

# Corporate Presentation

April 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.”



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

# Redefining Neurodegenerative Disease Therapy

## Advancing ATH434, a Potential First-in-Class, Disease-Modifying Therapy for Multiple System Atrophy (MSA)

### Differentiated, Disease-Modifying Approach for MSA

Oral iron chaperone ATH434 targets excess reactive iron and  $\alpha$ -synucleinopathies  
Blood brain barrier penetrant small molecule

### Compelling Phase 2 Efficacy on FDA-Endorsed Endpoint

Up to 48% slowing of disease progression vs. placebo on FDA-endorsed endpoint\*  
Favorable safety profile with no drug-related serious adverse events

### Unmet Need with Significant Commercial Potential

MSA is a rare, rapidly progressive disease (up to 50,000 U.S. patients)  
Independent assessment supports ~\$2.4B global peak sales opportunity in MSA

### Pivotal Advancement in 2026 with Clear Regulatory Path

End-of-Phase 2 FDA meeting planned for mid-2026 to align on Phase 3 design  
Veteran neurology team with proven FDA-approval track record

# Broad opportunity for ATH434 in neurodegenerative disease

Program:	Discovery / Pre-clinical	Phase 1	Natural History	Phase 2	Phase 3	Collaboration
Multiple system atrophy Double blind study						
Multiple system atrophy Open label study in advanced MSA						
Multiple system atrophy Natural history study						
Parkinson's disease						
Friedreich's ataxia						
Drug discovery						

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

**Rapidly progressive**

Highly debilitating

**Up to 50,000**

patients in U.S.

## Disease characteristics:

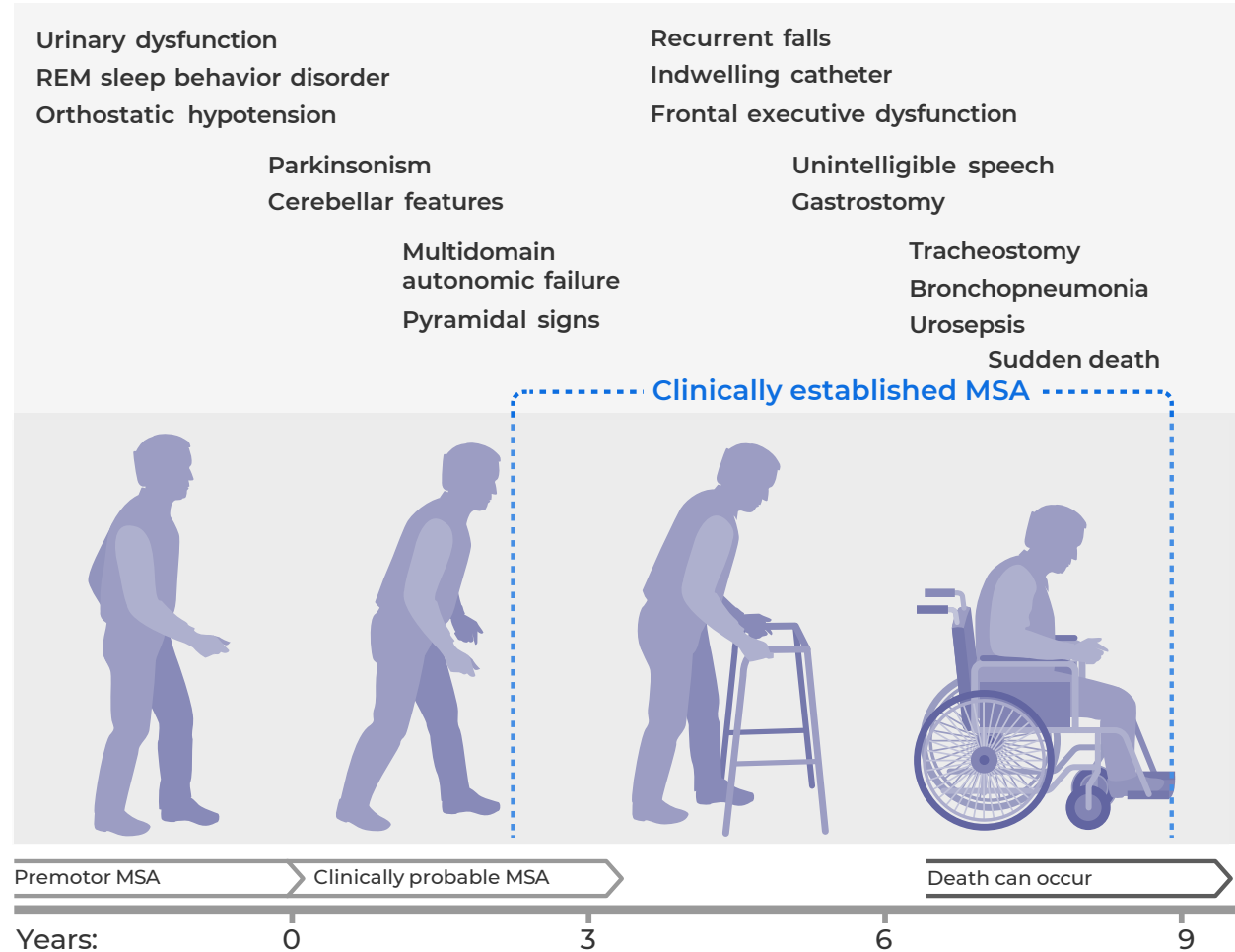
- Motor: Parkinsonism, uncoordinated movements, balance problems, falls
- Autonomic dysfunction: blood pressure maintenance, bladder control, bowel function
- Atrophy and  $\alpha$ -synuclein accumulation in multiple brain regions

**Over 50%**

require wheelchair  
in 5 years

**7.5 years**

median survival  
after symptom onset

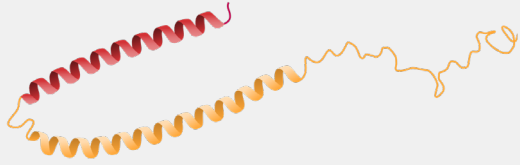


Targeting the pathology in  
Parkinsonian disorders



# Targeting key players in MSA pathology

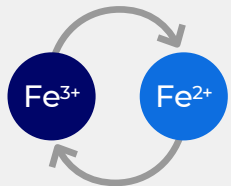
## Alpha-synuclein and iron balance in health and disease



### $\alpha$ -Synuclein protein

- Present in all neurons
- Enables neuronal communication

In disease:  *$\alpha$ -Synuclein aggregates in neurons in MSA impairing communication and leading to dysfunction*



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

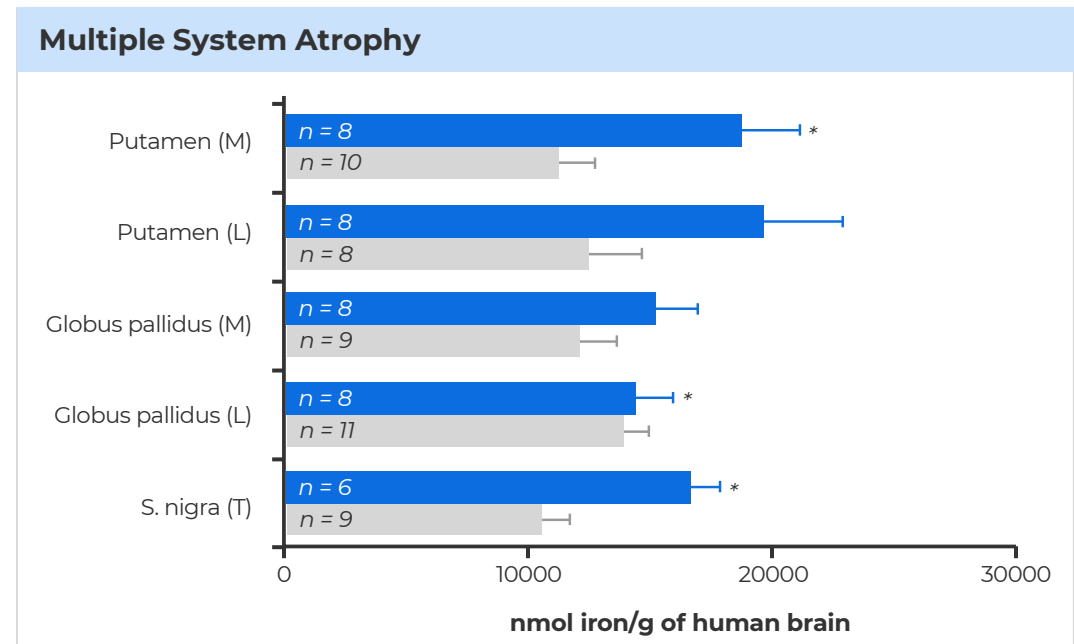
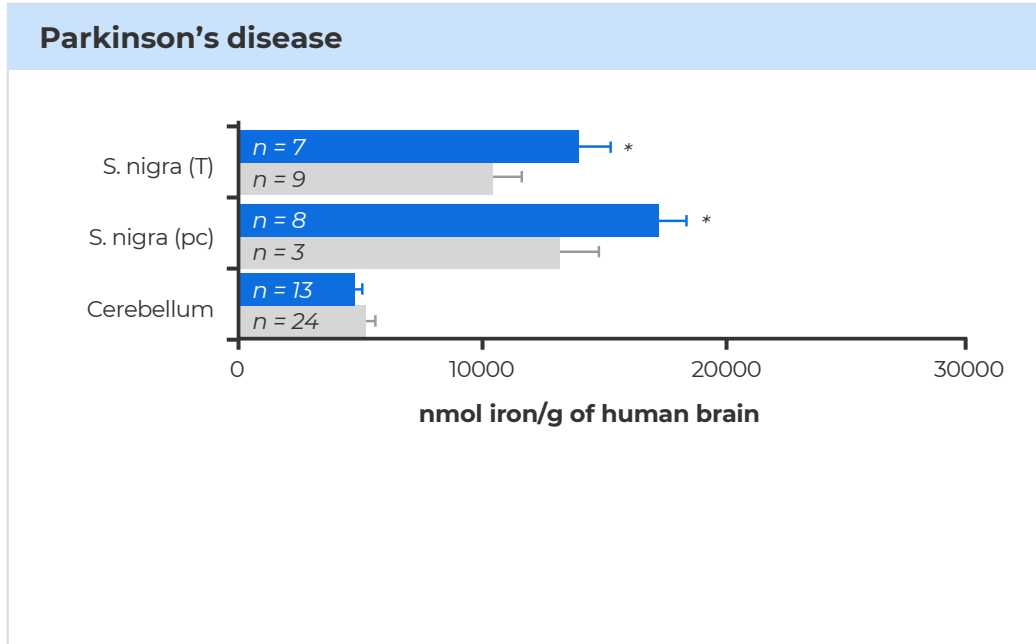
### Two forms of iron required for cellular function

- Neurotransmitter synthesis (e.g., dopamine)
- Myelin synthesis (allows fast signal transmission)

In disease: *Excess reactive iron drives  $\alpha$ -synuclein aggregation and oxidative injury*

# Pathology of Parkinsonian disorders

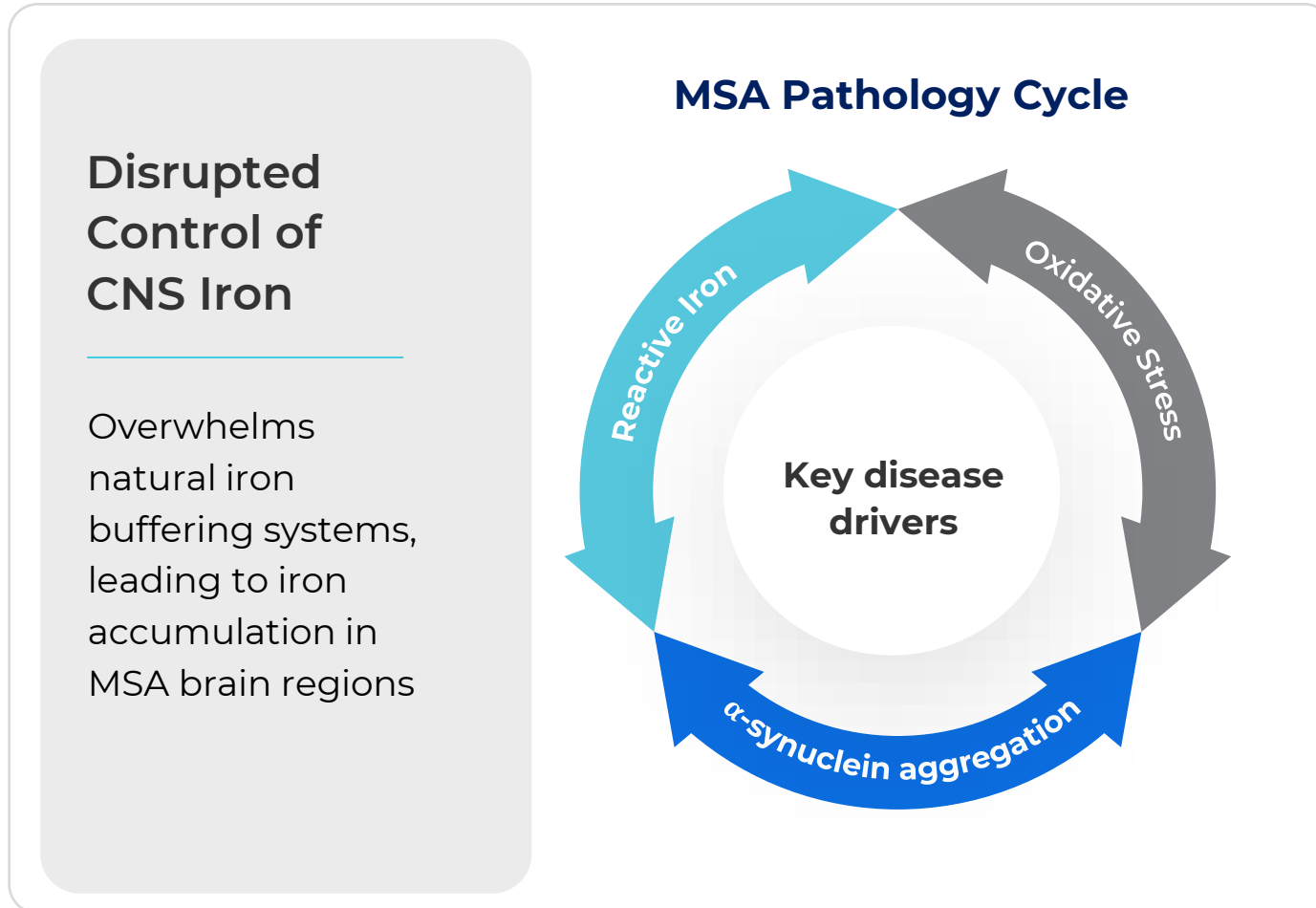
## Increased Brain Iron in Areas of Pathology



■ Patients    ■ Healthy controls

# Iron is a key driver of the MSA Pathology

**ATH434 chaperones excess iron to reduce neuronal injury**



## Disrupted Control of CNS Iron

Overwhelms natural iron buffering systems, leading to iron accumulation in MSA brain regions

## Reactive iron

Generates free radicals  
Promotes  $\alpha$ -synuclein aggregation

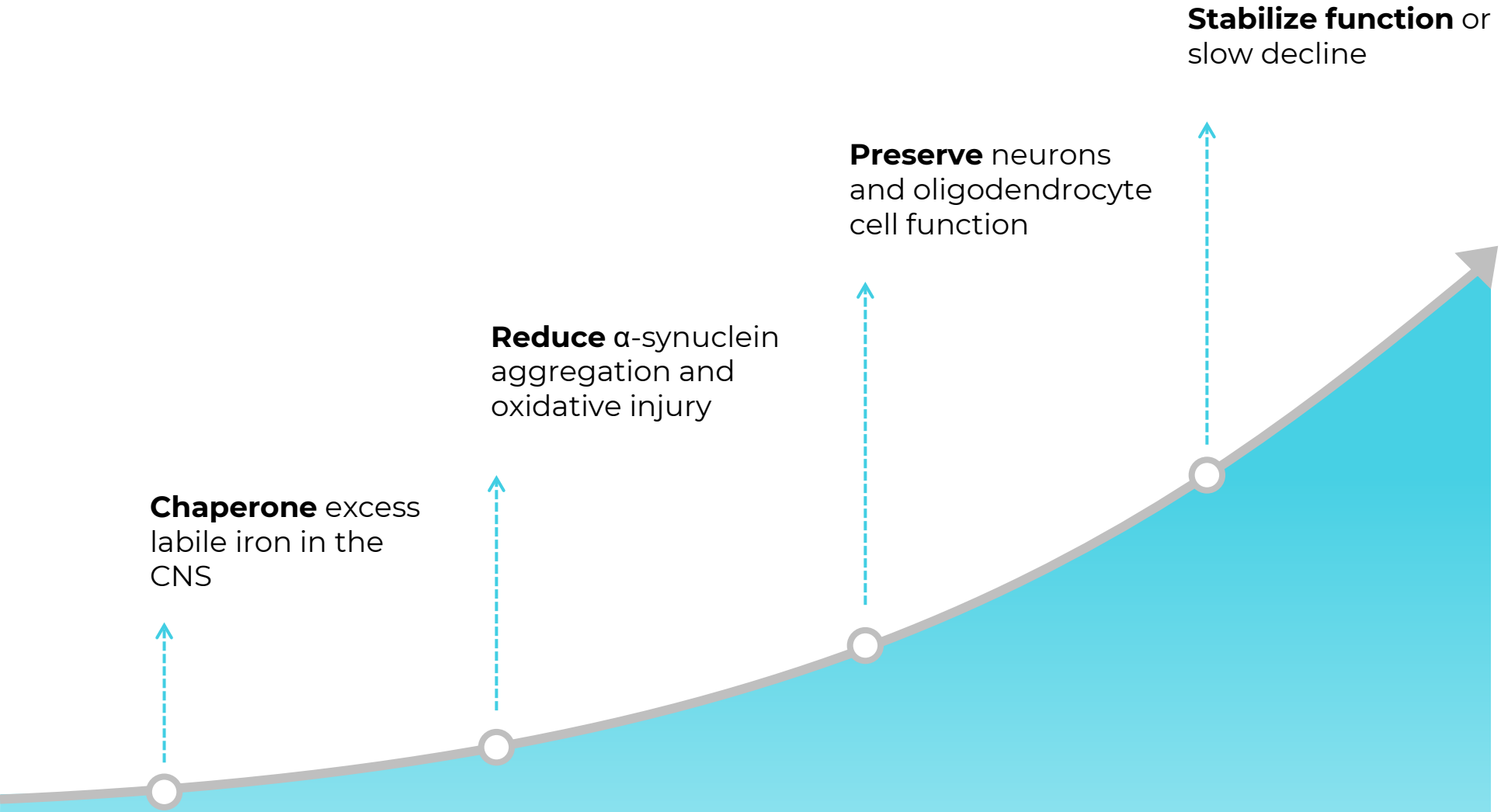
## Oxidative stress

Disrupts multiple cellular functions  
Promotes  $\alpha$ -synuclein aggregation

## $\alpha$ -synuclein aggregation

Neuronal toxicity  
Impaired myelin production

# Treatment approach: Address underlying pathology

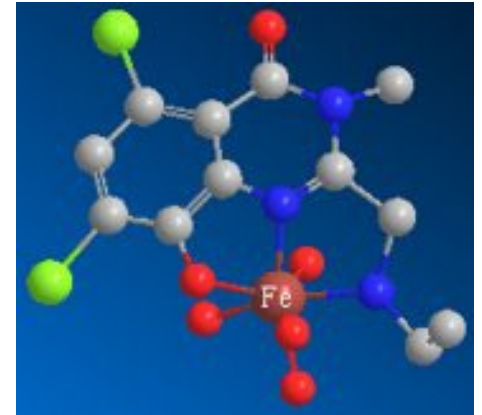


Based on mechanism of action, ATH434 is a potential disease modifying therapy

# 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



# Multiple models of neurodegenerative disease demonstrate ATH434 efficacy

Target Disease	Model	Midbrain iron (incl. s. nigra)	$\alpha$ -Synuclein	Preserve neurons/function	Clinical observations
MSA <sup>1</sup>	PLP- $\alpha$ -syn	↓	↓	↑	Improved motor performance
MSA <sup>2</sup>	PLP- $\alpha$ -syn	↔ to ↓	↓	↑	Improved motor performance
Parkinson's	Monkey MPTP	↔ to ↓	n/a	↑	Improved motor performance
Parkinson's	Mouse MPTP	↓	↓	↑	Improved motor performance
Parkinson's	Mouse A53T	↓	↓	↑	Improved motor performance
Parkinson's	Mouse tau knockout	↓	↓	↑	Improved motor performance

↔ Stable

**ATH434 consistently improved motor performance by reducing  $\alpha$ -synuclein aggregation and preserving neurons**



ATH434 clinical development  
program in MSA

# Diligent approach to de-risk development program

## Natural History Study

### bioMUSE

- Observational study in 21 participants with clinically probable 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

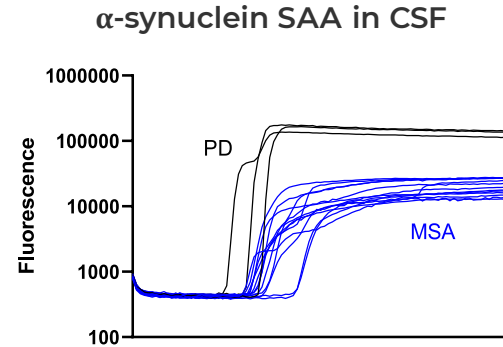
### ATH434-202

#### Open label trial in advanced MSA patients

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

## Optimized patient selection in Phase 2 trials

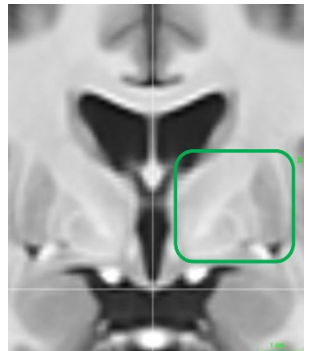
Advanced MRI methods



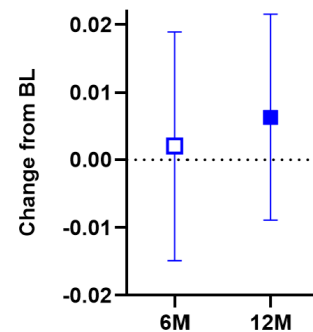
- ✓ Identified "iron signature" of early MSA
- ✓ Differentiated MSA from Parkinson's disease (PD)
- ✓ Revised selection criteria in ATH434-201 and ATH434-202 protocols to exclude PD patients

## 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

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

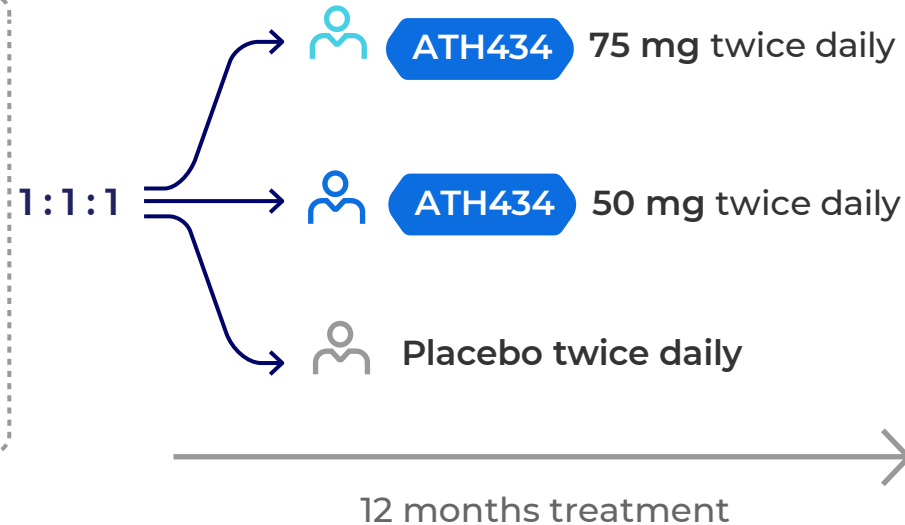
ATH434-201

## Patient criteria:

 **N = 77**

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

## Study design:



## Endpoints:

- ✓ **Key clinical endpoint:** MSA Rating Scale
- ✓ **Additional secondary endpoints:** CGI-S, OHSA, Wearable Sensors, Safety
- ✓ **Key biomarker endpoint:** brain iron content by MRI

# 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^

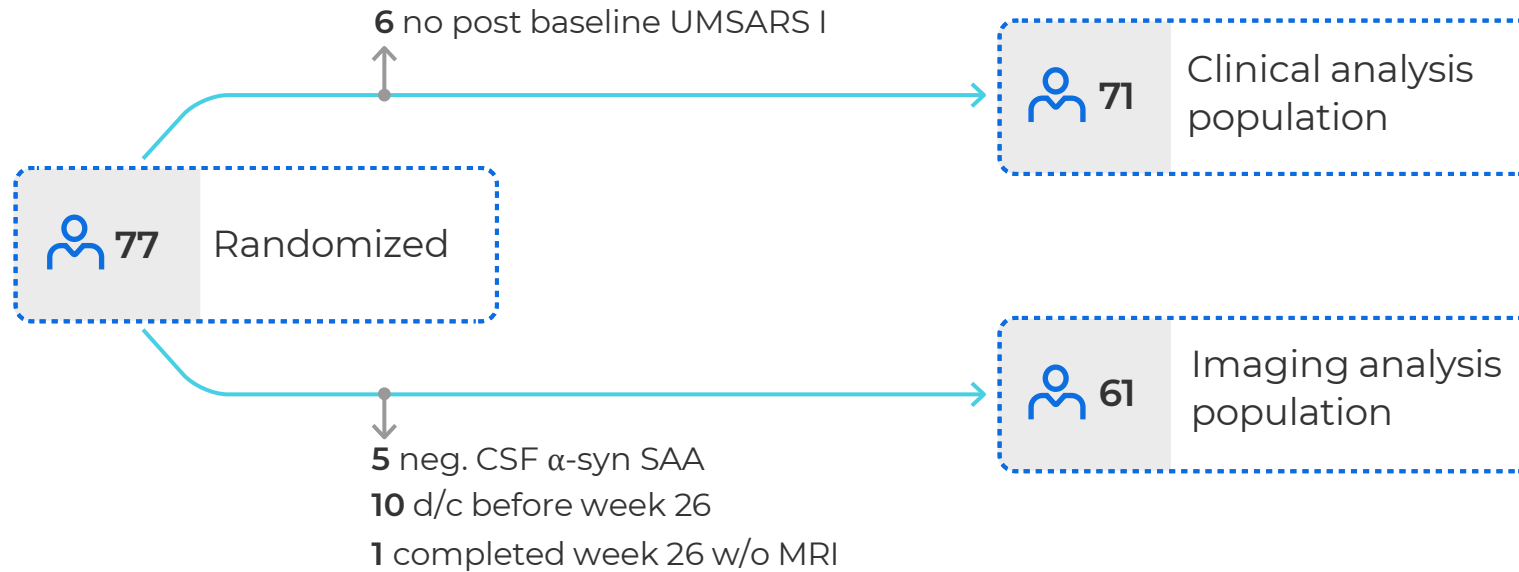
Rated from 0 to 48  
higher scores worse

**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**

# Populations and key endpoints



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

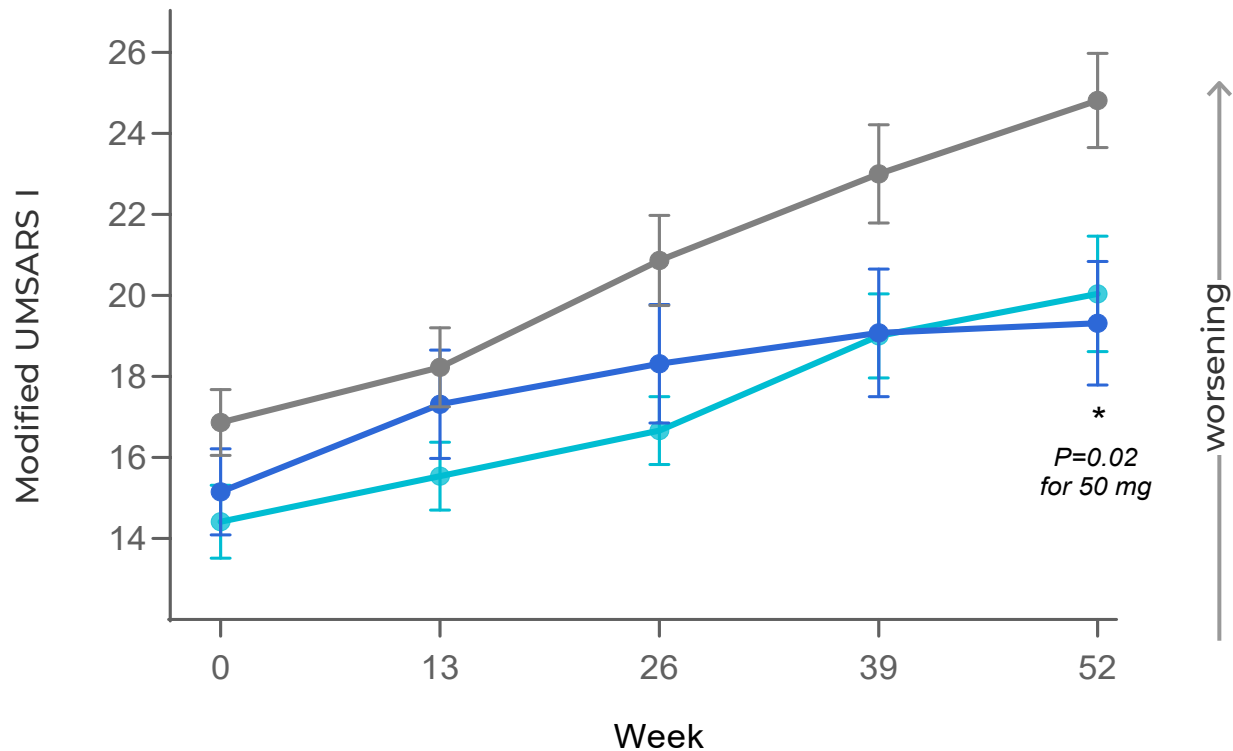
# Baseline characteristics

	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 <sup>1</sup>	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 $\alpha$ -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

# Clinically significant efficacy on modified UMSARS Part I

## Change from baseline to week 52



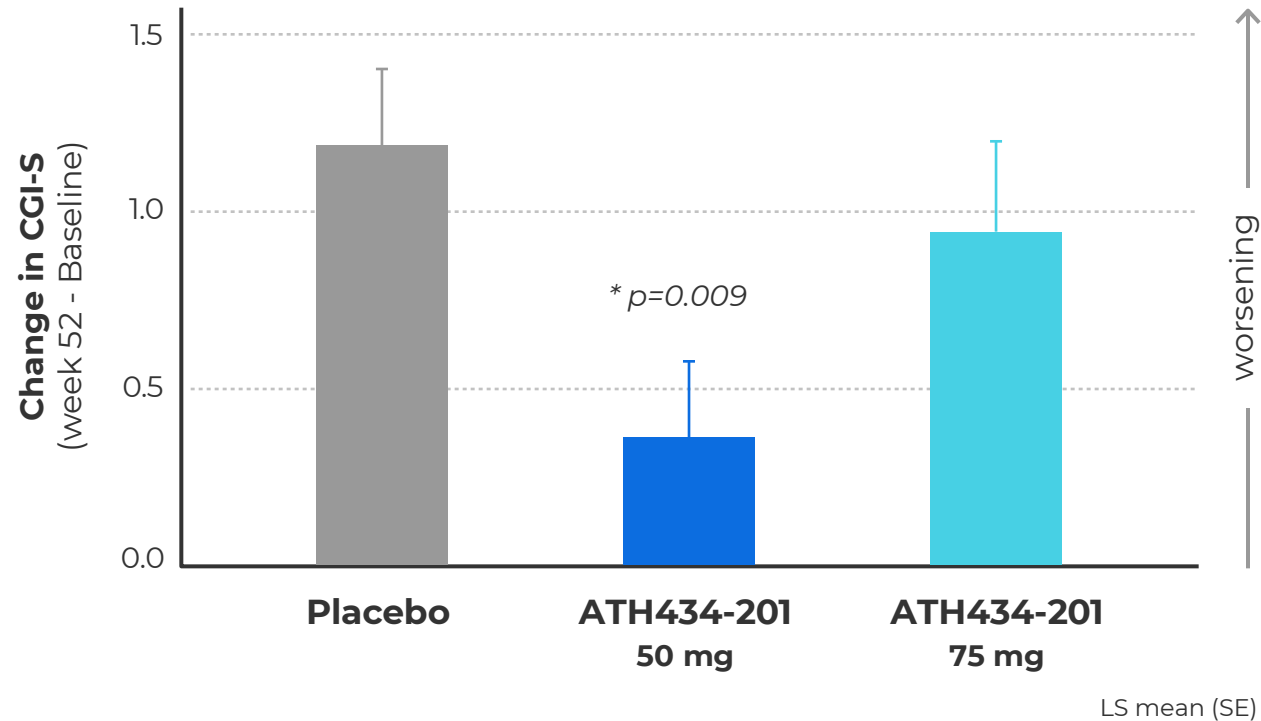
Placebo N=22	Difference vs. placebo LS mean (SE)	Relative treatment effect
ATH434 50 mg N=25	<b>- 3.8 (1.6)</b>	<b>48%</b>
ATH434 75 mg N=24	<b>- 2.4 (1.7)</b>	<b>30%</b>

Minimal clinically important difference (MCID) on UMSARS I = - 1.5 points

$$\text{Relative Treatment Effect} = \frac{\text{Change}_{\text{ATH434}} - \text{Change}_{\text{Placebo}}}{\text{Change}_{\text{Placebo}}}$$

# Efficacy on Clinical Global Impression of Severity (CGI-S) scale

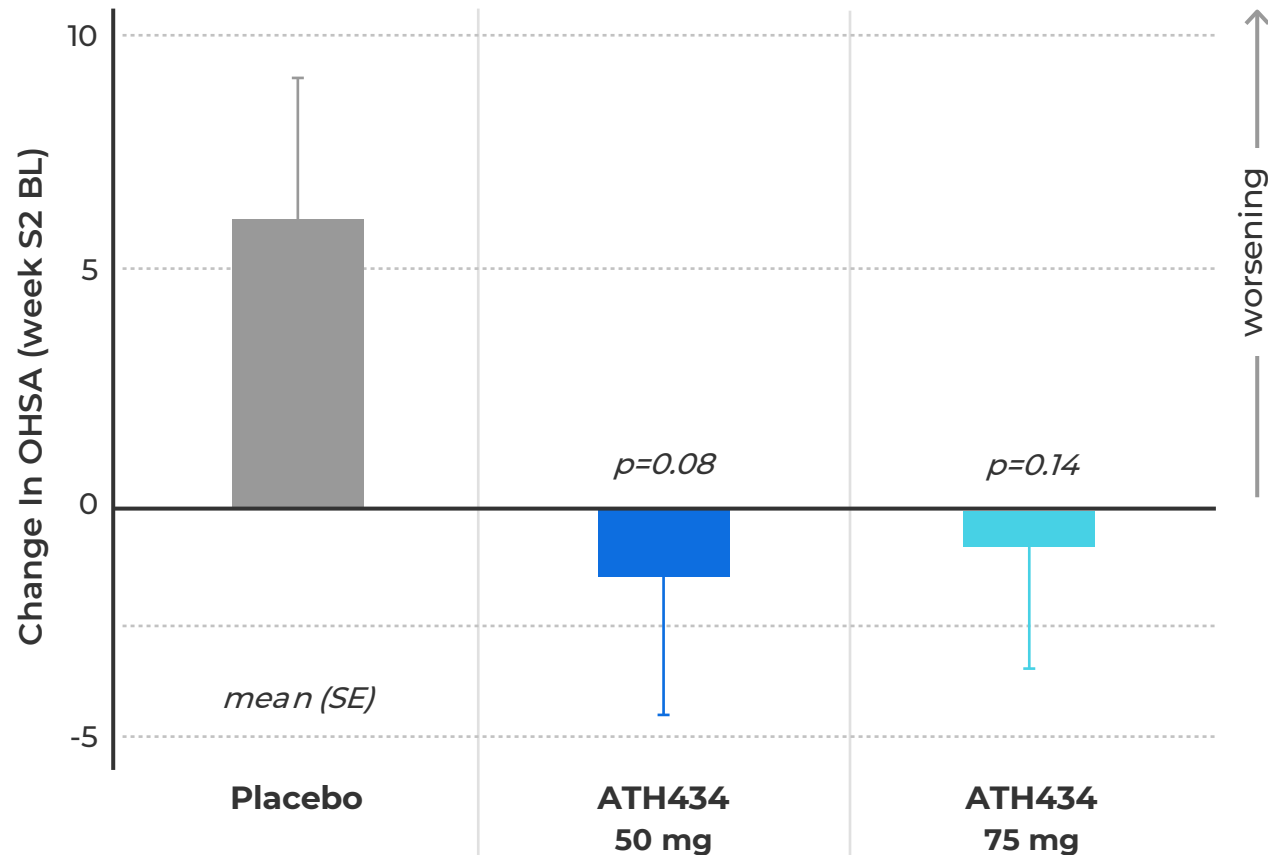
## Change from baseline to week 52



- CGI-S
  - 7-point scale
  - 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

# Orthostatic Hypotension Symptom Assessment (OHSA)

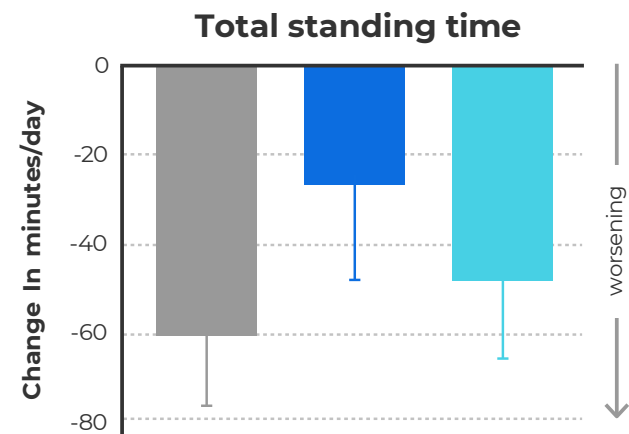
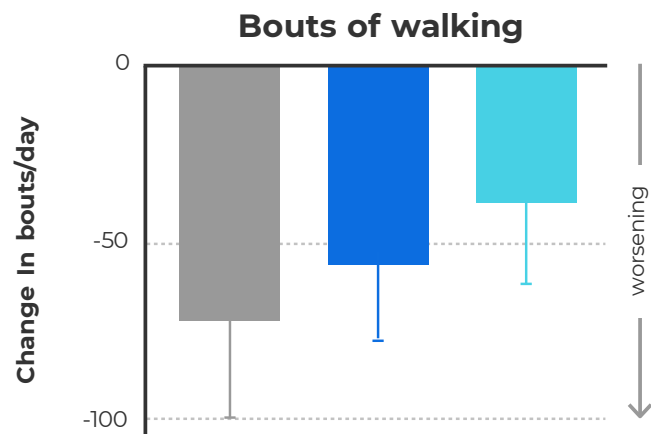
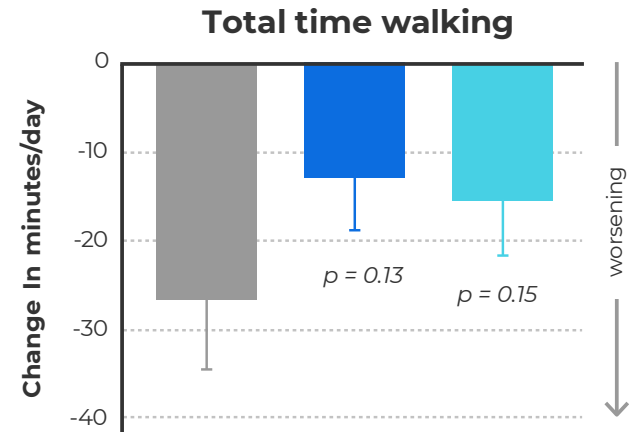
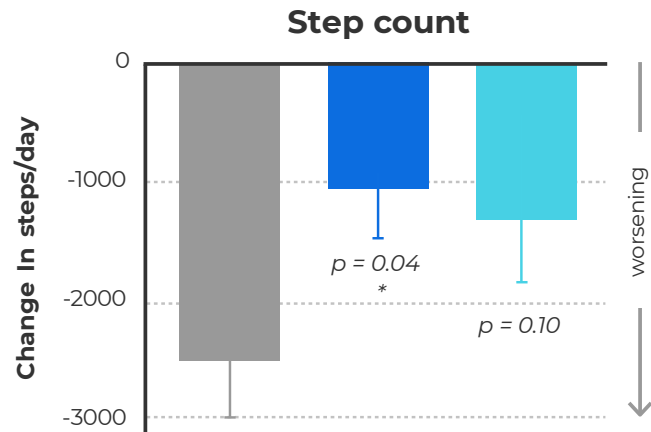
## Change from baseline to week 52



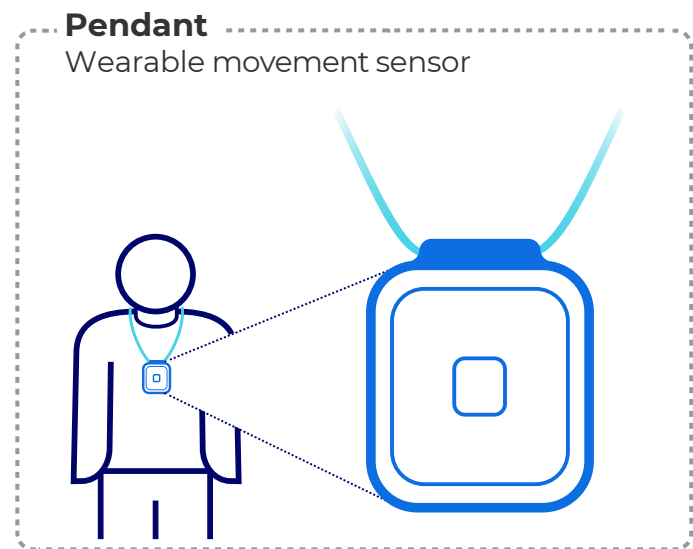
- Assesses symptoms of low blood pressure when going from sitting to standing (e.g., dizziness / feeling faint / lightheadedness)
- Patient reported outcome

# ATH434 preserved walking in outpatient setting

## Change from baseline to week 52






- Placebo
- ATH434-201 50 mg
- ATH434-201 75 mg



# Adverse Events

ATH434-201

	<b>Placebo</b> twice daily  N=26	<b>ATH434-201</b> 50 mg  N=25	<b>ATH434-201</b> 75 mg  N=26
<b>N (%) of subjects <sup>1</sup></b>			
<b>Any Adverse Event (AE)</b>	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%)
<b>Severe AEs <sup>2</sup></b>	8 (30.8%)	3 (12.0%)	6 (23.1%)
<b>Serious AEs <sup>2</sup></b>	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

# Neuroimaging showed target engagement and trends in reduced atrophy

## Reduced Iron Accumulation on MRI

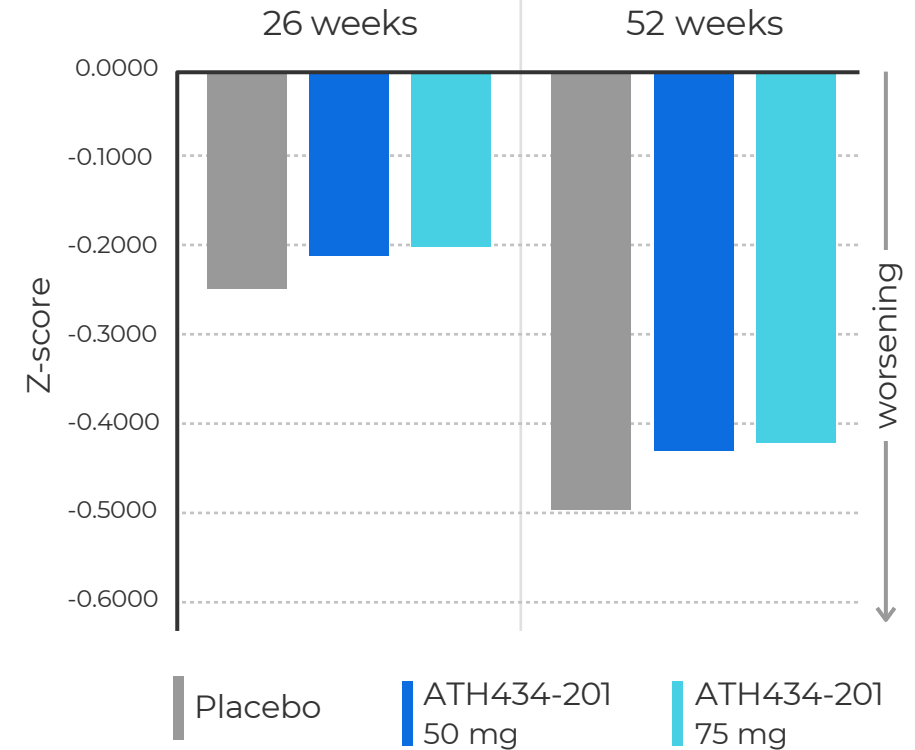
Region	50 mg		75 mg	
	Week 26	Week 52	Week 26	Week 52
Pallidum	↓	↓ <sup>†</sup>	↓	↓
Putamen	↓ <sup>^</sup>	↓	↔	↔
S. nigra	↔	↓	↔	↔

Compared to placebo: ↓ Iron content, ↔ No observable difference, <sup>^</sup>p = 0.03, <sup>†</sup>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

# ATH434-202: Open label study in advanced MSA

ATH434-202

<b>Design</b>	Single arm, open-label
<b>Objective</b>	Assess safety and efficacy in advanced MSA
<b>Population</b>	Advanced MSA (n=10)
<b>Treatment</b>	ATH434 75 mg BID x 12 months
<b>Brain MRI Biomarkers</b>	Volume, Iron
<b>Key Clinical Measure</b>	UMSARS I

## Outcomes:

- ✓ Comparable efficacy observed at same dose in double blind study
- ✓ No serious Adverse Events (AEs) related to study drug
- ✓ AEs consistent with underlying disease

The study indicates the potential of ATH434 to slow disease progression in advanced MSA

# Carefully designed Phase 2 program demonstrates potential for ATH434 in MSA

## ATH434 demonstrated clinically significant efficacy in slowing disease progression in MSA



Both dose levels efficacious on UMSARS I and important secondary endpoints



Demonstrated target engagement with reduced iron accumulation in MSA affected brain regions



Stabilized orthostatic hypotension, one of the most challenging MSA symptoms to manage



Preserved walking in outpatient setting as measured with objective digital biomarker



Open-label trial showed comparable safety and efficacy in advanced MSA



No safety signals and well-tolerated  
No serious AEs related to study drug

# Proposed Phase 3 trial design

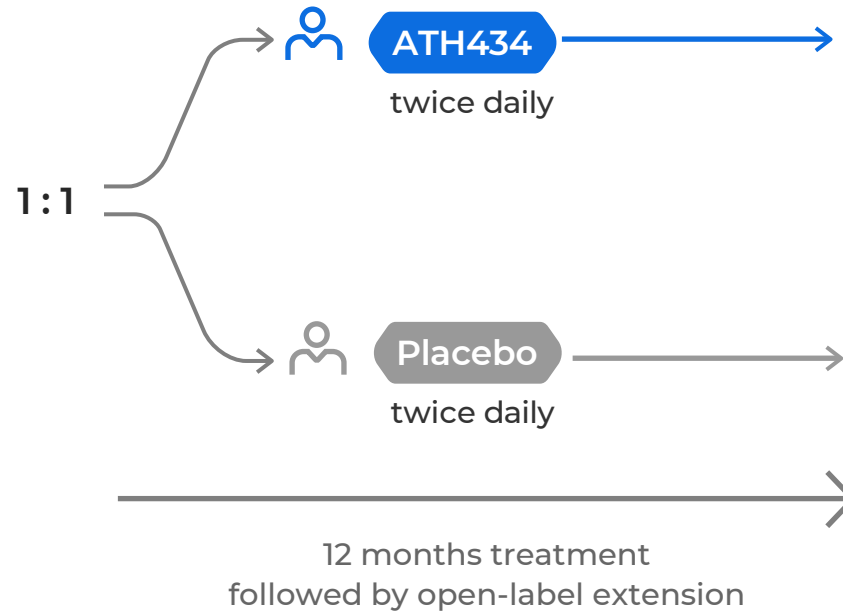
## Patient criteria:



N = ~200

- Clinical diagnosis of MSA
- Ambulatory without assistance
- No severe impairment
- Brain atrophy in MSA affected regions on MRI

## Study design:



## Endpoints:



### Primary endpoint:

MSA Rating Scale (UMSARS I)  
FDA endorsed clinical endpoint



### Secondary endpoints:

OHSA, Wearable Sensors,  
Brain Volume by MRI, Safety

- Expect to finalize Phase 3 program based on end-of-Phase 2 FDA feedback mid-year then initiate trial activities by YE 2026
- Orphan Drug Designation and Fast Track Designation provide valuable support



Commercial assessment &  
corporate overview

# Independent commercial assessment in MSA

## Target product profile based on positive Phase 2 data



### 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  $\alpha$ -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<sup>^</sup>, one of the most challenging symptoms in MSA, strongly positions ATH434

**USD \$2.4 Billion**

Potential worldwide annual peak sales for ATH434 in MSA

# 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 supports 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\$49.2M as of 31 December 2025

## Finalize Regulatory Strategy

- **Align with 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

## Phase 3 Preparations

- **Commence trial preparation activities**
  - Clinical site identification and qualification
  - Manufacture and packaging of clinical drug supply

## Build for Scalable Growth

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

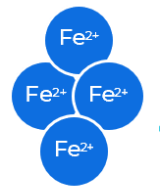
ASX: ATH  
NASDAQ: ATHE





# APPENDIX

# Inadequately chaperoned cellular iron drives MSA pathology



Excess  
labile iron

Promotes  $\alpha$ -synuclein cross linking<sup>1</sup>

Directly increases  $\alpha$ -synuclein translation<sup>2</sup>

ODG toxicity due to limited endogenous glutathione<sup>3</sup>

Free radicals promote  $\alpha$ -synuclein aggregation<sup>4</sup>

Impaired lysosomal autophagy<sup>5</sup>

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

Christine Kaindlstorfer, Kurt A Jellinger, Sabine Eschlböck, Nadia Stefanova, Günter Weiss, Gregor K Wenning

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

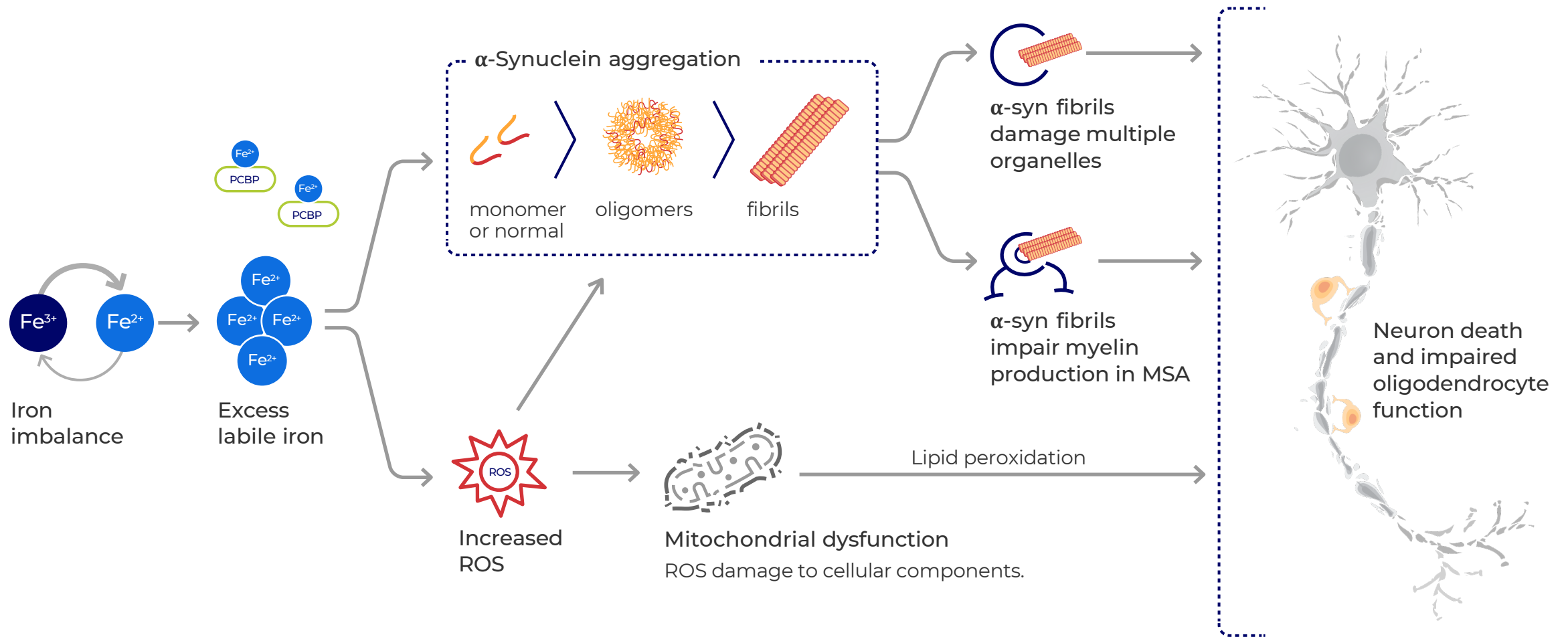
*The disturbance of iron homeostasis leads to abnormal iron deposition in the brain and causes neurotoxicity via generation of free radicals and oxidative stress.*

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

Seojin Lee, Gabor G Kovacs

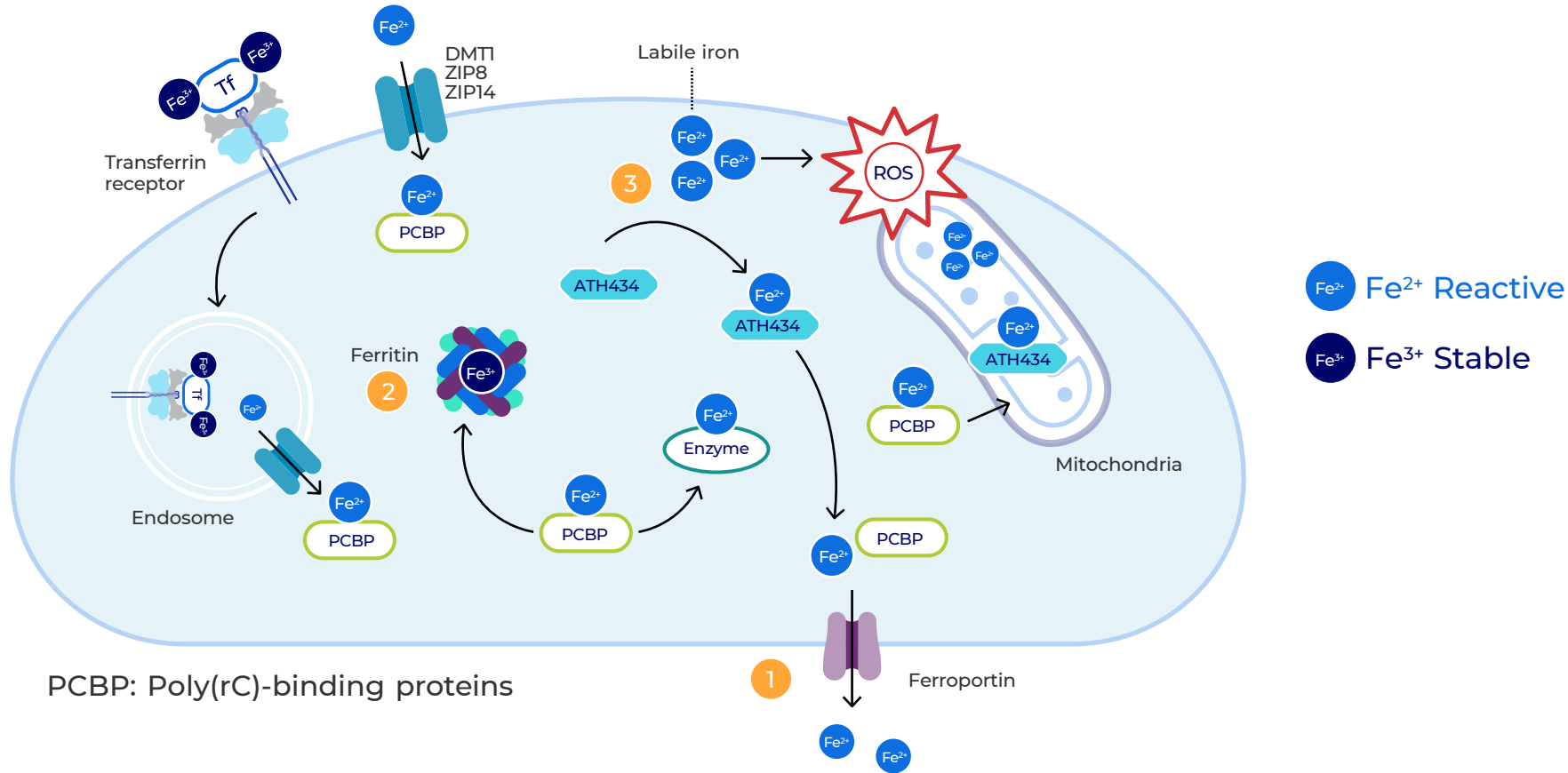
**The close association of iron accumulation with distinct  $\alpha$ -synuclein pathology-related anatomical regions of the two disease subtypes supports the critical involvement of pathological iron in disease progression and further suggests the two disease subtypes as distinct pathological identities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

# Excess labile iron is the key driver of pathology causing $\alpha$ -synuclein aggregation and oxidative injury



# ATH434 mechanism of action: Iron chaperone

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





## Chaperone mechanisms:

- 1 Efflux iron from cell (ferroportin)
- 2 Increase iron storage (ferritin)
- 3 Buffering Fe<sup>2+</sup> in labile iron pool

# ATH434-202: Open label study in advanced MSA

ATH434-202



Parameter	ATH434-202 75 mg BID	ATH434-201 75mg BID
	 N=10	 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 <sup>1</sup>	19.2 (5.3)	14.4 (4.4)
Motor score of Parkinson Plus Scale <sup>2</sup>	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**

# 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 <sup>1</sup>	-0.44 (0.14)	-0.42 (0.29)

Mean (SD)

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

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