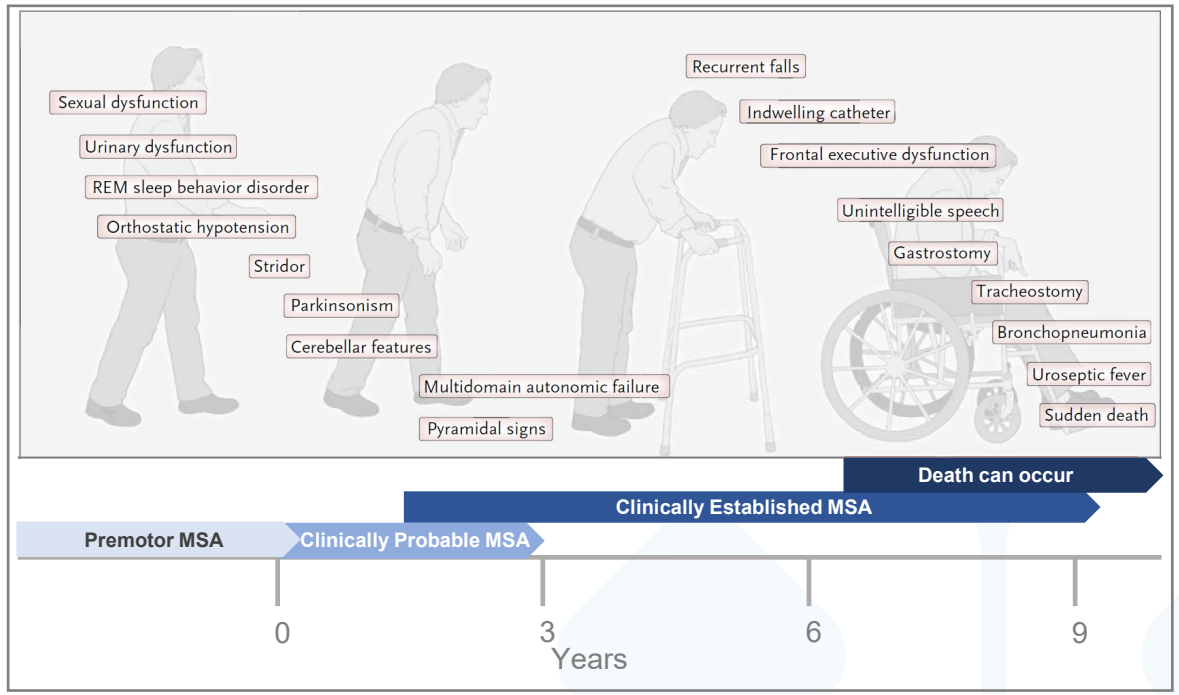
ATH434 consistently improved motor performance across diverse animal models of disease by redistributing iron and preserving neurons

Source: Finkelstein, Acta Neuropath Comm 2017; Beauchamp et al, Neurotherapeutics 2022; 1 Heras-Garvin et al, Mov Disord. 2021; 2 Finkelstein et al, J Park Dis 2022; Bradbury et al, Am Acad. Neurol 2024

Understanding Multiple System Atrophy

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

- Parkinsonian disorder with no approved treatment
- Orphan disease: up to 50,000 patients in U.S.
- Disease characteristics
  - Motor: Parkinsonism, uncoordinated movements, balance problems and falls
  - Autonomic dysfunction: blood pressure maintenance, bladder control, bowel function
  - Brain atrophy and α-synuclein accumulation 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 | Multiple System Atrophy: National Institute of Neurological Disorders and Stroke (nih.gov)

bioMUSE Natural History Study Informs and De-Risks Treatment Studies

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

- Strategy: Optimize patient selection and choose endpoints for Phase 2
- Iron content: Significant increase in iron observed at 12 months in key brain region (substantia nigra)
- Brain volume: Significant decrease in volume observed over 12 months in MSA affected regions

BioMUSE Natural History Study
Learnings to Date

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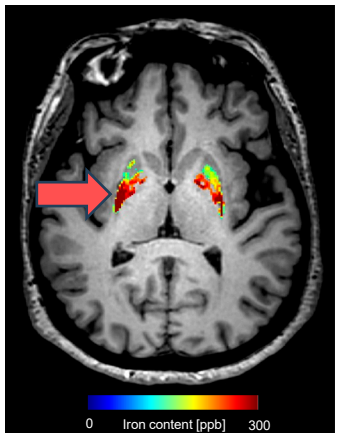
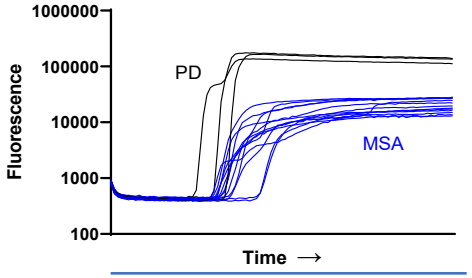
Optimize Patient Selection in Phase 2 Trials

Advanced MRI methods



Identify "iron signature" of early MSA

α-synuclein in CSF

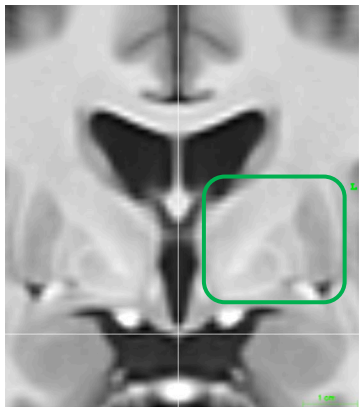


Differentiate MSA from PD

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

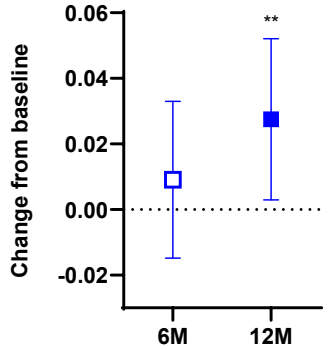
Precision Endpoint Assessment

Structural mapping



Improve precision of volume measurements

Iron Content in Substantia Nigra



Novel strategies for measuring brain iron in individual regions

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

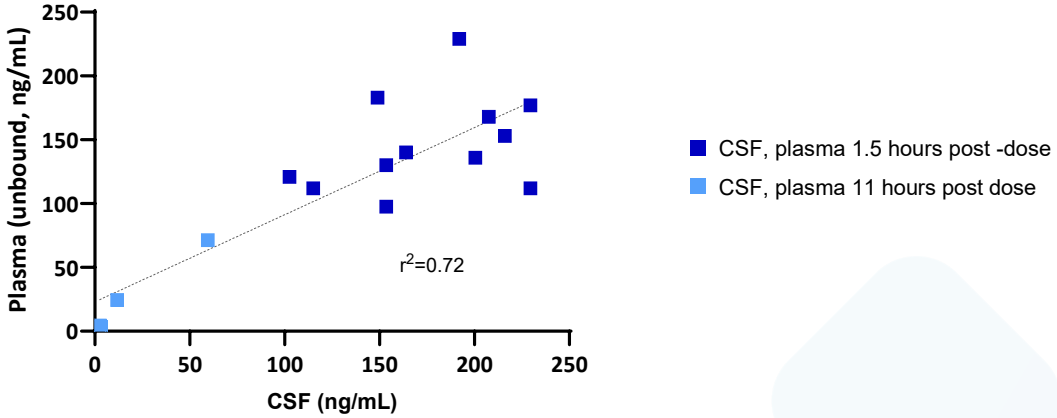
Sources: Presentations/Posters on file, including Claassen et al, MDS Conference 2021 and 2022.

ATH434 Clinical Development Program in Multiple System Atrophy

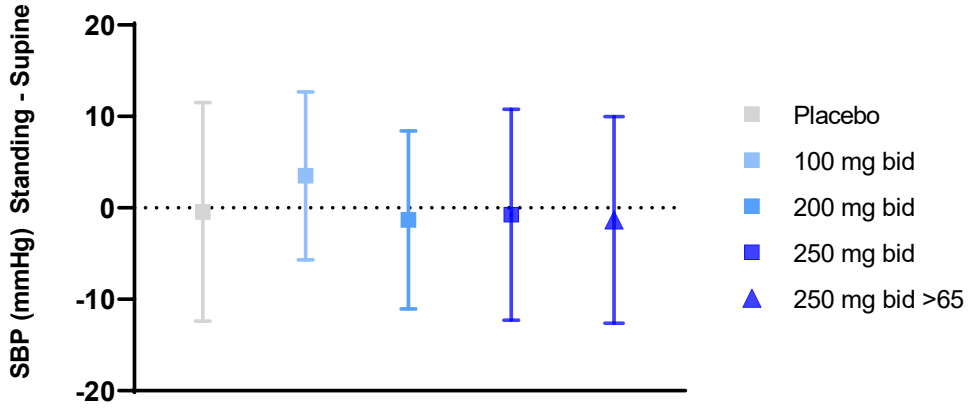
Phase 1 Demonstrated Favorable Safety Profile

- 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

Ongoing Treatment Studies with ATH434

Study	ATH434-201 – Phase 2	ATH434-202 – Phase 2
Design	**Randomized, double-blind**	**Single arm, open-label**
Objectives	Efficacy and safety of ATH434	Efficacy and safety of ATH434
Population	**Early-stage MSA**	**Advanced MSA**
Sample Size	N = 77	N = 10
Treatment	12 months	12 months
Brain MRI Biomarkers	Iron, volume	Iron, volume, glial pathology
Fluid Biomarkers	NfL^, Aggregated α-synuclein	NfL^, Aggregated α-synuclein
Other Biomarkers	Wearable movement sensors	—
Clinical Measures	Motor exam, autonomic function, activities of daily living, global measures	Motor exam, autonomic function, activities of daily living, global measures

^NfL: Neurofilament light chain

ATH434-202 Interim Clinical Data Confirms Development Approach

Population: 10 with advanced MSA
Treatment: ATH434 75 mg bid
Assessment: 6 months

UMSARS: Unified MSA Rating Scale (Part I)
Activities of Daily Living Scale

- Group change (n=10)^ compares favorably to patients with similar disease severity*

Areas Assessed

- Speech
- Swallowing
- Handwriting
- Cutting food
- Dressing
- Hygiene
- Walking
- Falling
- Orthostatic symptoms
- Urinary Function
- Sexual Function
- Bowel Function

Global Impression of Change

- Overall rating from patient or clinician perspective

Question

With respect to your overall neurological symptoms, how would you describe yourself now compared to immediately before starting treatment?

Clinical Responders

- 30% of participants showed stable or improved neurological symptoms, based on UMSARS I and Global Impression of change scores

^ Claassen. Mov. Disord. 2024.

* Wenning. Lancet Neurol 2013;12: 264–74.

ATH434-202 Interim Biomarker Data Support Clinical Observations

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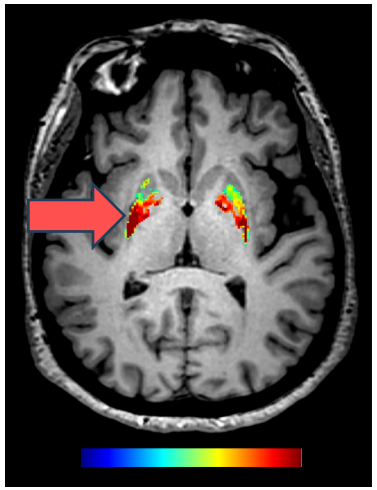
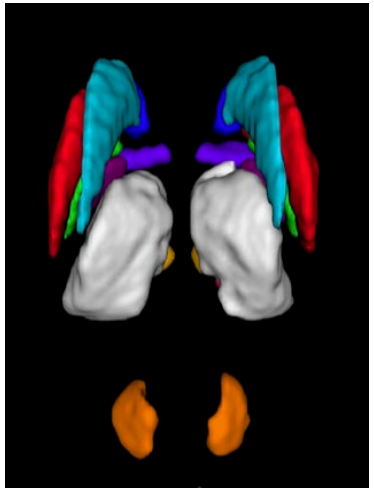
Brain Iron



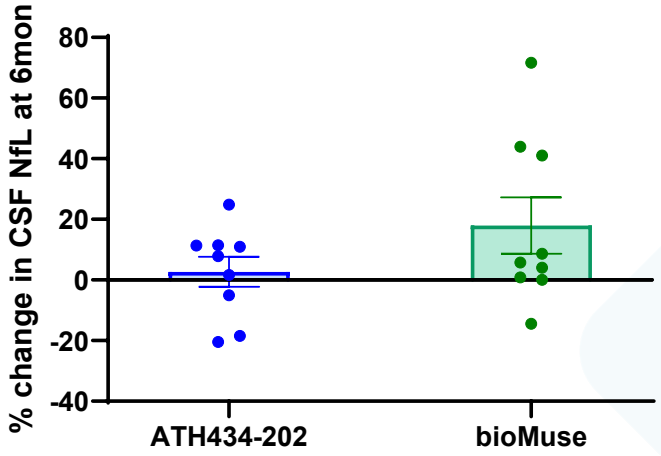
Iron content was stable in the s. nigra, putamen and globus pallidus over 12 mo in clinical responders

Brain Volume



Brain volume stable between 6 and 12 mo in clinical responders

Neuronal Injury Marker



Mean levels of NfL, a marker of neuronal injury only ↑2.7% in ATH434-patients compared to ↑17.9% in untreated patients (bioMUSE)

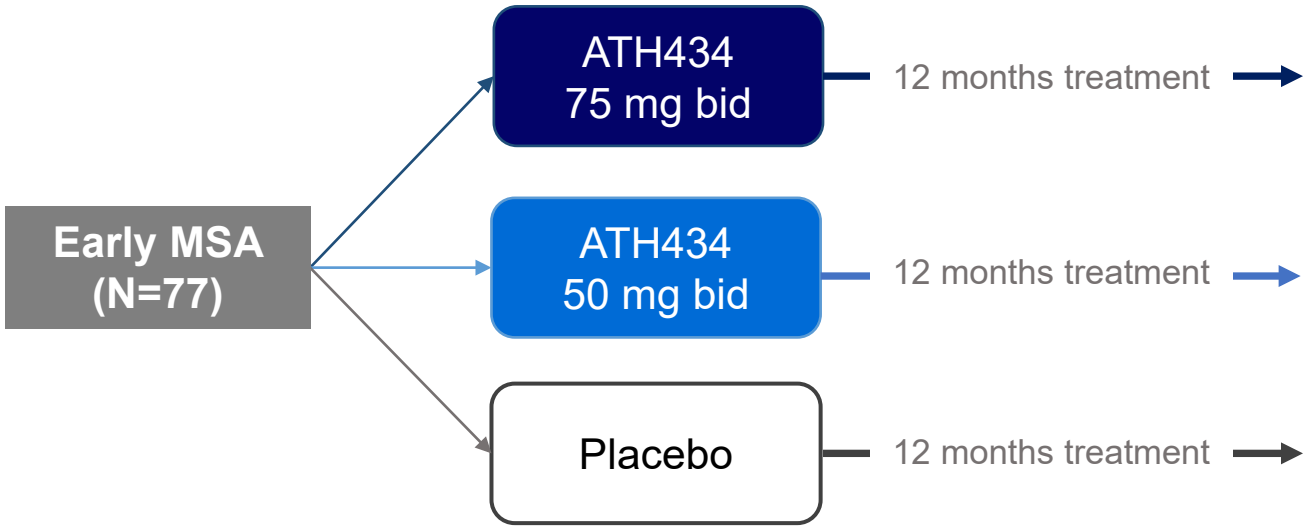
MRI data at 6 months (n=10) and 12 months (n=3)
NfL (neurofilament light chain) data at 6 months.

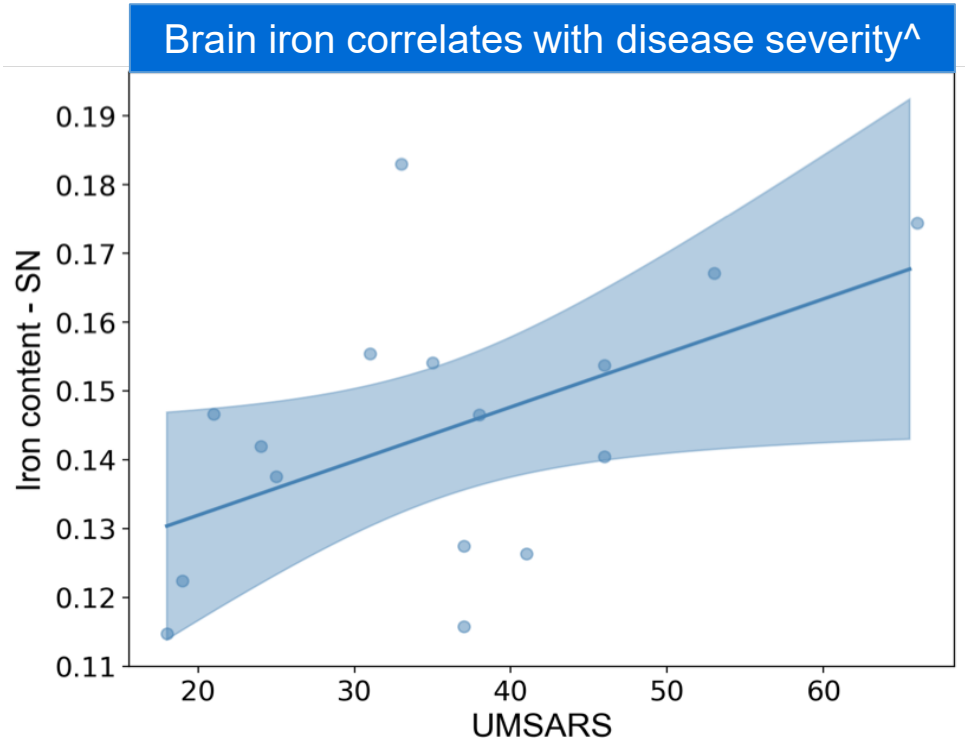
Encouraging Clinical and Biomarker Results ATH434-202 Interim Analysis

- **Clinical response observed in rapidly progressive, unremitting disease**
  - 30% had stable or improved overall neurological symptoms
- Objective biomarkers demonstrated improvement consistent with clinical findings
- ATH434 well-tolerated and had no serious adverse events related to study drug

Participants who stabilized or improved had less advanced disease

ATH434-201 Phase 2 Double-Blind Design with Topline Data Expected in January 2025



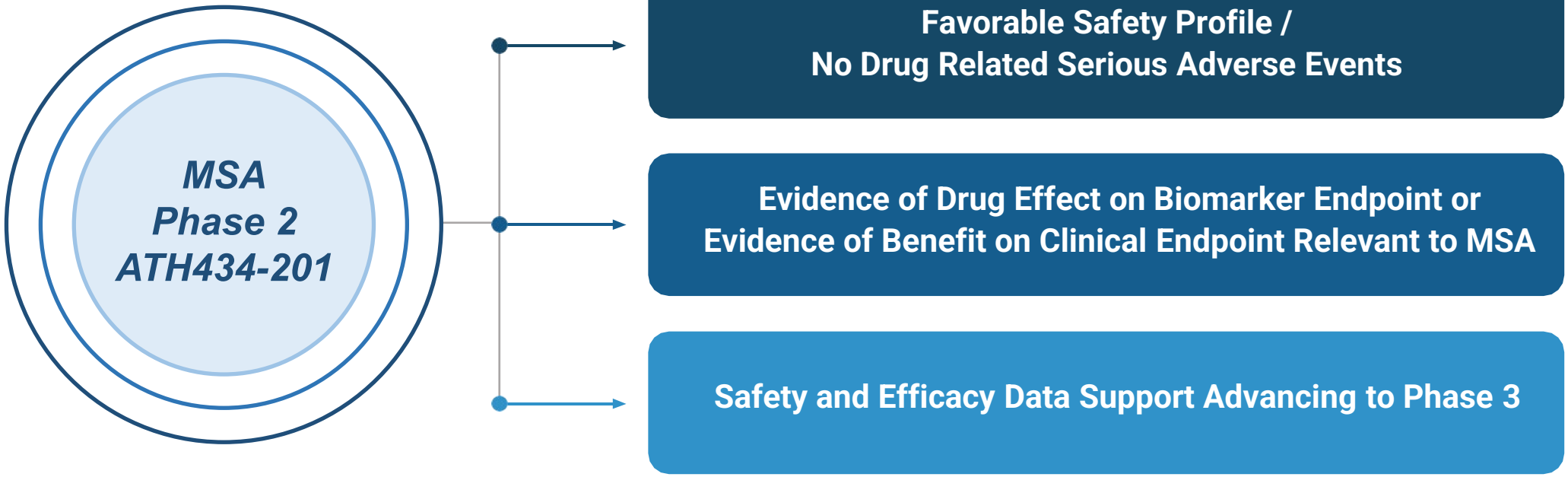


BioMUSE Natural History Study

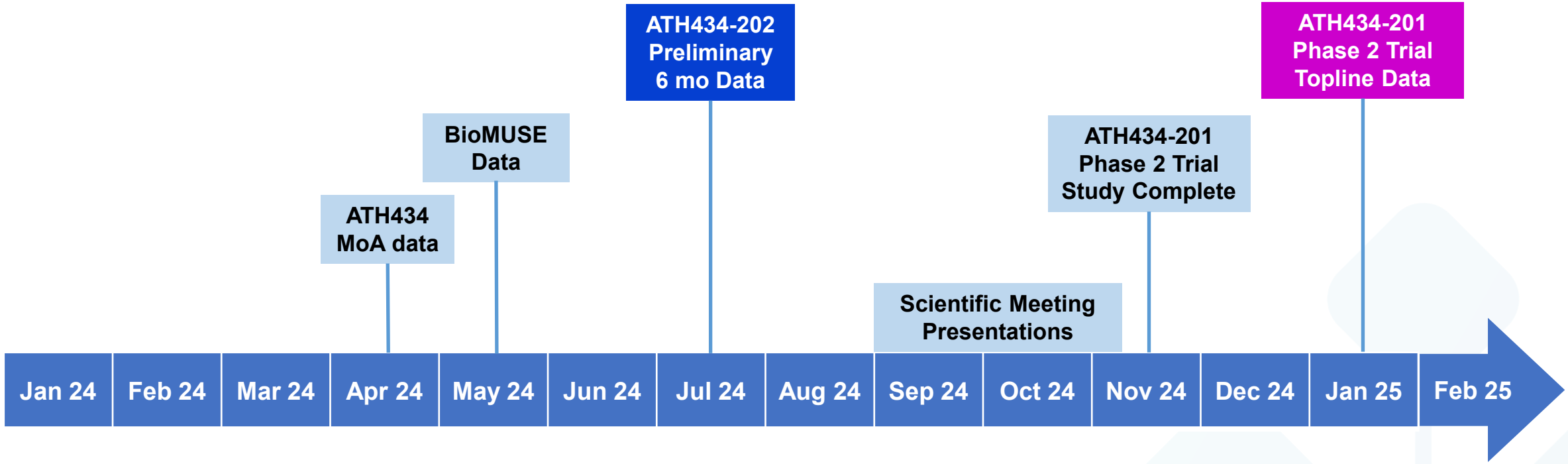
^Baseline ($p<0.05$), Over 12 months ($p=0.004$)

Source: Claassen, et al. Mov Disorders 2021

Target Measures for Success



Key Milestones



Alterity: Poised for Progress

- Targeting Orphan disease with no approved treatments
- Natural History Study de-risked Phase 2
- Positive interim data in open label study confirms clinical development approach
- Phase 2 double-blind data expected in January 2025
- Development team with multiple FDA approvals
- Cash balance of AU$9.28M as of 30 Sept 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 Open label Trial

- ✓ Jul 2024: Preliminary 6-mo Data
- H1 2025: 12-month Data

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ASX:ATH | NASDAQ:ATHE