Corporate Presentation

Alterity THERAPEUTICS

January 2026

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 2025 Form 20-F, filed with US Securities and Exchange Commission, in particular Item 3, Section D, titled “Risk Factors.”

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THERAPEUTICS

Alterity is a late clinical stage biopharmaceutical company dedicated to developing treatments for neurodegenerative diseases

- Alterity means the state of being different
- Our goal is to slow the course of disease progression
- We strive to create an alternate future and improve patient quality of life

Investment highlights

Positive Phase 2 data in Multiple system atrophy, a Parkinsonian disorder

Robust efficacy on functional endpoint in double-blind study

Large market potential in neurodegenerative diseases

Potential to treat Parkinson's disease and related disorders

Oral administration preferred over competition

Patient friendly administration

Highly experienced leadership team in movement disorders

Three FDA approvals in neurology

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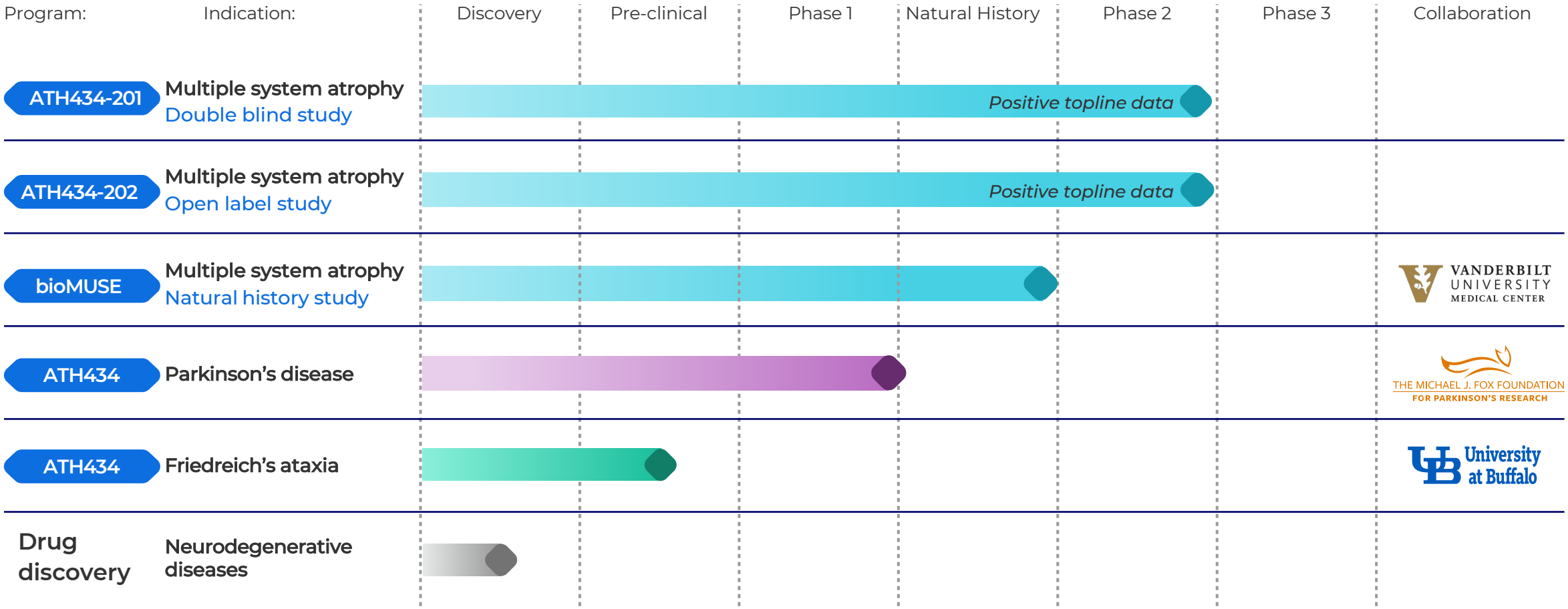
Promising portfolio in neurodegenerative diseases



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Multiple System Atrophy (MSA): Parkinsonian disorder with no approved treatment

Rapidly progressive
Highly debilitating

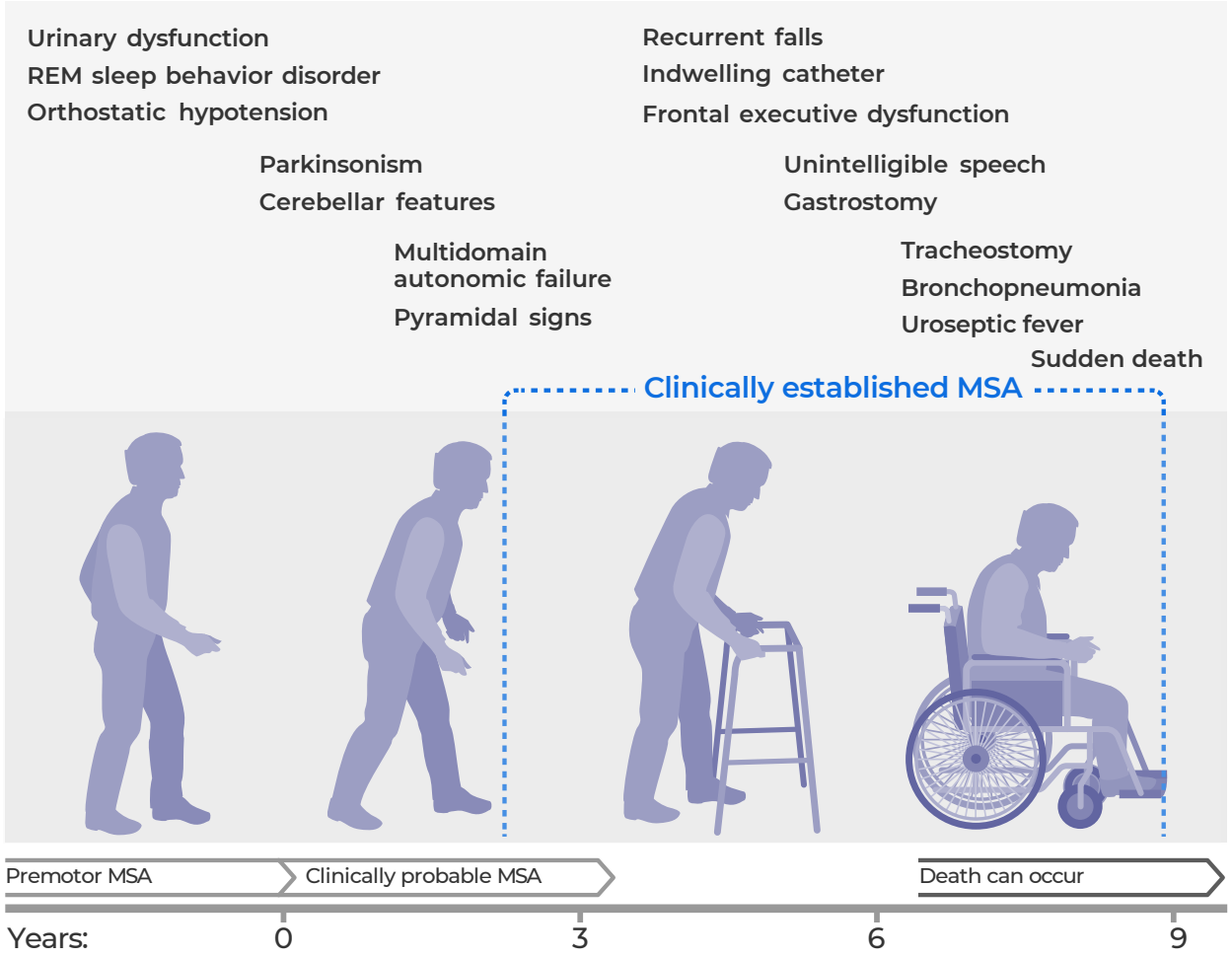
Up to 50,000
patients in U.S.

Disease characteristics:

- Motor: Parkinsonism, uncoordinated movements, balance problems, falls
- Autonomic dysfunction: blood pressure maintenance, bladder control, bowel function
- Atrophy and α-synuclein accumulation in multiple brain regions

Over 50%
require wheelchair in 5 years

7.5 years
median survival after symptom onset



Sources: Fanciulli, Wenning. NEJM 2015 | Wenning, et al. Mov Disorders 2022 | Coon, et al. Brain 2015 | Multiple System Atrophy: National Institute of Neurological Disorders and Stroke (nih.gov)

Targeting the pathology in Parkinsonian disorders

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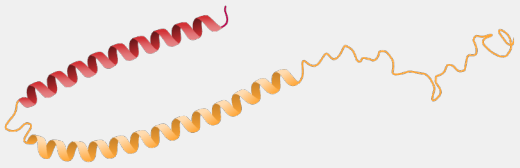
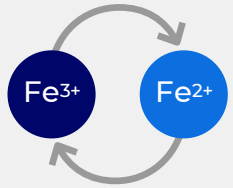
Alpha-synuclein and iron balance vital for normal CNS function



α-Synuclein protein:

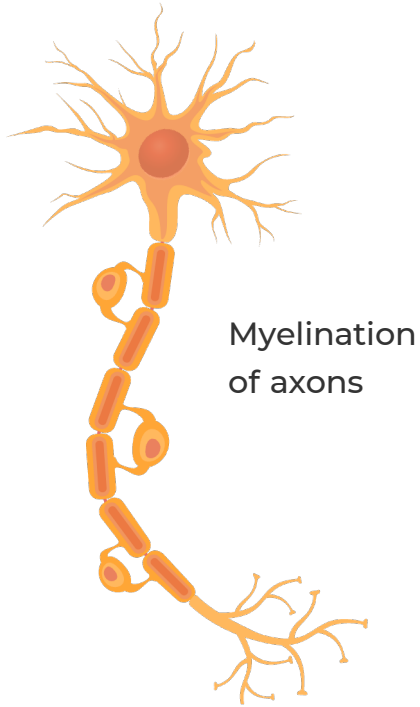
- Present in all neurons
- Regulates neurotransmitter release
- Facilitates neuronal communication



Fe^{2+} Reactive
Fe^{3+} Stable

Two forms of iron required for cellular function:

- Energy production and activity of many enzymes
- Neurotransmitter synthesis (e.g., dopamine)
- Myelin synthesis



Myelination of axons

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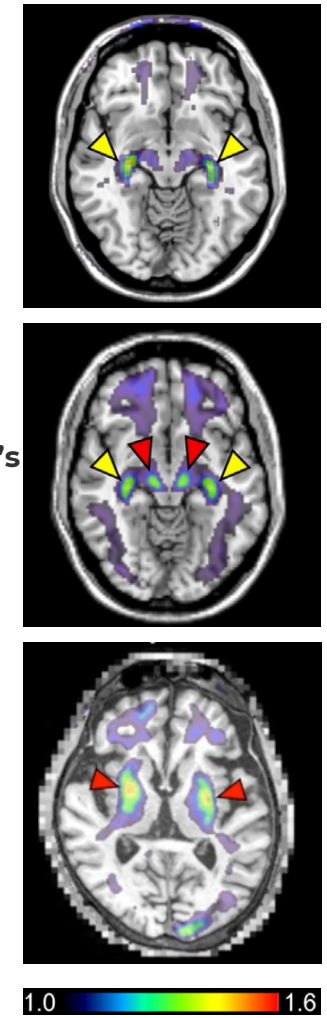
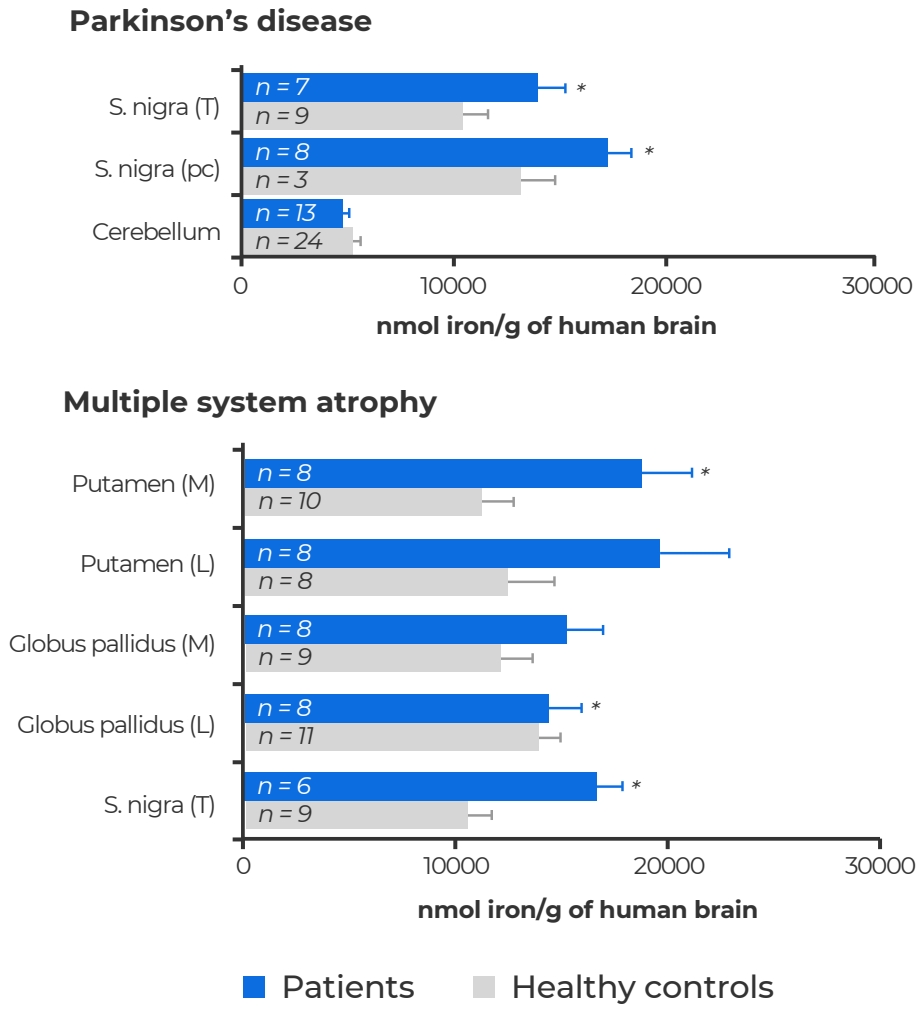
Pathology of Parkinsonian disorders

α-synuclein Aggregation



PET imaging of α-synuclein pathology (18F-C05-05)

Increased Brain Iron



Endo et al., Neuron 2024; Dexter et al. Brain.1991

Role of iron and α-synuclein in disease pathogenesis

The Relevance of Iron in the Pathogenesis of Multiple System Atrophy: A Viewpoint

Christine Kaindlstorfer [1], Kurt A Jellinger [2], Sabine Eschlböck [1], Nadia Stefanova [1], Günter Weiss [3], Gregor K Wenning [1]

Iron converts native α-SYN into a β-sheet conformation and promotes its aggregation *either directly or via increasing levels of oxidative stress.*

The disturbance of iron homeostasis leads to abnormal iron deposition in the brain and causes neurotoxicity via generation of free radicals and oxidative stress.

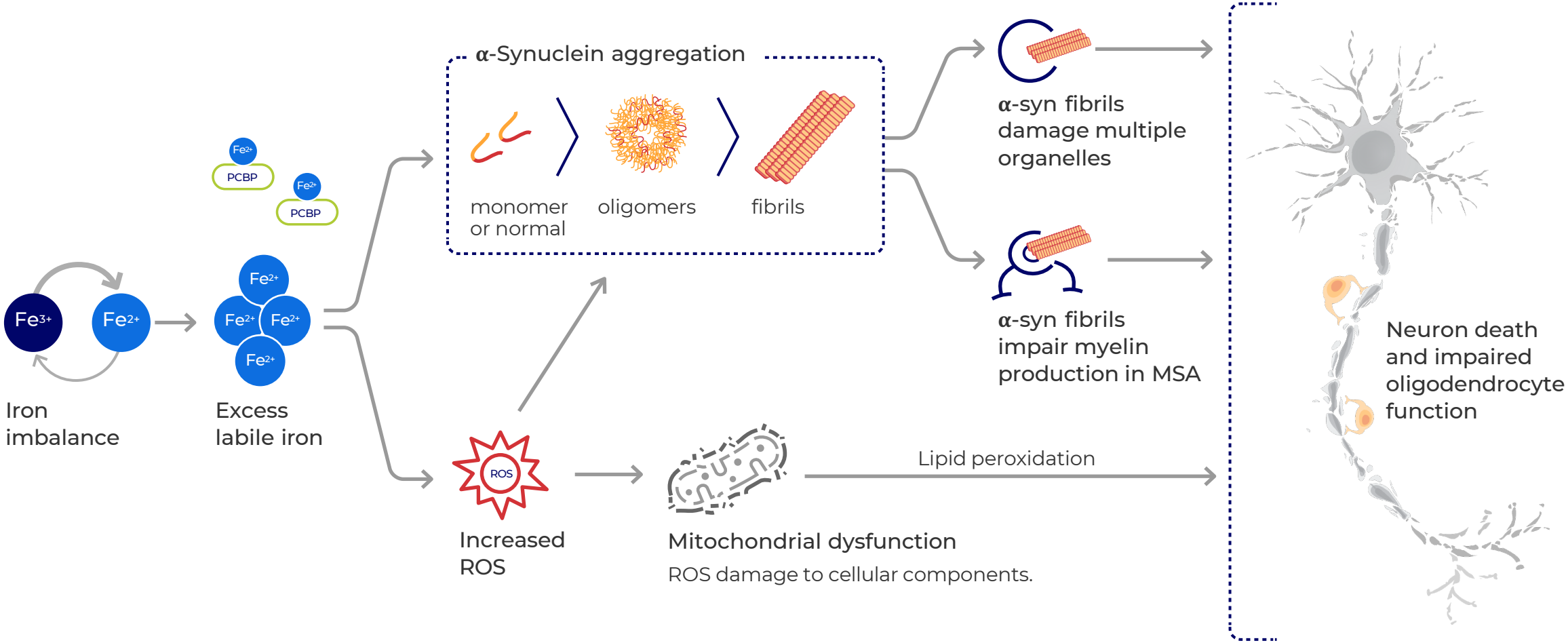
The Irony of Iron: The Element with Diverse Influence on Neurodegenerative Diseases

Seojin Lee [1 2], Gabor G Kovacs [1 2 3]

The close association of iron accumulation with distinct α-synuclein-pathology-related anatomical regions of the two disease subtypes supports the critical involvement of pathological iron in disease progression *and further suggests the two disease subtypes as distinct pathological identities in relation to disease pathogenesis.*

doi 10.3233/JAD-170601 (2018); doi.org/10.3390/ijms25084269 (2024)

Excess labile iron is the key driver of pathology causing α-synuclein aggregation and oxidative injury



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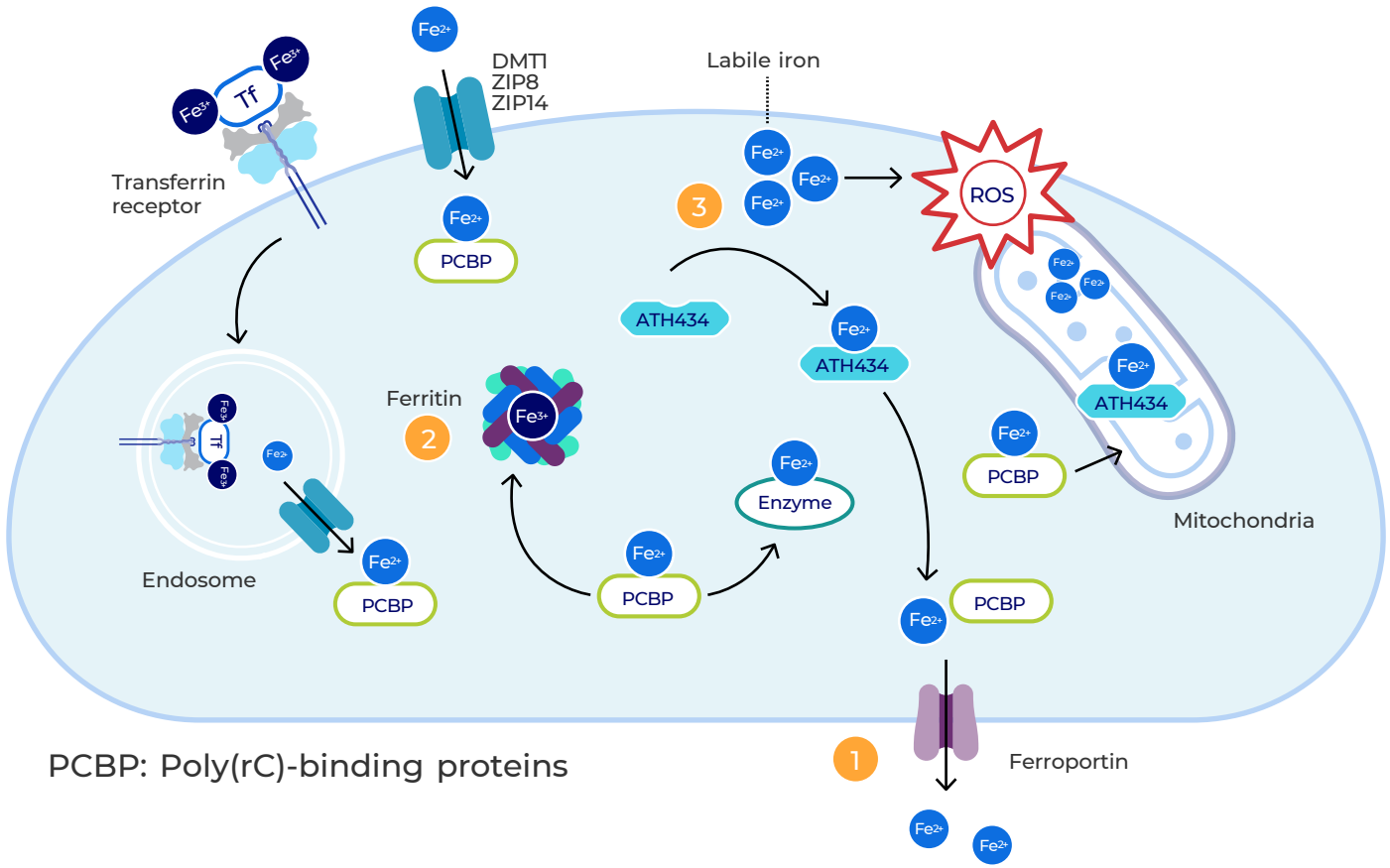
ATH434 mechanism of action: Iron chaperone

ATH434 chaperones excess labile (reactive) iron to reduce neuronal injury



PCBP: Poly(rC)-binding proteins

Fe^{2+} Reactive

Fe^{3+} Stable

Chaperone mechanisms:

1. Efflux iron from cell (ferroportin)
2. Increase iron storage (ferritin)
3. Buffering Fe^{2+} in labile iron pool

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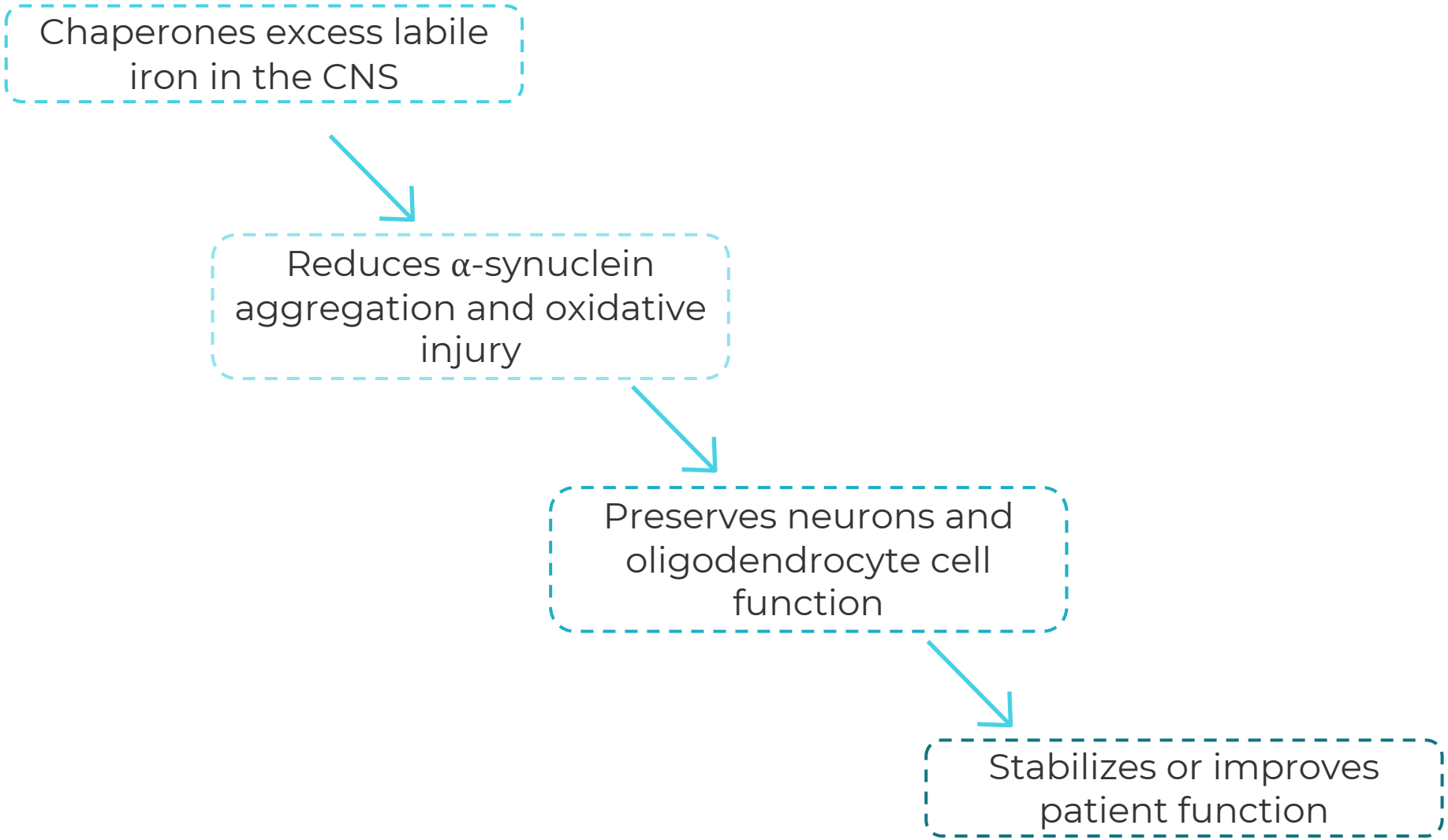
Sources: Adapted from Yanatori et al., BBA 2020 and Philpott et al., Frontiers Mol Bio. 2023 | Pall, et al. Metallomics, 2024.

Treatment approach: Address underlying pathology



Based on mechanism of action, ATH434 is a potential disease modifying therapy

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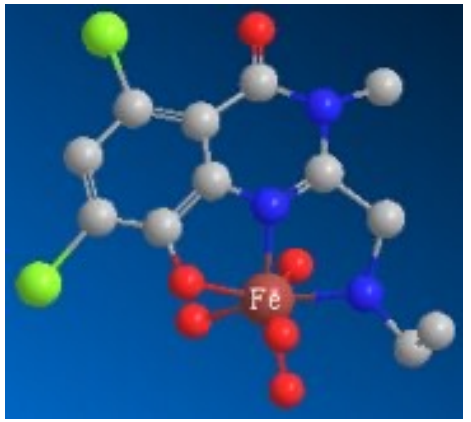
ATH434: Small molecule drug candidate

Oral administration	Preferred by patients and doctors vs infusions (IV, intrathecal) or injections
Blood-brain barrier penetrant	Acts intracellularly to address underlying pathology
Iron chaperone	Moderate binding affinity, redistributes excess labile iron in CNS
Broad treatment potential	Potential to treat many neurodegenerative diseases (e.g., Parkinson's, Frederich Ataxia)
Orphan & Fast Track designations	US FDA Fast Track Designation and Orphan drug designation in U.S. and EU

ATH434 binding to labile iron



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Accumulated evidence of ATH434 efficacy

Target disease	Model	Midbrain iron incl. s. nigra	α-Synuclein	Preserve neurons / function	Clinical observations
Parkinson's disease	Monkey MPTP	⟷	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	⟷	↓	↑	Improved motor performance

⟷ **Stable**

ATH434 consistently improved motor performance by reducing α-synuclein aggregation and preserving neurons

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Sources: Bradbury et al, Am Acad. Neurol 2024; 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

ATH434 clinical development program in MSA

Diligent approach to de-risk development program

Natural History Study

bioMUSE

- Observational study in individuals with MSA
- Designed to de-risk clinical development program
- Identify biomarkers to improve accuracy of patient selection

Phase 2

ATH434-201

Randomized double-blind placebo-controlled trial

Results: clinically meaningful efficacy on MSA rating scale, measures of orthostatic hypotension, disease severity

ATH434-202

Open label trial in advanced MSA patients

Results: showed improved neurological symptoms in more advanced patients and favorable safety

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BioMUSE natural history study informs and de-risks clinical development program

N=21

Patient criteria:

Clinically Probable MSA

Biomarkers:

- MRI: iron, volume, glial pathology
- Fluid: NfL, aggregated α-synuclein
- Digital: Wearable movement sensors

Clinical: UMSARS 1, autonomic function, motor function

global measures

12 months of observation

Objective:

Track clinical and biomarker endpoints over observation period

BioMUSE natural history study allowed us to optimize patient selection in our Phase 2 trials

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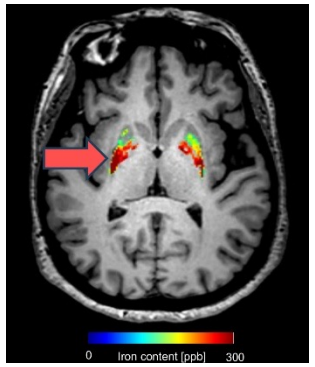
*Biomarkers of progression in Multiple System Atrophy (bioMUSE).; 1NfL: Neurofilament light chain

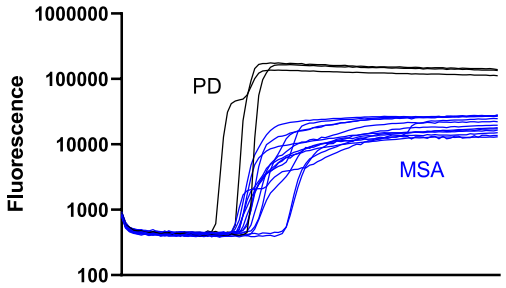
BioMUSE natural history study results

Optimized patient selection in Phase 2 trials

Advanced MRI methods



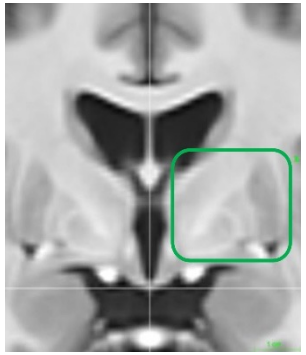
α-synuclein SAA in CSF



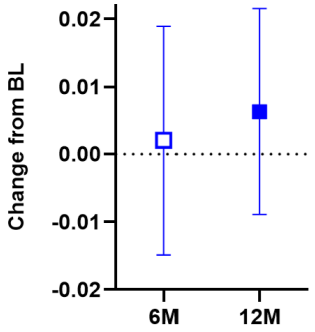
- Identified "iron signature" of early MSA
- Differentiated MSA from Parkinson's disease (PD)
- Revised selection criteria in ATH434-201 and ATH434-202 protocols to exclude PD patients

Precision biomarker assessment

Structural mapping



Iron content in pallidum



- Improved precision of volume measurements
- Novel strategies for measuring brain iron in individual regions
- State of the art methods enabled precise measurements of brain iron and volume with MRI

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

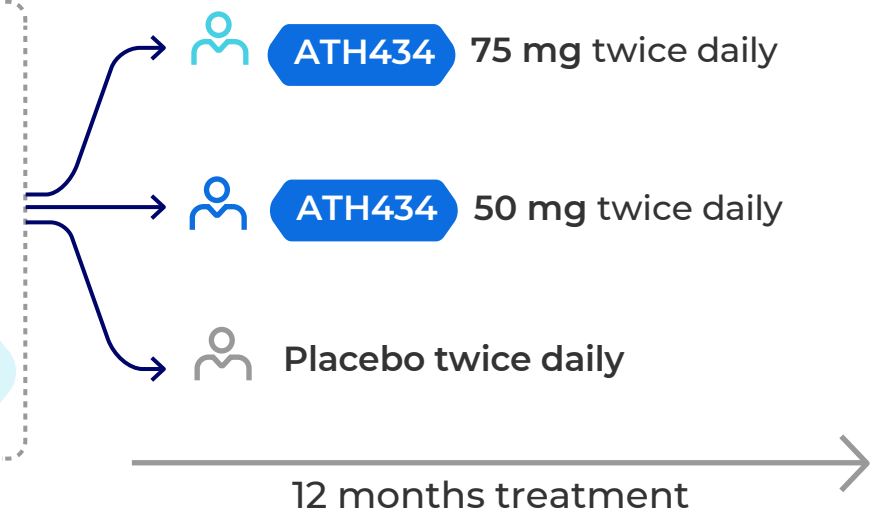
ATH434-201: Randomized, double-blind, placebo-controlled study

Patient criteria:

N=77

- Clinical diagnosis of MSA
- Motor symptoms ≤4 years
- No severe impairment
- Elevated brain iron on MRI
- Elevated plasma NfL

Study design:



Endpoints:

Key clinical endpoint:
modified UMSARS Part 1

Additional secondary endpoints:
CGI-S, OHSA, Wearable Sensors, Safety

Key biomarker endpoint:
brain iron content by MRI

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MRI - Magnetic Resonance Imaging; **UMSARS -** Unified MSA Rating Scale (UMSARS) Scale– measures activities of daily living
CGI-S - Clinical Global Impression-Severity scale; **OHSA** - Orthostatic Hypotension Symptom Assessment

Importance of the Unified MSA Rating Scale Part I (UMSARS I)

UMSARS Part I Items:

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

Rated from 0 to 48
higher scores worse

UMSARS is the FDA endorsed clinical endpoint to support approval for the treatment of MSA

Validated rating scale to assess MSA disease severity

Rates functional impairment in domains affected in MSA

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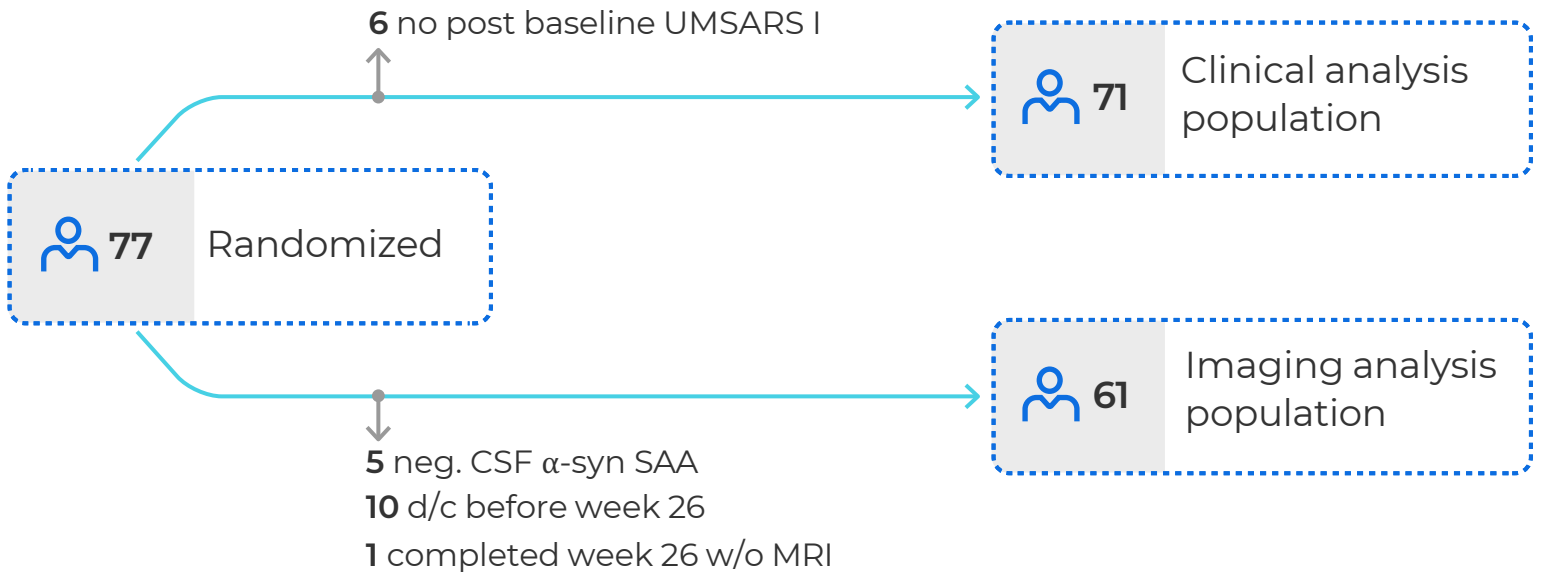
^ Modified version of UMSARS I excludes sexual function item

Populations and key endpoints



Endpoint	Change from BL to week 52	Population
Biomarker (Primary)	Iron content in s. nigra by MRI	Imaging
Clinical (Key secondary)	Change in Modified UMSARS Part I	Clinical

All patients in Imaging and Clinical analysis populations were randomized and treated

Baseline characteristics

	Placebo N=22	ATH434-201 50 mg twice daily N=25	ATH434-201 75 mg twice daily N=24
Age (y)	61.3 (6.6)	63.1 (6.1)	63.9 (6.7)
Gender (% male)	63.6%	52.0%	62.5%
Duration of motor symptoms (y)	2.5 (0.8)	2.6 (0.8)	2.3 (0.9)
Modified UMSARS I	16.9 (3.9)	15.2 (5.4)	14.4 (4.4)
Motor score of Parkinson plus scale[1]	57.6 (14.2)	47.8 (18.4)	48.9 (16.8)
Plasma NfL (pg/mL)	34.9 (12.5)	31.1 (9.1)	32.3 (9.0)
CSF aggregating α-syn SAA (+)	91%	92%	96%
OH symptom assessment	13.5 (9.8)	13.8 (13.2)	15.0 (12.2)
Clinical phenotype: MSA-P (%)	59.1%	60.0%	70.8%
Severe orthostatic hypotension	4.5%	4.0%	29.2% ↑

Groups balanced at baseline except for severe orthostatic hypotension – a predictor of rapid disease progression

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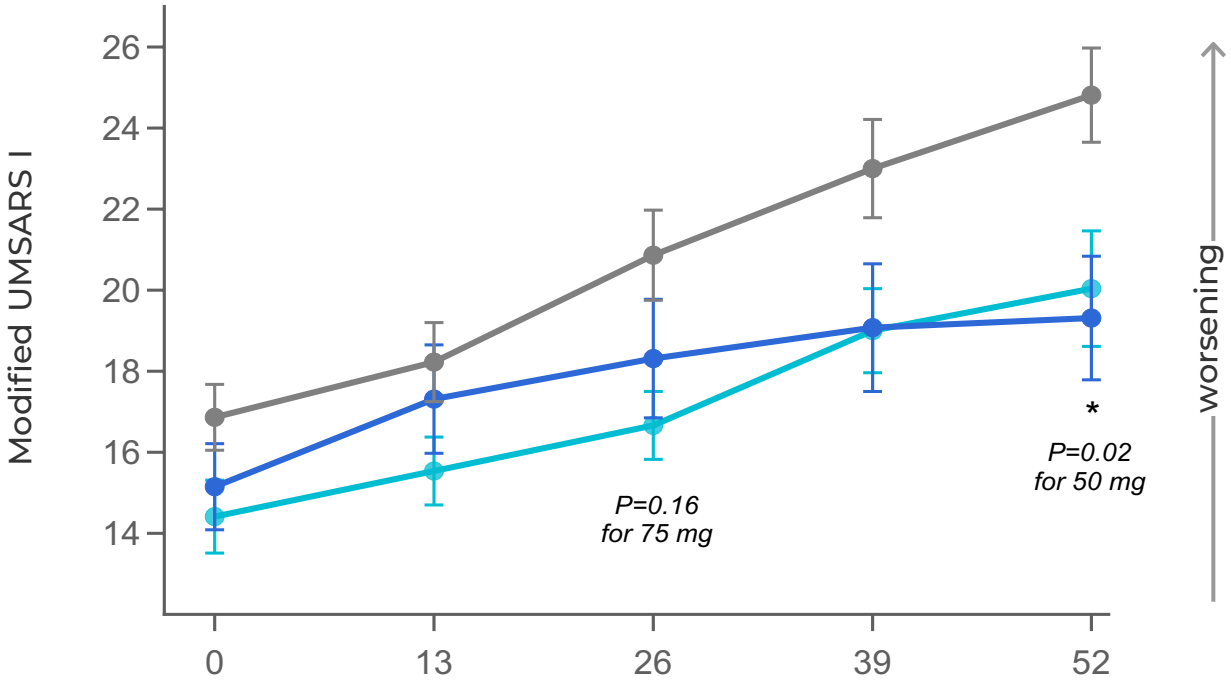
Clinical Analysis Population

[1] Payan et al. PlosOne 2011

Clinically significant efficacy on modified UMSARS Part I
Change from baseline to week 52



	Difference vs. placebo LS mean (SE)	Relative treatment effect	
Placebo N=22			
ATH434 50 mg N=25	**- 3.8 (1.6)**	**48%**	
ATH434 75 mg N=24	**- 2.4 (1.7)**	**30%**	
ATH434 75 mg N=24	**- 2.8 (1.7)**	**35%**	***P*-value 0.11**

Effect of ATH434 with Baseline OH change as covariate given imbalance of severe OH at baseline

Relative Treatment Effect

$$\frac{\text{Change}_{\text{ATH434}} - \text{Change}_{\text{Placebo}}}{\text{Change}_{\text{Placebo}}}$$

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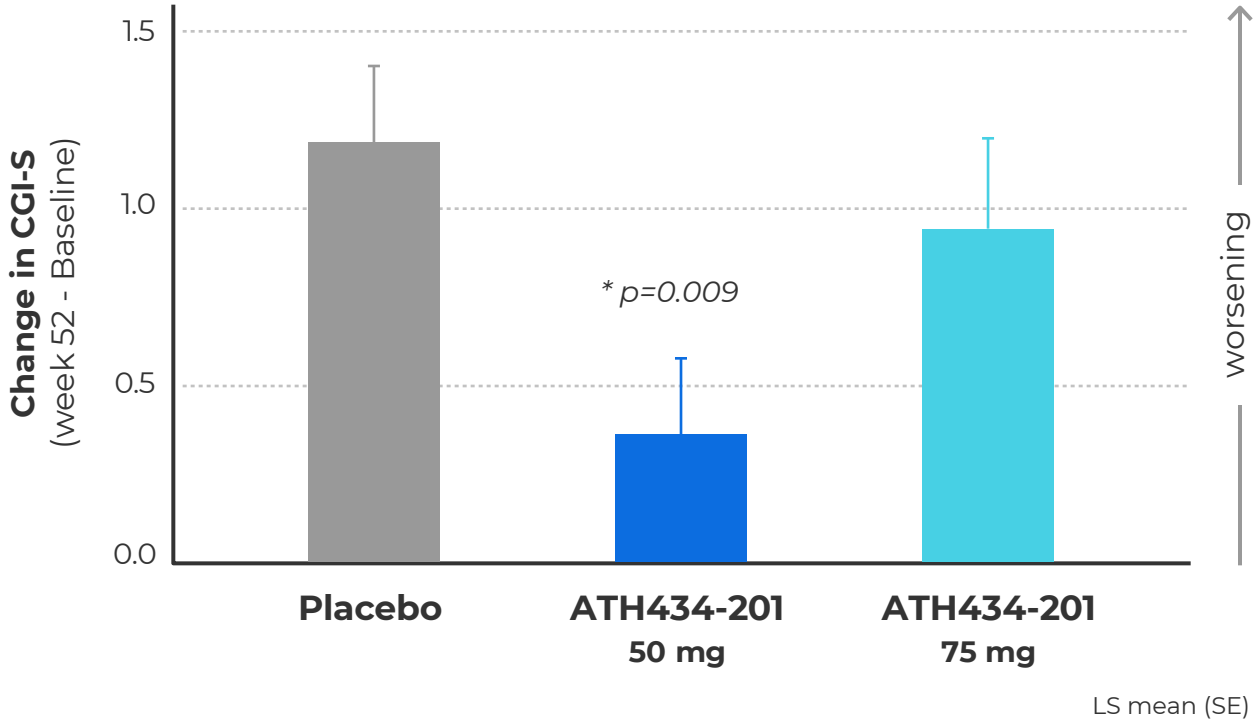
Clinical Analysis Population

Efficacy on Clinical Global Impression of Severity (CGI-S) scale
Change from baseline to week 52



- CGI-S
  - 7-point scale, ranging from 1 to 7
  - higher score indicates a worse outcome
- Assesses total picture over prior 28 days
  - illness severity, impact of illness on function, level of distress and any other aspects of impairment

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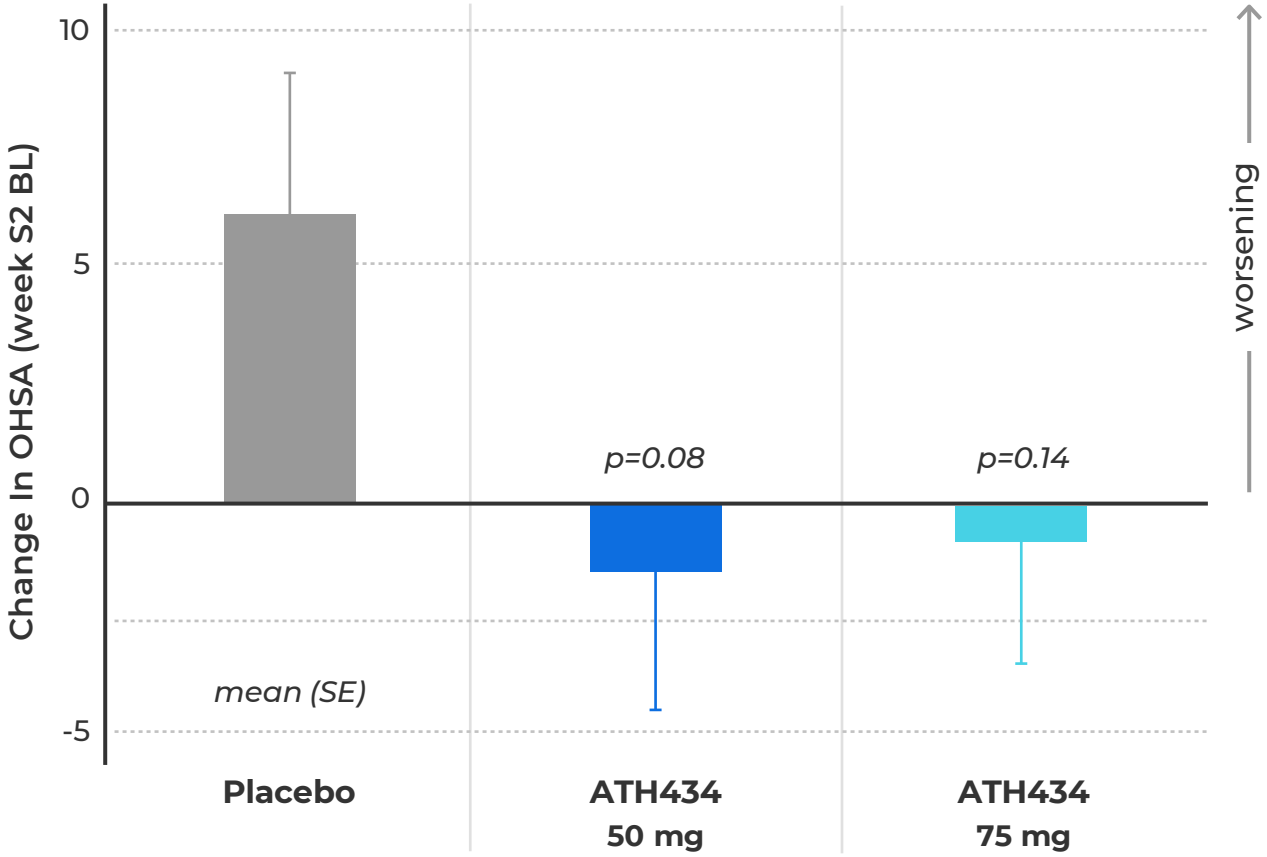
Clinical Analysis Population

Orthostatic Hypotension Symptom Assessment (OHSA)
Change from baseline to week 52



- Assesses symptoms of low blood pressure when going from sitting to standing (e.g., dizziness / feeling faint / lightheadedness)
- Patient reported outcome

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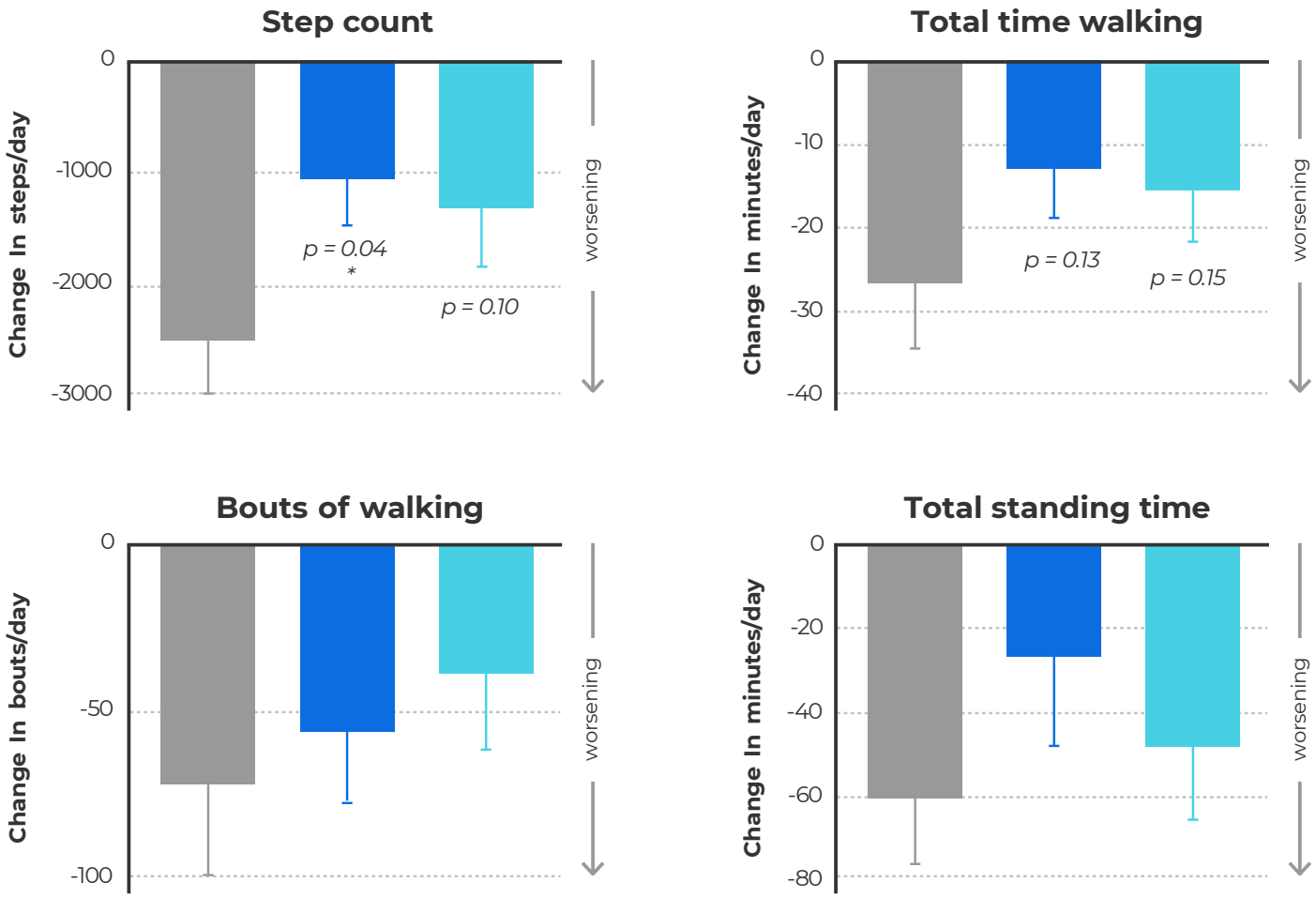
Clinical Analysis Population

Kaufmann, et al. Clin Auton Res 2012..

ATH434 preserved walking in outpatient setting
Change from baseline to week 52

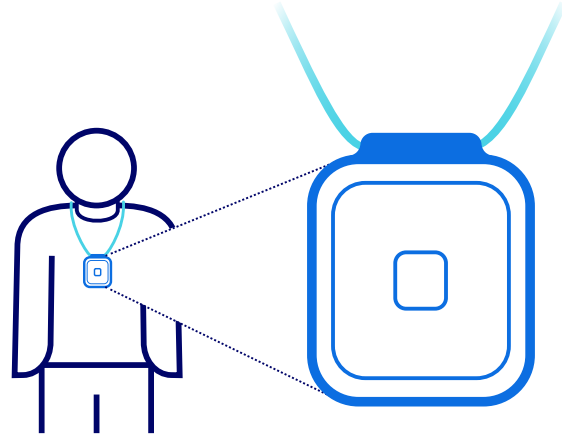


Placebo

ATH434-201
50 mg

ATH434-201
75 mg

Pendant
Wearable movement sensor



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Clinical Analysis Population

Adverse Events

N (%) of subjects [1]	Placebo twice daily N=26	ATH434-201 50 mg N=25	ATH434-201 75 mg N=26
Any Adverse Event (AE)	24 (92.3%)	21 (84.0%)	25 (96.2%)
UTI	14 (53.8%)	10 (40.0%)	7 (26.9%)
Fall	8 (30.8%)	7 (28.0%)	8 (30.8%)
Covid-19	1 (3.8%)	6 (24.0%)	4 (15.4%)
Fatigue	2 (7.7%)	1 (4.0%)	5 (19.2%)
Back pain	1 (3.8%)	3 (12.0%)	2 (7.7%)
Severe AEs [2]	8 (30.8%)	3 (12.0%)	6 (23.1%)
Serious AEs [2]	10 (38.5%)	5 (20.0%)	7 (26.9%)

- **Similar rates of AEs in ATH434 and placebo participants**
- **No severe or serious AEs related to study drug**
- **No hematologic side effects**

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1 - Reporting one or more event
2 - None related to Study Drug

Neuroimaging Endpoints

Change in Iron Content by MRI

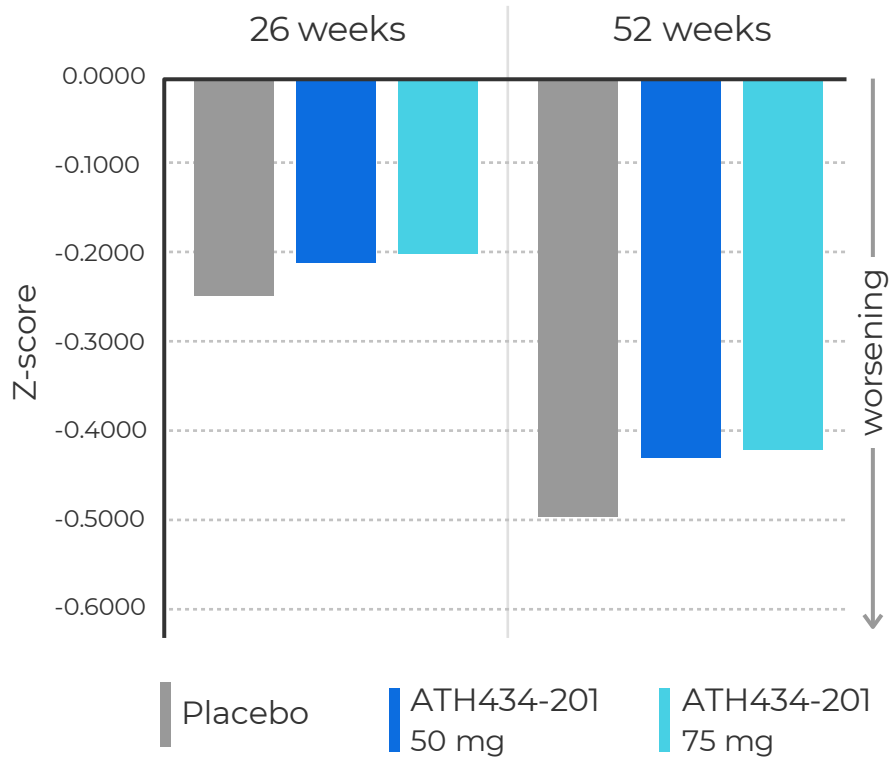
	50 mg		75 mg	
Region	Week 26	Week 52	Week 26	Week 52
Pallidum	↓	↓¶	↓	↓
Putamen	↓^	↓	↔	↔
S. nigra	↔	↓	↔	↔

Compared to placebo: ↓ Iron content, ↔ No observable difference, ^p = 0.03, ¶p = 0.08

ATH434 demonstrated target engagement on reducing iron on MRI

- Reduced/stabilized iron content in Pallidum (GP) > Putamen
- Reduced iron content in s. nigra at 50 mg dose but not 75 mg (primary endpoint)

Change in Brain Volume*



ATH434 showed trends in preserving brain volume

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* MSA Atrophy Index: composite z-score of putamen, GP, cerebellum and brainstem vs. healthy age-matched population

ATH434-202: Open label study in advanced MSA

Design	Single arm, open-label
Population	Advanced MSA (n=10)
Treatment	ATH434 75 mg BID x 12 months
Brain MRI Biomarkers	Iron, volume
Clinical Measures	UMSARS I, clinical/patient global impressions of change

Parameter	**ATH434-202** 75 mg BID N=10	**ATH434-201** 75mg BID N=24
Age (yr)	64.5 (7.5)	63.9 (6.7)
Duration of motor symptoms (yr)	3.9 (1.8)	2.3 (0.9)
Modified UMSARS I[1]	19.2 (5.3)	14.4 (4.4)
Motor score of Parkinson Plus Scale2	57.5 (20.4)	48.9 (16.8)
Plasma NfL (pg/mL)	42.1 (14.1)	32.3 (9.0)
OH Symptom Assessment	16.7 (14.8)	15.0 (12.2)
Severe Orthostatic Hypotension	40.0%	29.2%

Mean (SD)

Key objective was to assess efficacy and safety of ATH434 75 mg dose for comparison to 75 mg dose in 201 double-blind study

[1] MSA affected areas by MSA-atrophy index. Trujillo, P. et al Annals of Clin and Trans Neuro, 2025

ATH434-202: Key data at 75 mg dose
Comparison to double blind study at 12 mo

Change over 12 Months	ATH434-202 75 mg BID N=10	ATH434-201 75mg BID N=24
Modified UMSARS I	3.5 (4.7)	5.6 (5.6)
Clinical global impression of change (% stable)	30%	21%
Patient global impression of change (% stable)	30%	26.4%
Brain volume[1]	-0.44 (0.14)	-0.42 (0.29)
		Mean (SD)

- No serious AEs related to study drug
- AEs consistent with underlying disease

The 75 mg dose demonstrated comparable efficacy to that observed in the double-blind study

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[1] In MSA affected areas by MSA-atrophy index. Trujillo, P. et al. Annals of Clin and Trans Neuro, 2025

ATH434 Phase 2 summary

Double-blind trial: ATH434 demonstrated clinically significant efficacy in slowing disease progression in MSA

- Both dose levels efficacious on UMSARS I and important secondary endpoints
- Efficacy signal at 75 mg strengthens when accounting for baseline differences in severe OH, a predictor of rapid progression
- Demonstrated target engagement with reduced iron accumulation in MSA affected brain regions
- No safety signals and was well-tolerated

Open-label trial: Similar efficacy in advanced MSA as observed in double-blind study

- Data consistent on key efficacy endpoints
- Biomarkers demonstrated target engagement and similar effect on brain volume
- Comparable safety to double-blind study

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Commercial assessment & corporate overview

Approach to commercial assessment
Conducted by independent marketing research and forecasting group

Exploratory Research

- **Conduct secondary market research** Assess unmet needs and competitive landscape
- **Develop target product profile** based on Phase 2 clinical data
- **Qualitative research**

  Conduct In-depth interviews and Focus groups with general neurologists, movement disorder neurologists and autonomic specialists to identify decision-making behavior and key drivers and barriers to adoption leveraging the target product profile

- **Develop physician screener and discussion guide** for Quantitative Research

Quantitative Research

- **Conduct ~30-minute online survey among 100 neurologists (~50% general, ~50% specialists)** to determine their awareness, interest, market demand and likelihood of product adoption
- **Assess the Target Product Profile** to better understand its viability, differentiation opportunities and potential barriers to adoption
- **Rigorous methods used to ensure data quality and integrity**

Opportunity Analysis and Forecast

- **Develop forecast assumptions** based on qualitative and quantitative findings.
- **Build a financial valuation** of ATH434 in treatment of MSA

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Key attributes of ATH434 drive significant commercial opportunity in MSA

Strong Intent to Prescribe

Over 70% of neurologists were “extremely likely” or “very likely’ to prescribe ATH434 based on its profile

Substantial Unmet Need

Severely debilitating illness with no approved treatment ripe for new entrants

Critical need for a tolerable, disease modifying therapy

Targeted Mechanism of Action

Importance of inhibiting α-synuclein aggregation to address the underlying pathology of disease

Efficacy is the Key Driver

Slowing disease progression is key driver of physician interest

Stabilizing orthostatic hypotension^, one of the most challenging symptoms in MSA, strongly positions ATH434

USD $2.4 Billion

Potential worldwide annual peak sales for ATH434 in MSA

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^Orthostatic hypertension is the drop in blood pressure on standing; Global peak sales number in U.S. Dollars; Independent market research survey conducted in 2025. Peak sales estimate based on U.S. prevalence of ~19,000

Key Objectives for 2026

The Foundation is Set

- Robust efficacy in Phase 2 study in MSA, a rapidly progressive rare disease with no approved treatment
- Commercial assessment demonstrated significant opportunity: USD $2.4B potential peak sales
- Moving into Phase 3 program led by an accomplished team with multiple FDA approvals in neurology
- Cash Balance of A$54.5M as of 30 September

Finalize Regulatory Strategy

- **Align with the U.S. FDA on pivotal Phase 3 clinical trial protocol**
  - Conduct meetings related to non-clinical data and chemistry/manufacturing
  - End of Phase 2 meeting mid-year

Deepen External Reach

- **Publish Phase 2 results in peer-reviewed journal**
- Deliver poster and presentations at key medical and advocacy meetings
- Expand global IR, PR and BD outreach

Build for Scalable Growth

- **Expand intellectual property protection**
- Evaluate additional high-value indications to grow the pipeline
- Strengthen the team to enhance organizational capabilities

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ASX: ATH
NASDAQ: ATHE

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