

# Corporate Presentation

June 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

## *A Potential First-in-Class, Disease-Modifying Therapy for Multiple System Atrophy (MSA)*

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

Up to 46% slowing of disease progression v. placebo ( $p < 0.05$ ) 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 ~\$US2.4B global peak sales opportunity in MSA

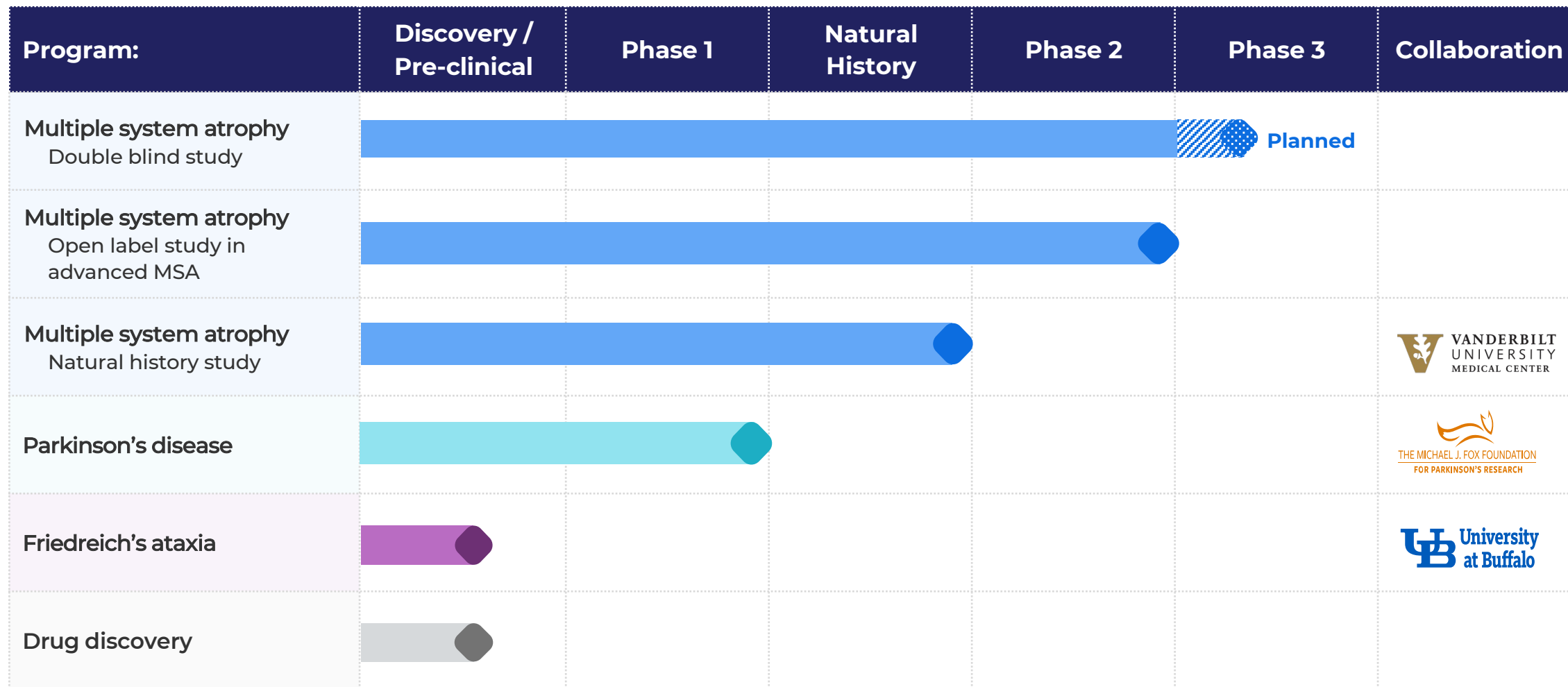
### Differentiated, Disease-Modifying Approach for MSA

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

### Pivotal Advancement in 2026 with Clear Regulatory Path

Successful End-of-Phase 2 FDA meeting obtained alignment on Phase 3 design  
Veteran development team with 3 FDA approvals in Neurology area

# Broad opportunity for ATH434 in neurodegenerative disease



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

**Rapidly progressive**

Highly debilitating

**Up to 50,000**

patients in U.S.

## Disease characteristics:

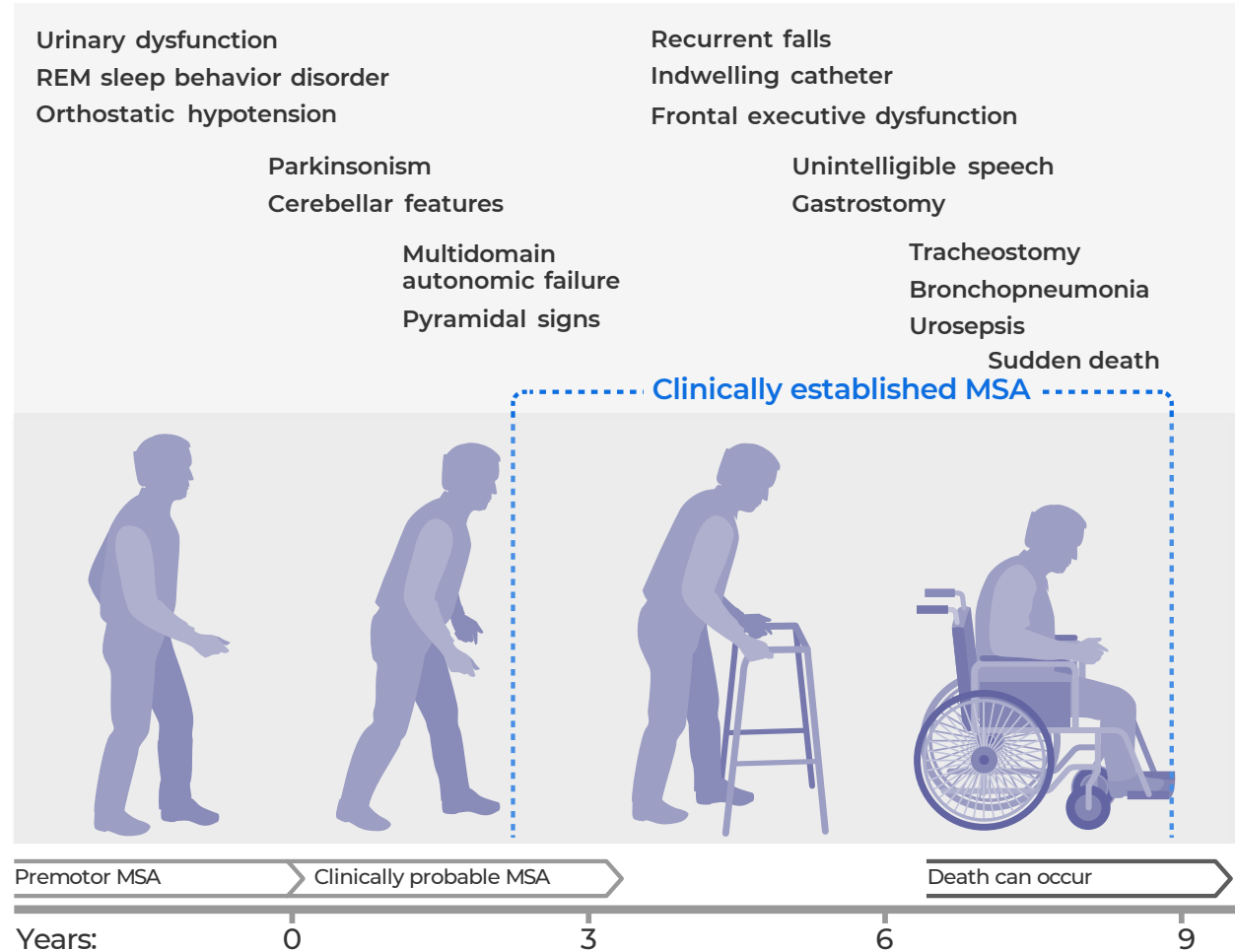
- Motor: Parkinsonism, uncoordinated movements, balance problems, falls
- Autonomic dysfunction: blood pressure maintenance, bladder control, bowel function
- Atrophy and  $\alpha$ -synuclein accumulation in multiple brain regions

**Over 50%**

require wheelchair  
in 5 years

**7.5 years**

median survival  
after symptom onset

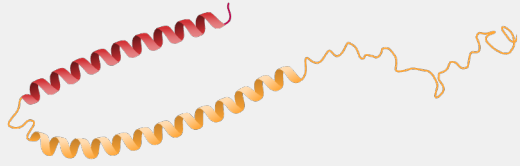


Targeting the pathology in  
Parkinsonian disorders



# Targeting key players in MSA pathology

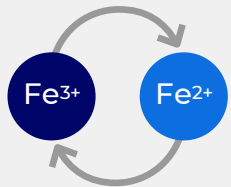
## Alpha-synuclein and iron balance in health and disease



### $\alpha$ -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<sup>2+</sup> Reactive  
Fe<sup>3+</sup> Stable

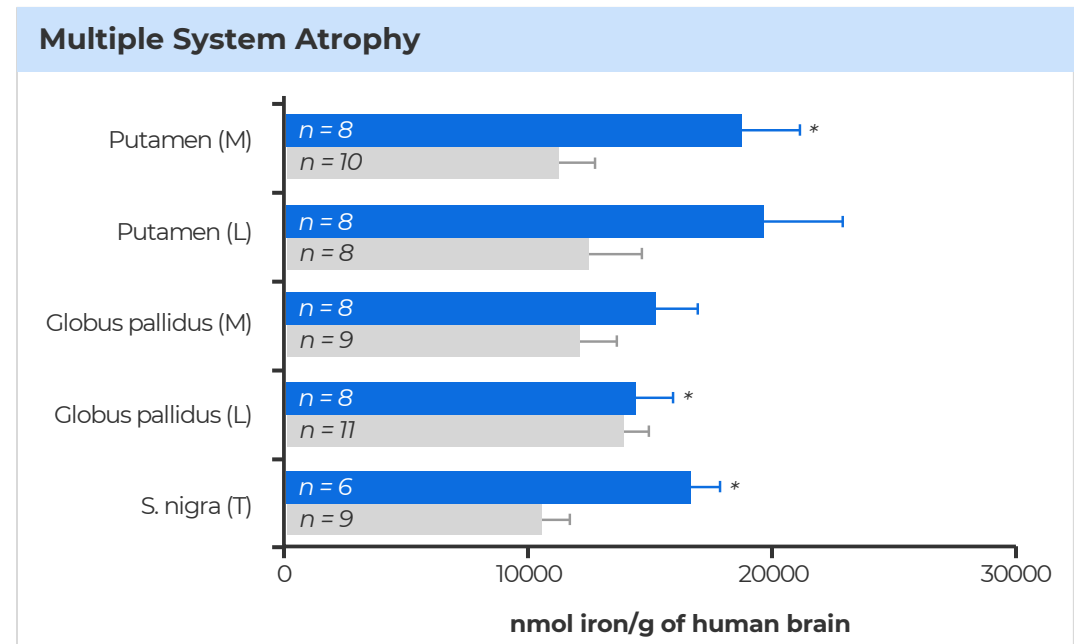
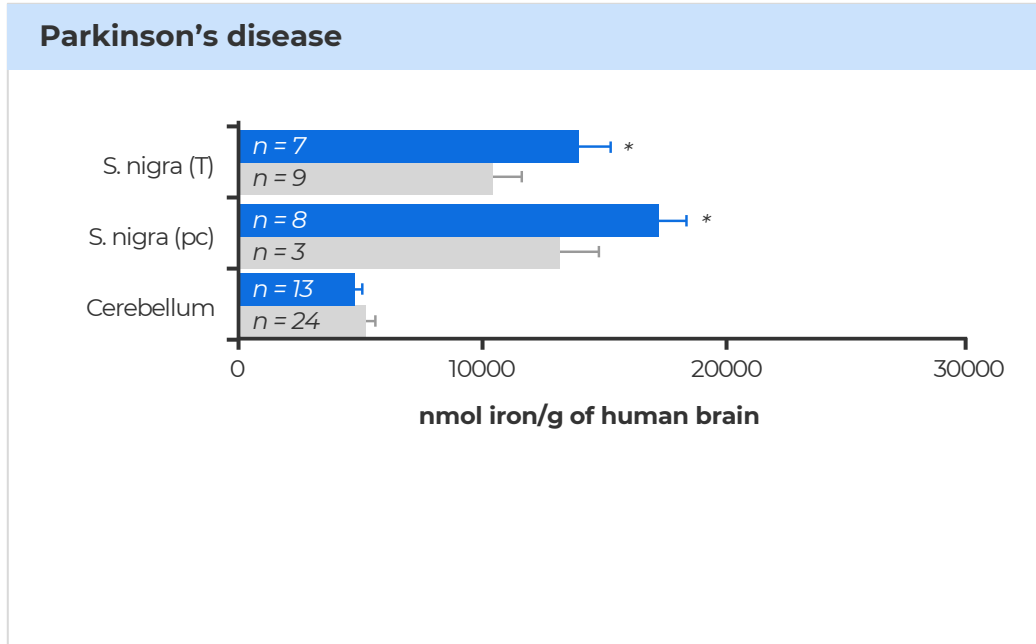
### Two forms of iron required for cellular function

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

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

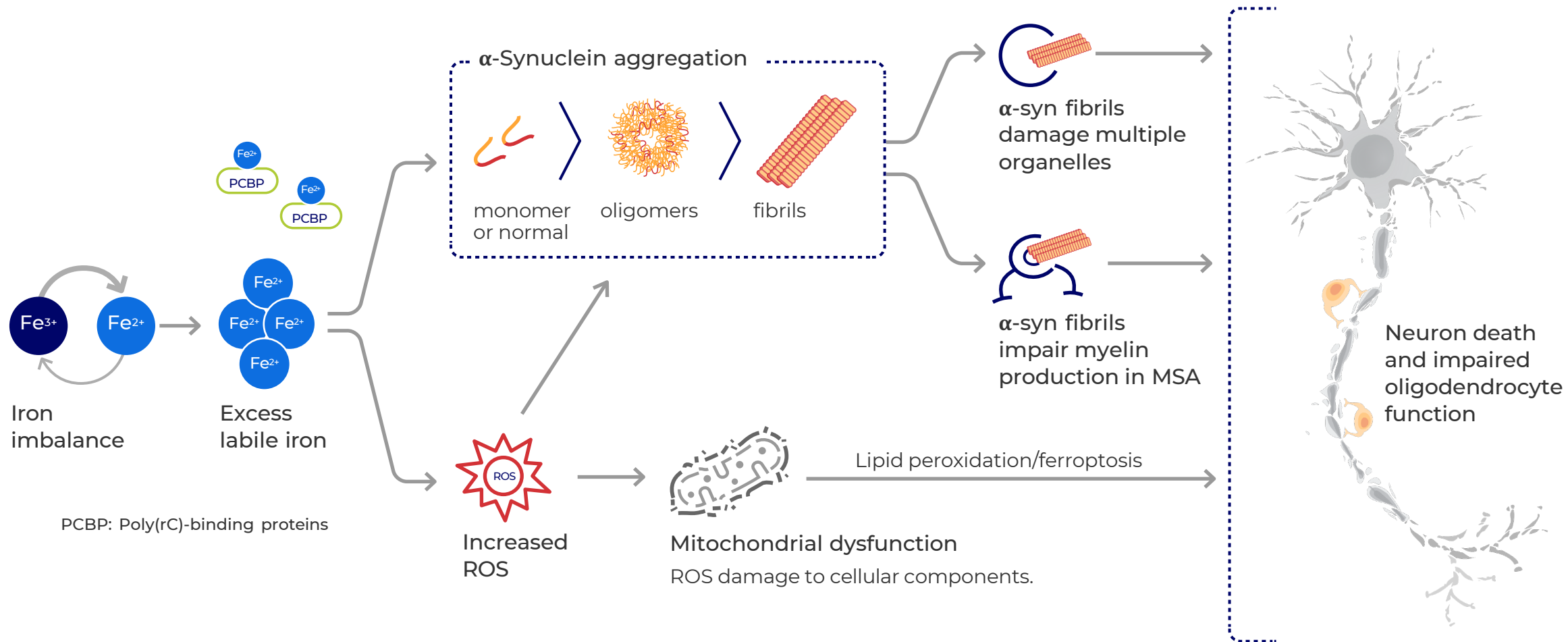
# Pathology of Parkinsonian disorders

## Increased Brain Iron in Areas of Pathology



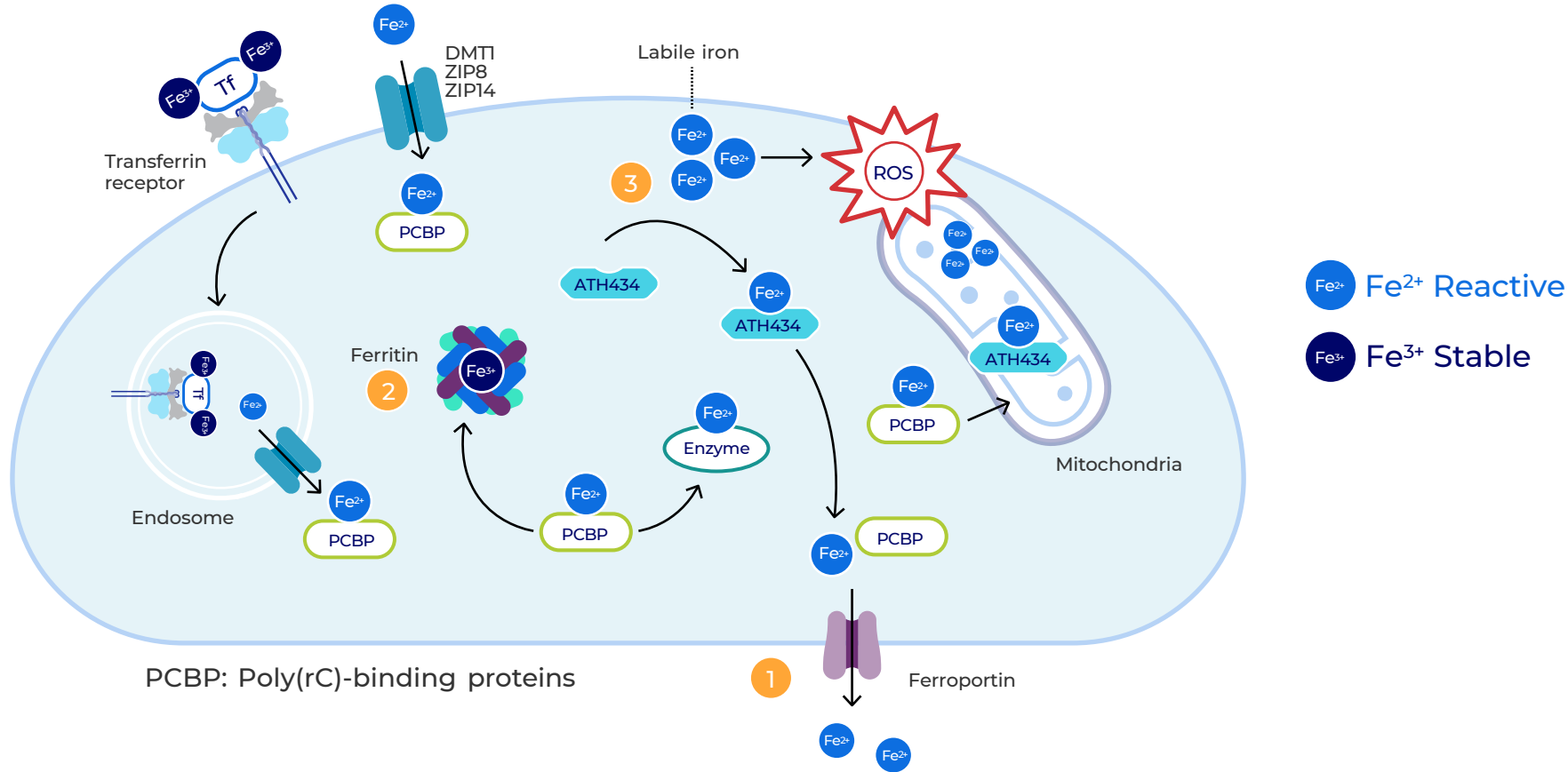
■ Patients ■ Healthy controls

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



# ATH434 mechanism of action: Iron chaperone

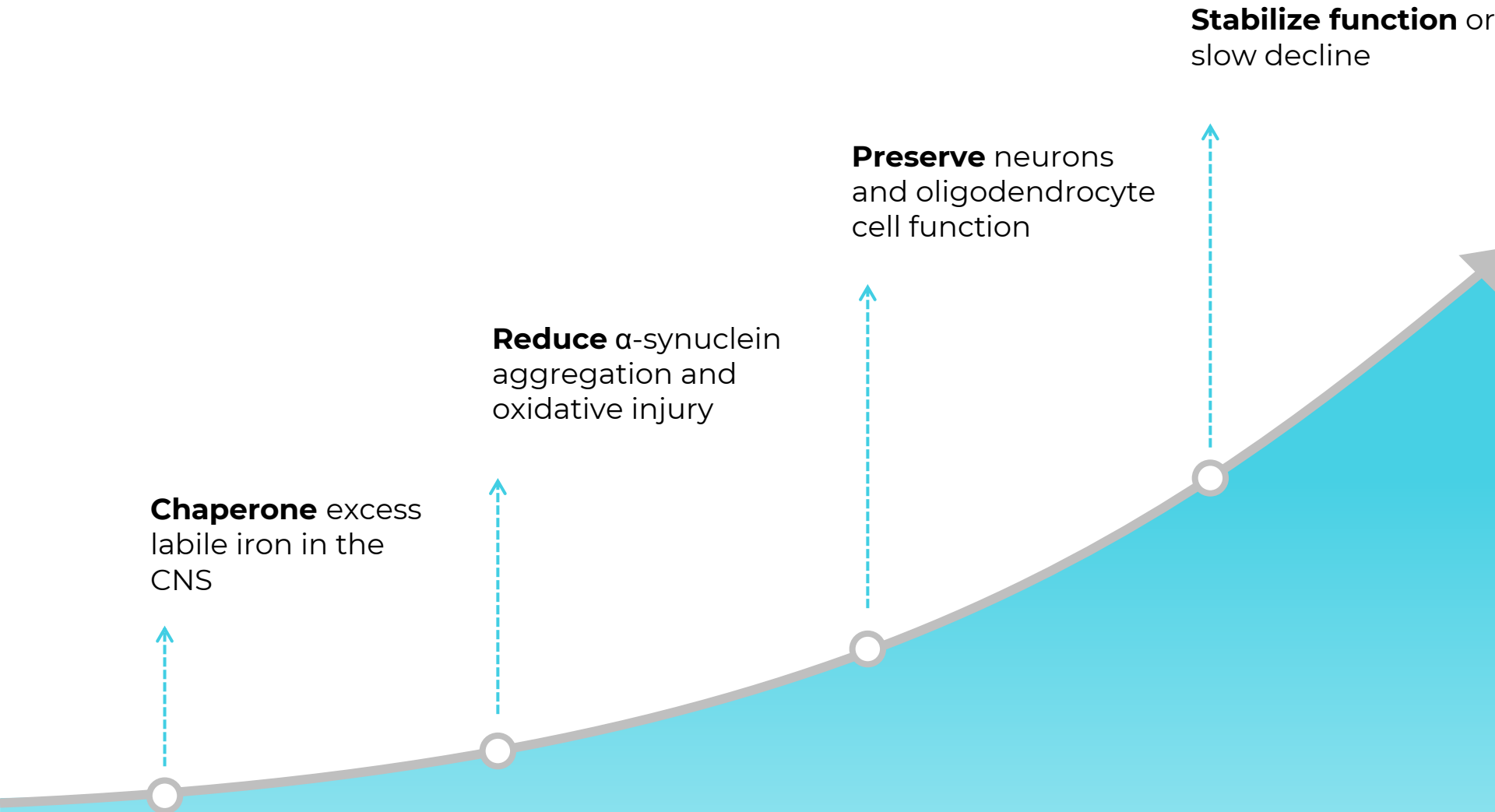
ATH434 chaperones excess labile (reactive) iron to reduce neuronal injury



## Chaperone mechanisms:

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

# Treatment approach: Address underlying pathology

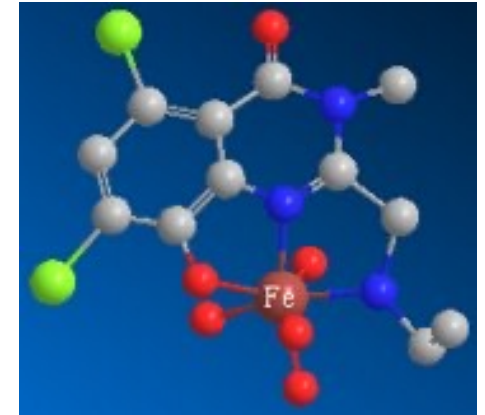


Based on mechanism of action, ATH434 is a potential disease modifying therapy

# 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, Friedreich 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

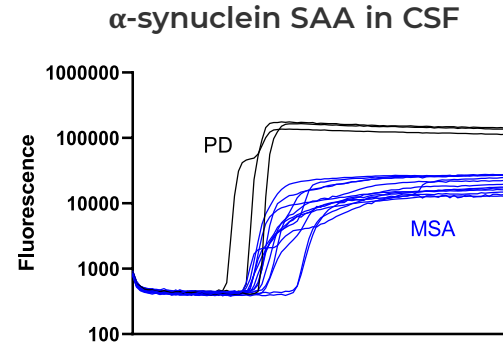
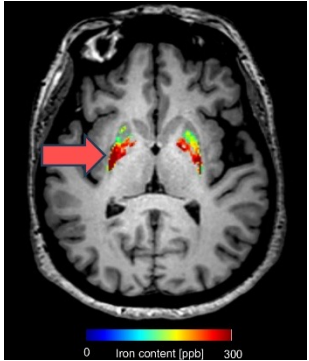
### ATH434-202

#### 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

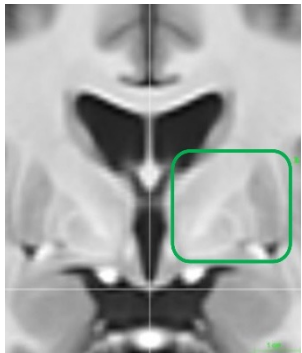
Advanced MRI methods



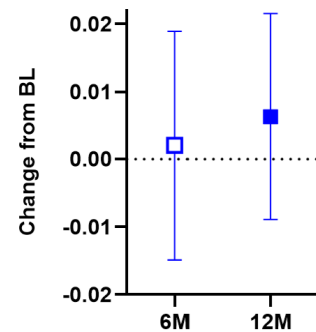
- ✓ Identified "iron signature" of early MSA
- ✓ Differentiated MSA from Parkinson's disease (PD)
- ✓ Revised selection criteria in ATH434-201 and ATH434-202 protocols to exclude PD patients

## 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

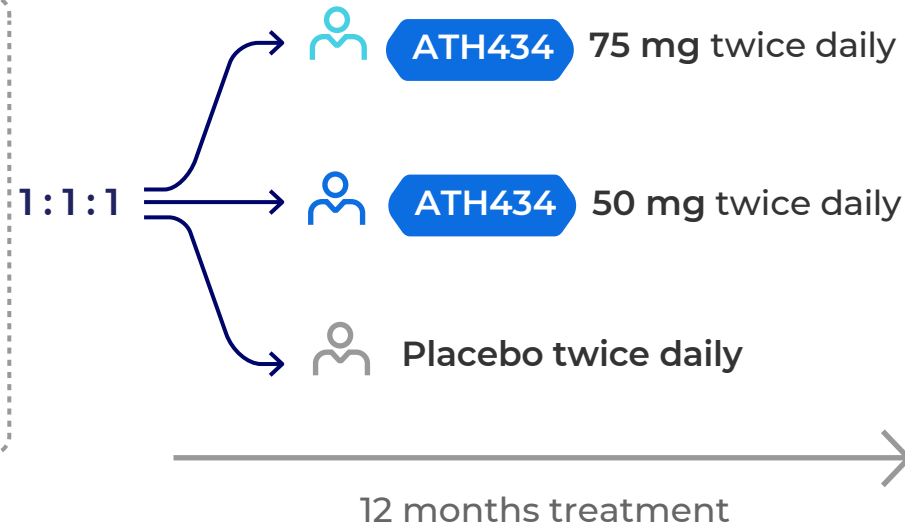
ATH434-201

## Patient criteria:




 **N = 77**

- Clinical diagnosis of MSA
- Motor symptoms ≤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<sup>^</sup>

Rated from 0 to 48  
higher scores worse

Validated rating scale to assess MSA disease severity  
Rates functional impairment in domains affected in MSA

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

Primary endpoint in Phase 3

# Baseline characteristics

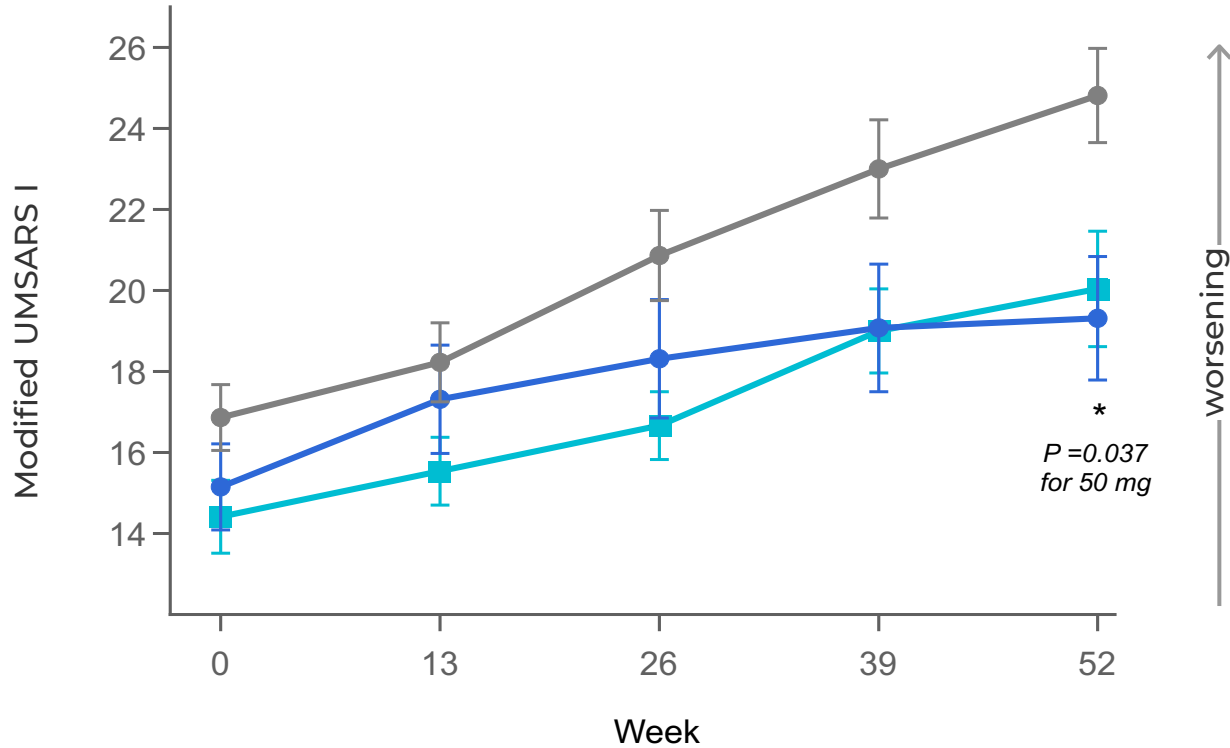
ATH434-201

	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 11-Item UMSARS I

## Change from Baseline to Week 52



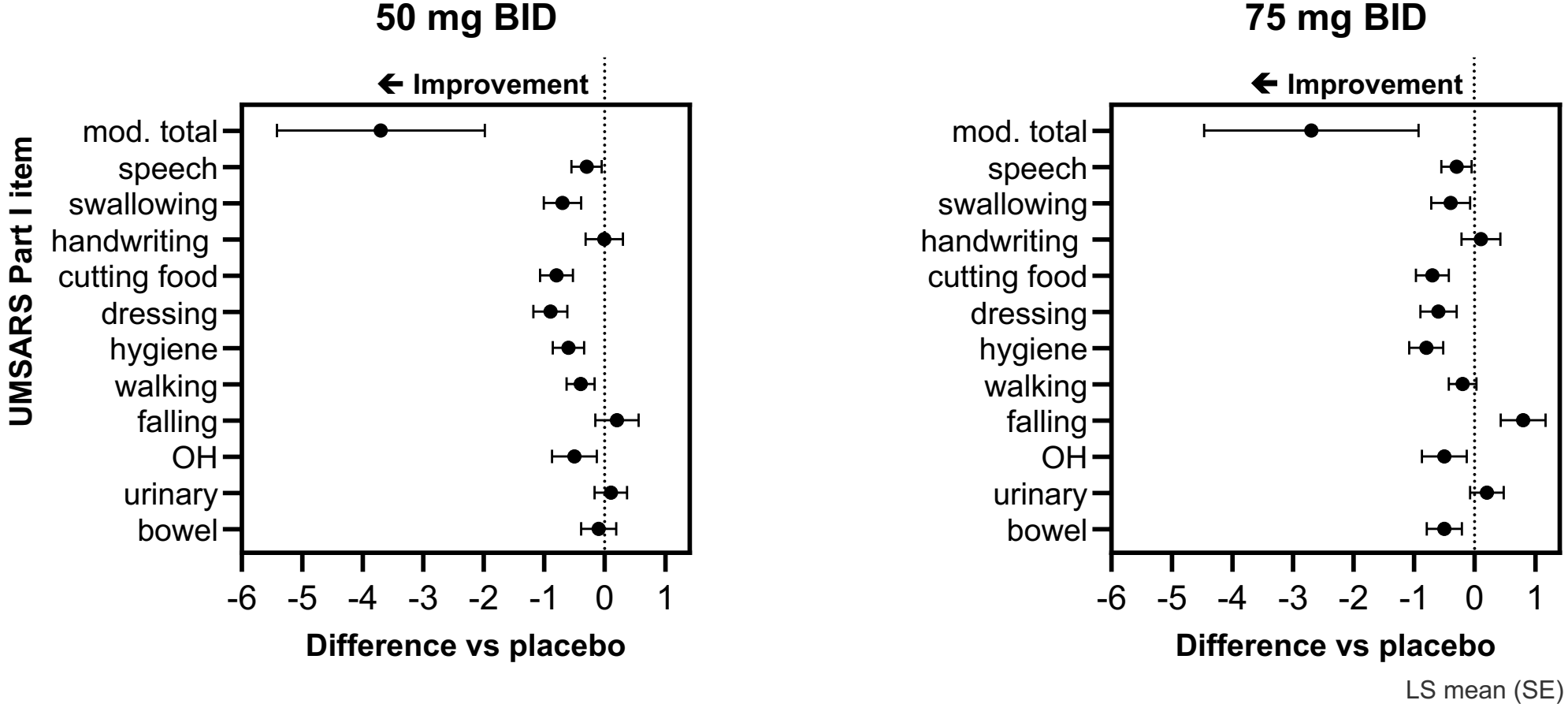
	Difference v. placebo LS mean (SE)	Relative treatment effect
<b>Placebo</b> N=22		
<b>ATH434 50 mg</b> N=25	<b>-3.7 (1.7)</b>	<b>46%</b>
<b>ATH434 75 mg</b> N=24	<b>-2.7 (1.8)</b>	<b>34%</b>

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

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

# Item Analysis of 11-Item UMSARS I: Consistent efficacy across multiple domains

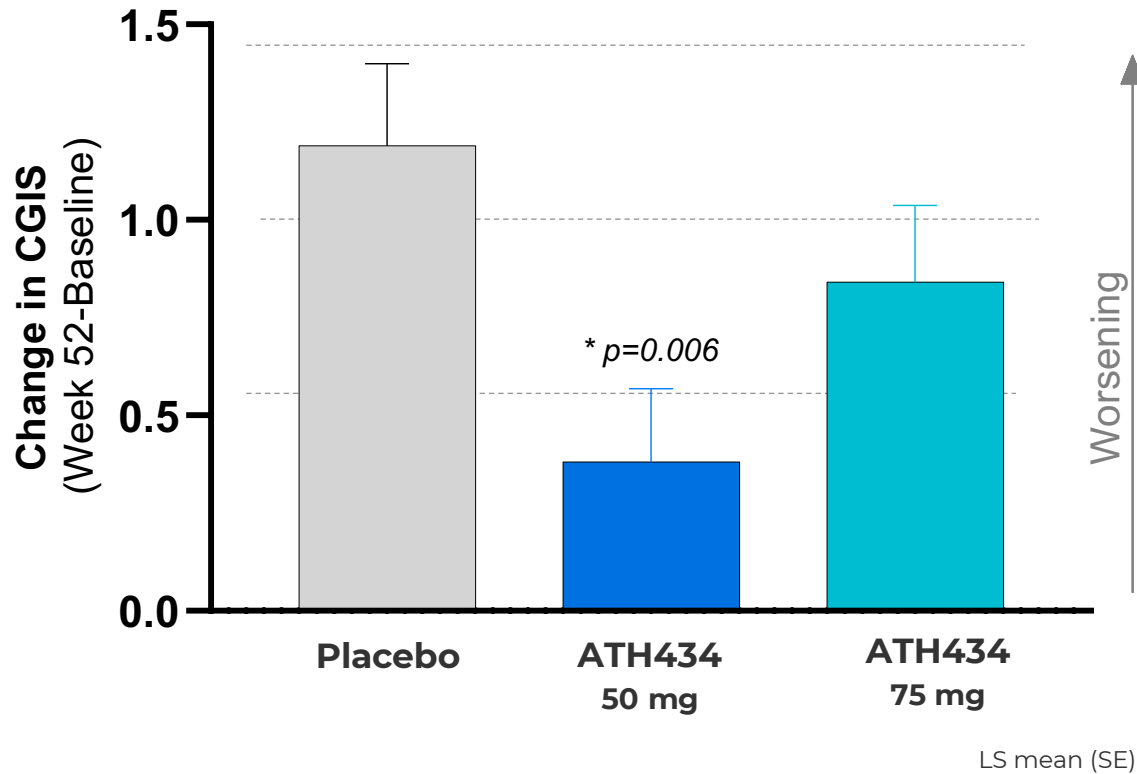
## ATH434 treatment effect vs. placebo



Similar pattern of efficacy in both dose groups

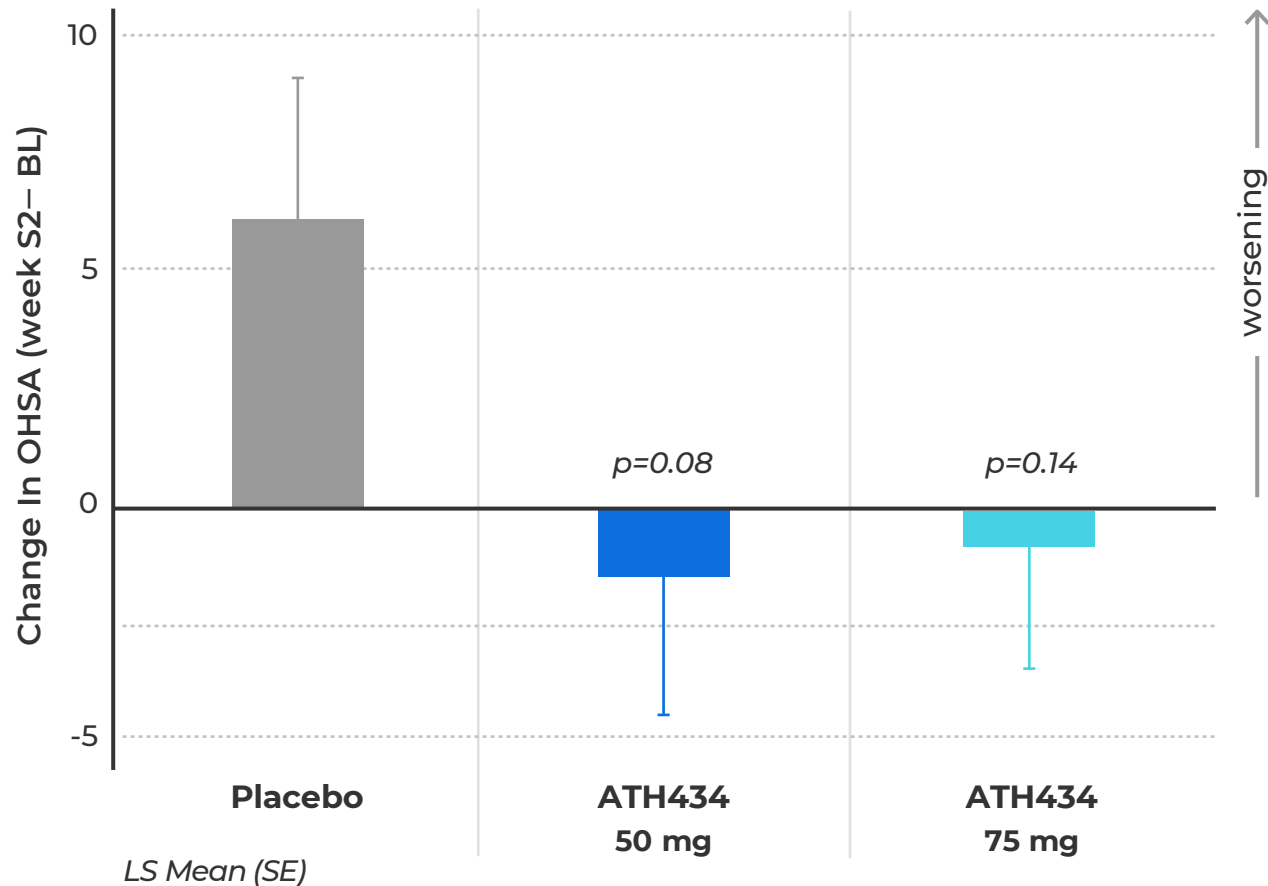
# Efficacy on Clinical Global Impression of Severity (CGI-S) scale

## Change from baseline to week 52



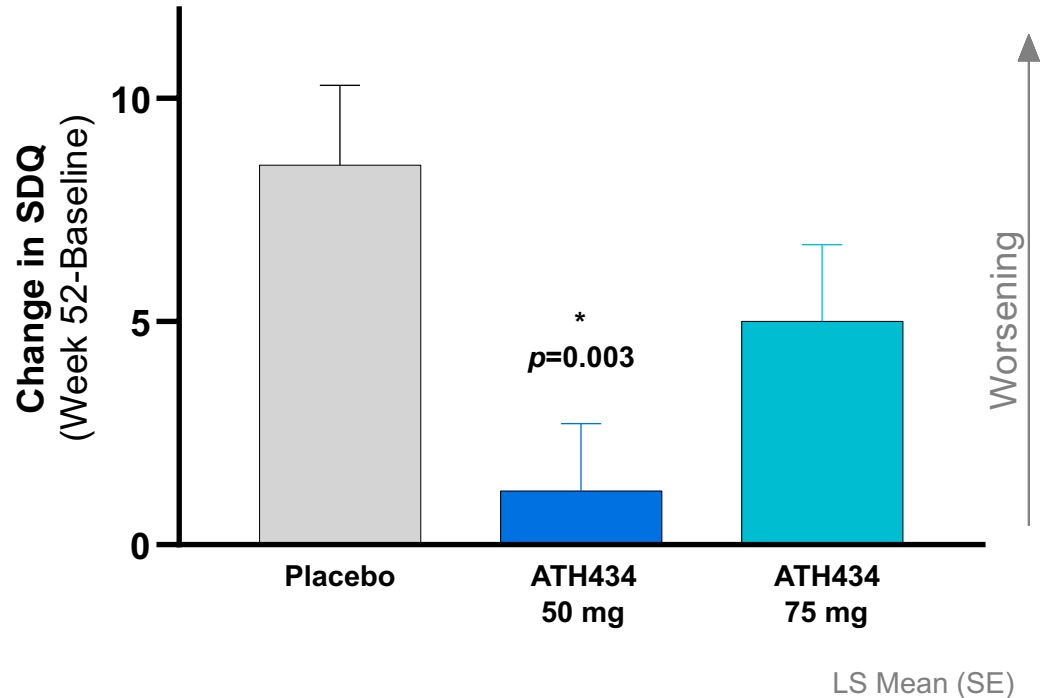
- CGI-S
  - 7-point scale
  - higher score indicates a worse outcome
- Assesses total picture over prior 28 days
  - illness severity, impact of illness on function, level of distress and any other aspects of impairment

# 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

# Swallowing Disturbance Questionnaire (SDQ) Change from baseline to week 52



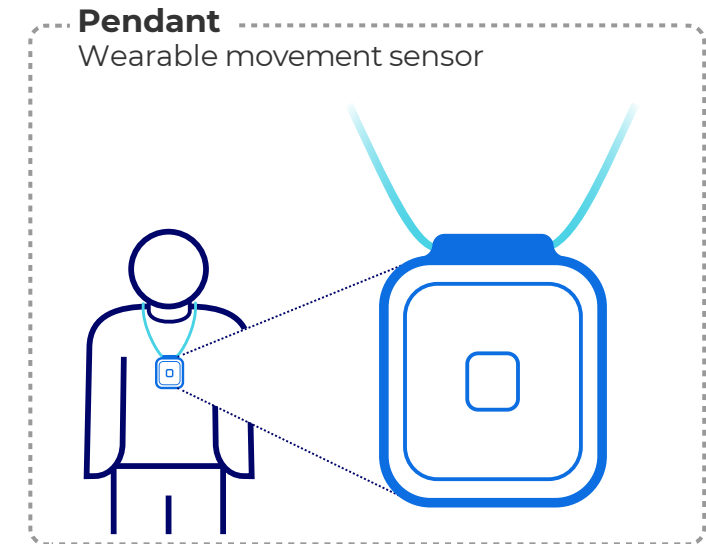
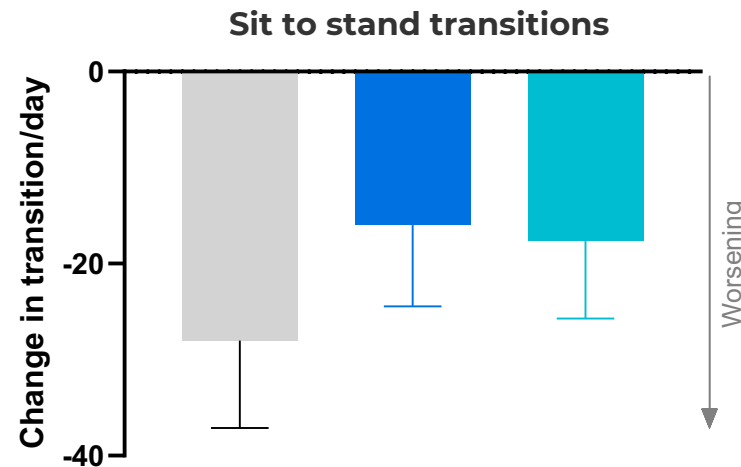
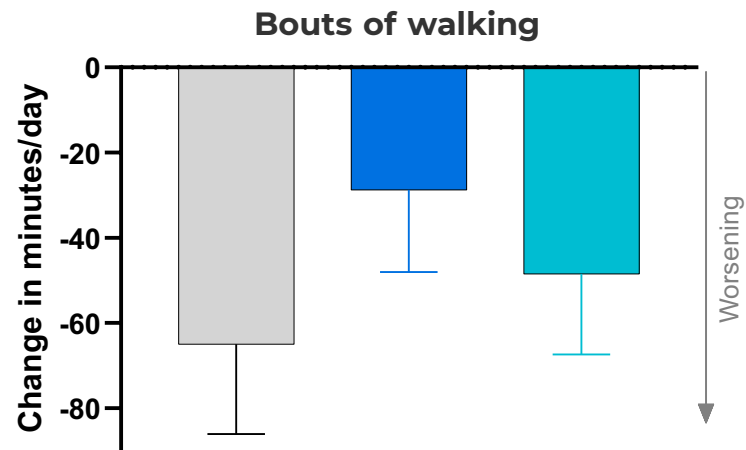
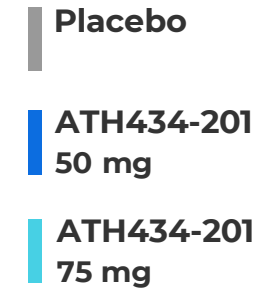
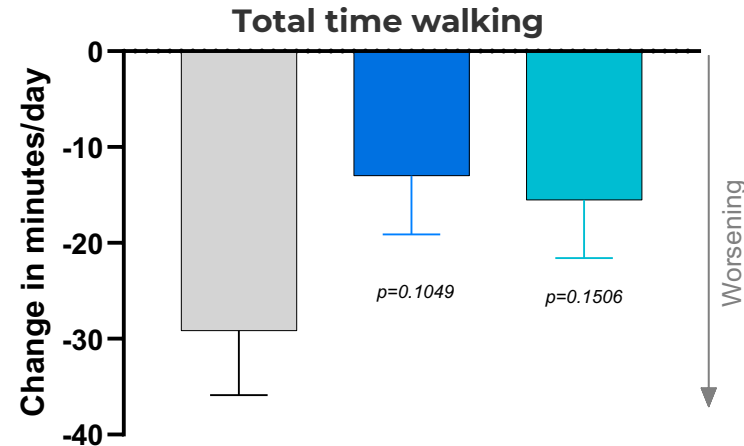
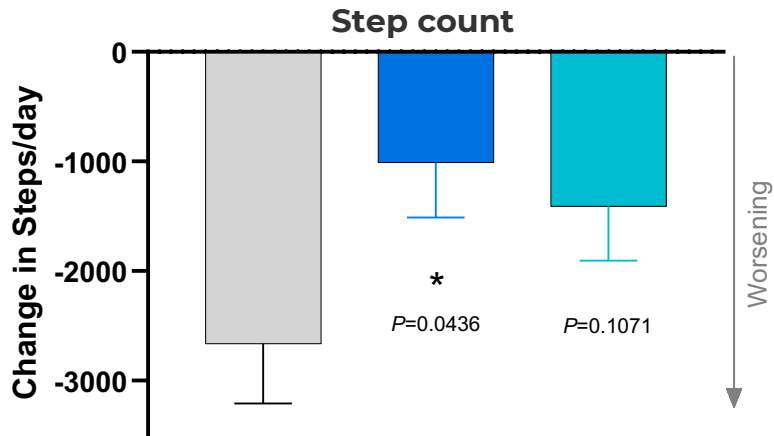
Patient Reported Outcome

## Validated Scale for Detecting Dysphagia

1. Do you experience difficulty chewing solid food like an apple, cookie or a cracker?
2. Are there any food residues in your mouth, cheeks, under your tongue or stuck to your palate after swallowing?
3. Does food or liquid come out of your nose when you eat or drink?
4. Does chewed up food dribble from your mouth?
5. Do you feel you have too much saliva in your mouth; do you drool or have difficulty swallowing your saliva?
6. Do you swallow chewed up food several times before it goes down your throat?
7. Do you experience difficulty in swallowing solid food (i.e., do apples or crackers get stuck in your throat)?
8. Do you experience difficulty in swallowing pureed food?
9. While eating, do you feel as if a lump of food is stuck in your throat?
10. Do you cough while swallowing liquids?
11. Do you cough while swallowing solid foods?
12. Immediately after eating or drinking, do you experience a change in your voice, such as hoarseness or reduced?
13. Other than during meals, do you experience coughing or difficulty breathing as a result of saliva entering your windpipe?
14. Do you experience difficulty in breathing during meals?
15. Have you suffered from a respiratory infection (pneumonia, bronchitis) during the past year?




# ATH434 preserved walking in outpatient setting

## Change from baseline to week 52



# 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



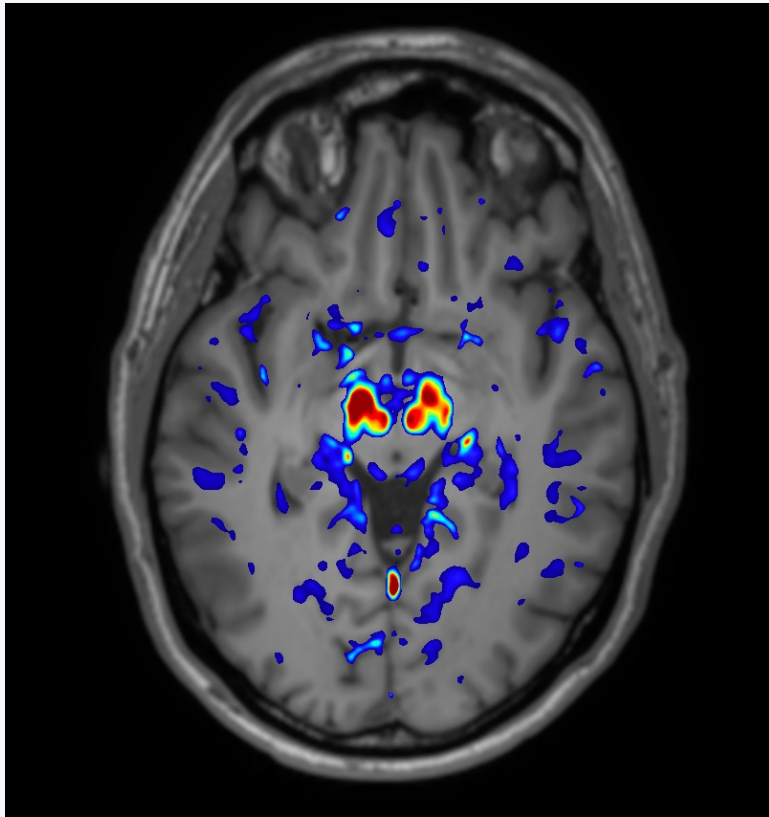
# Neuroimaging

# Measuring Iron Content with MRI (QSM)

## Regional increases in iron in MSA Patient

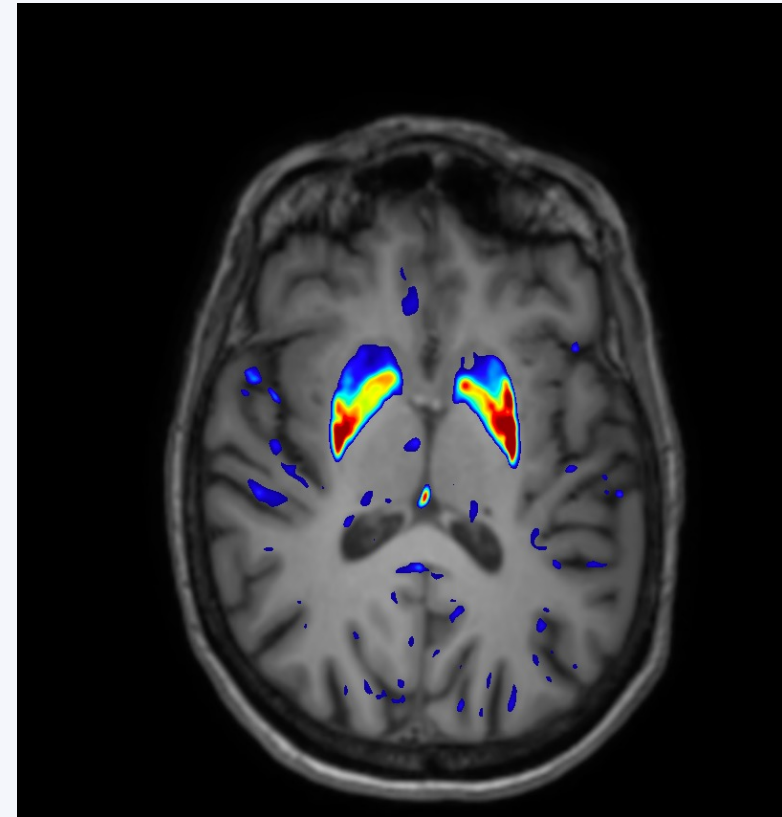
### Substantia Nigra

*Midbrain axial view*

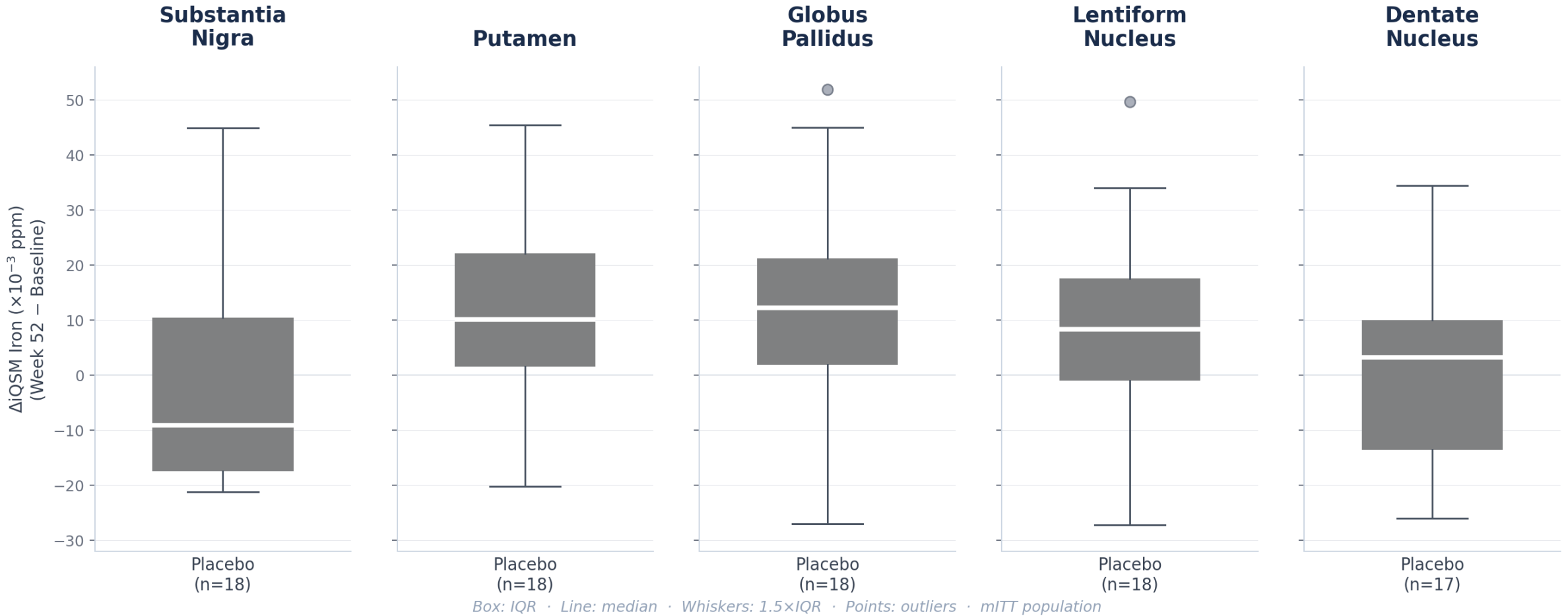


### Putamen / Globus Pallidus

*Basal ganglia axial view*



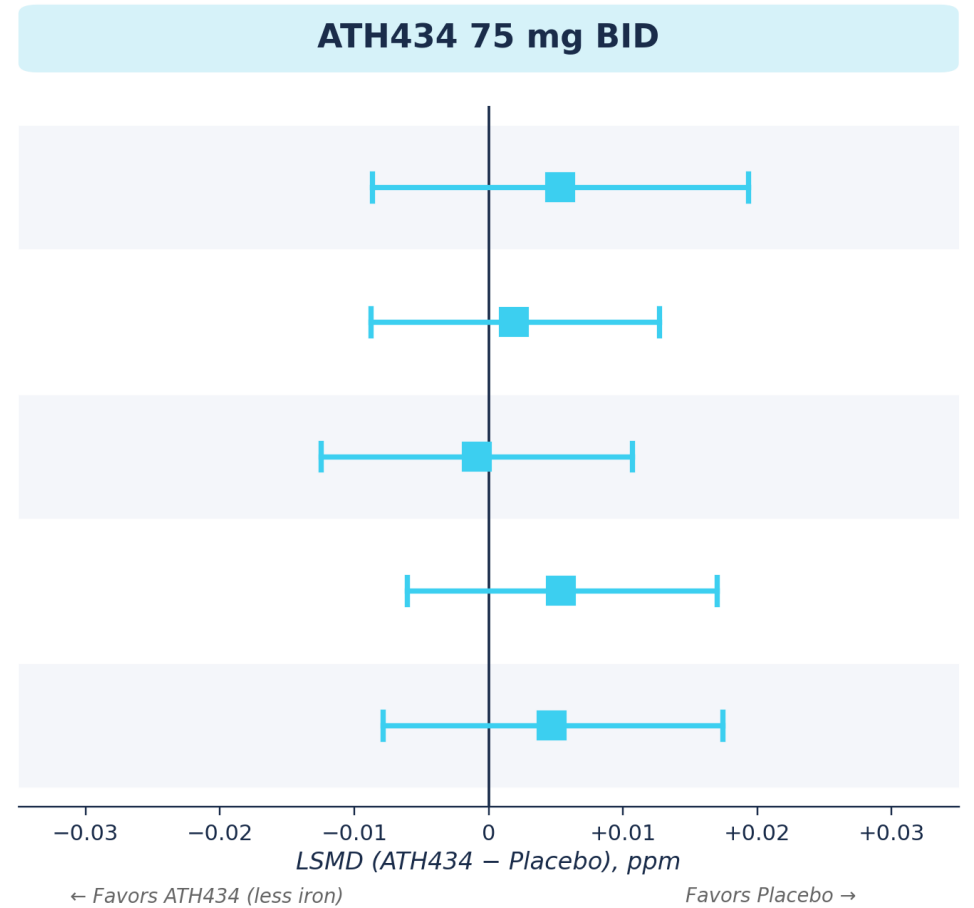
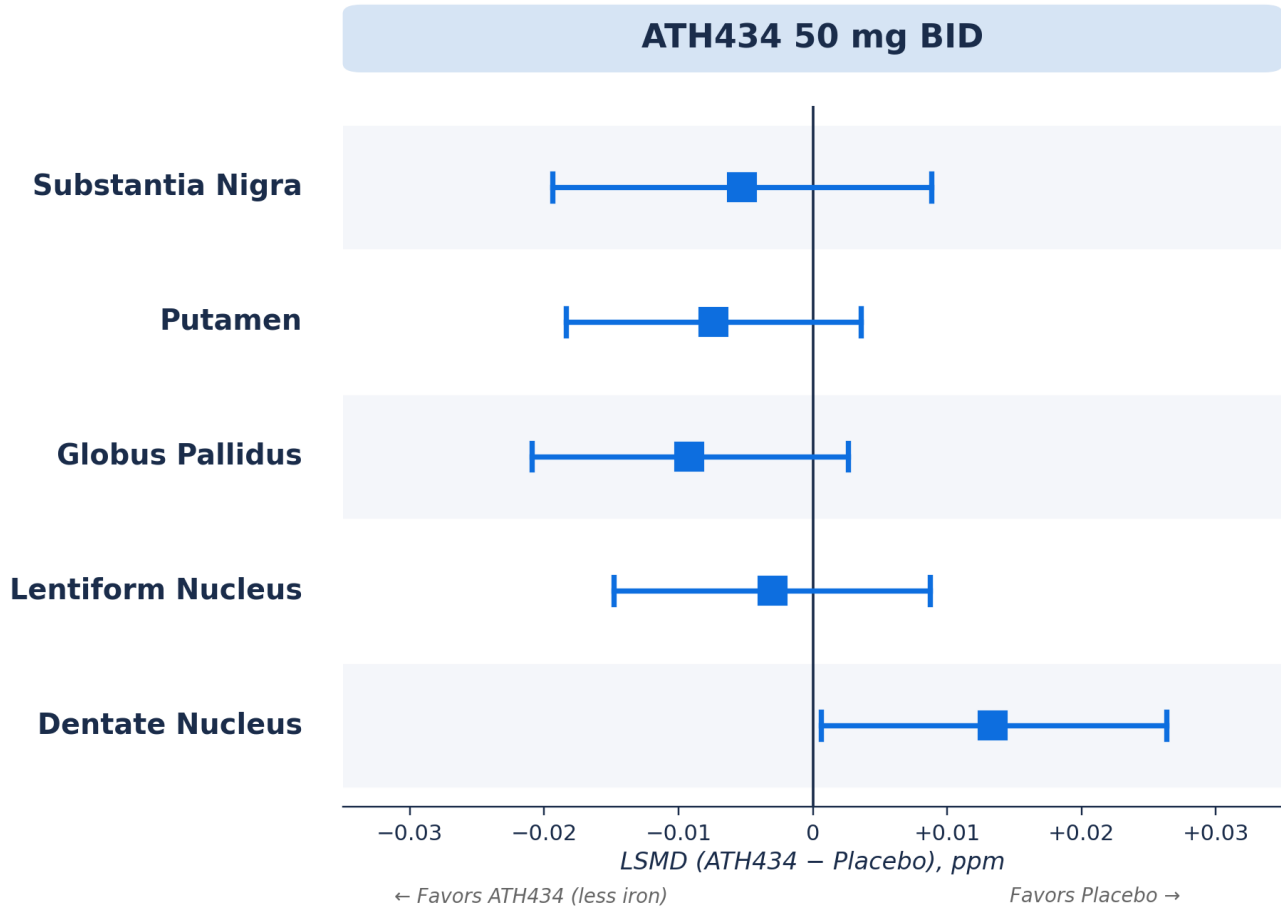
# Iron Deposition on MRI in Placebo: Change Baseline → Week 52



Mean  $\pm$  95% CI

# Iron Deposition on MRI: ATH434 vs. Placebo

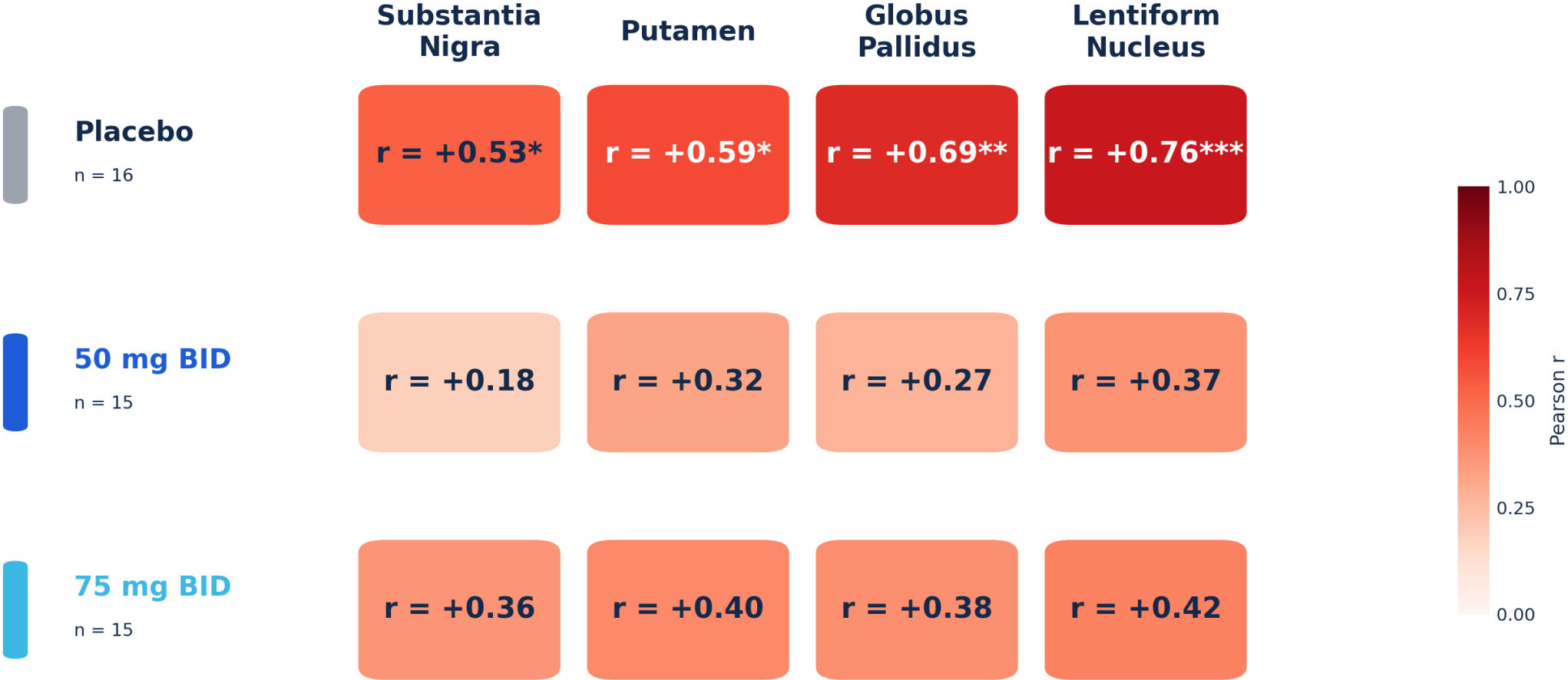
ATH434-201



MMRM with sex, age, baseline CSF NfL, and baseline iron as covariates

# Correlation Between Change in Iron and Change in UMSARS I Score at Week 52

*ATH434 decouples iron accumulation from clinical worsening*

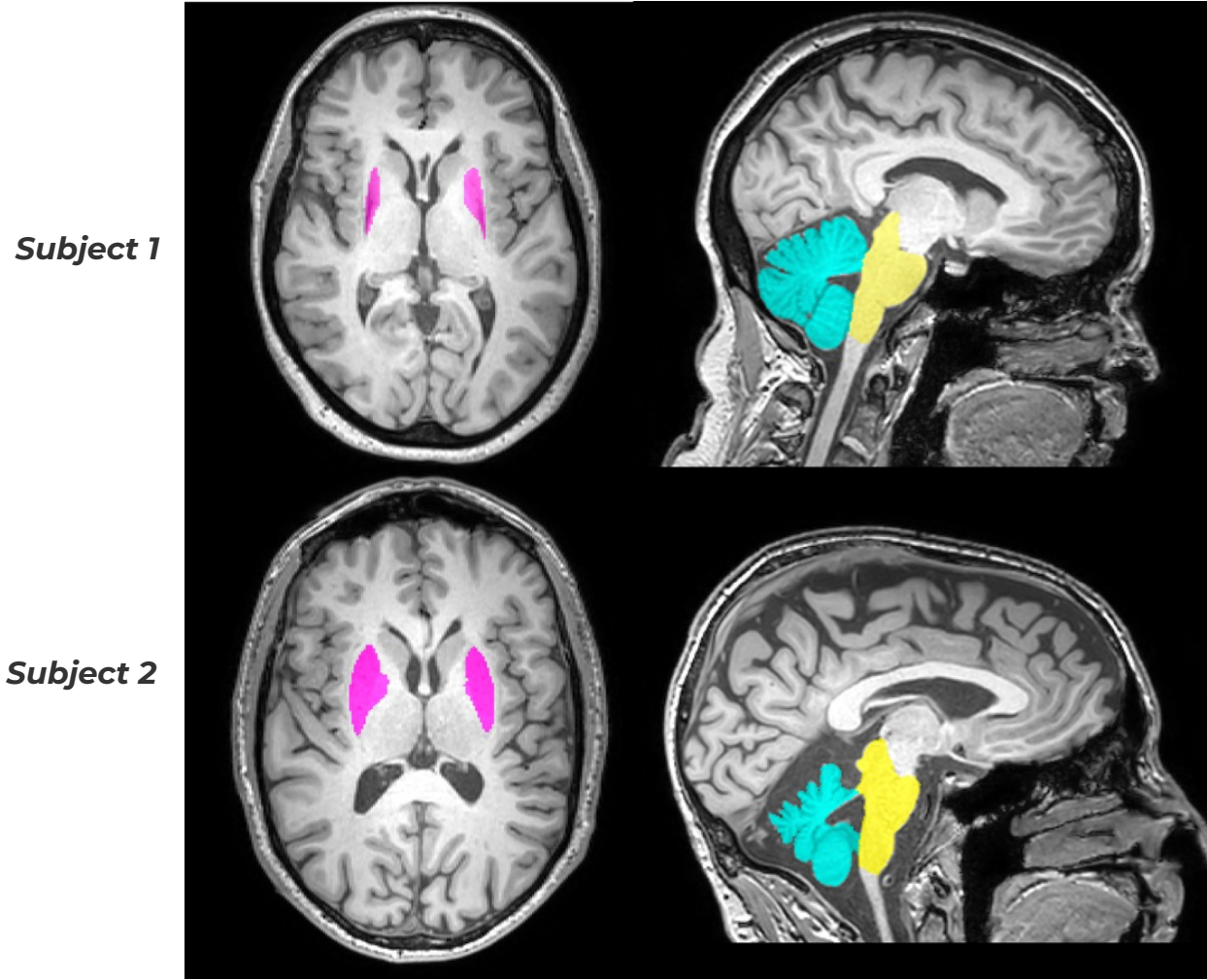


† p<0.10 \* p<0.05 \*\* p<0.01 \*\*\* p<0.001 | Residual partial correlation Controlling for Sex, Age, Baseline CSF NfL, Baseline QSM

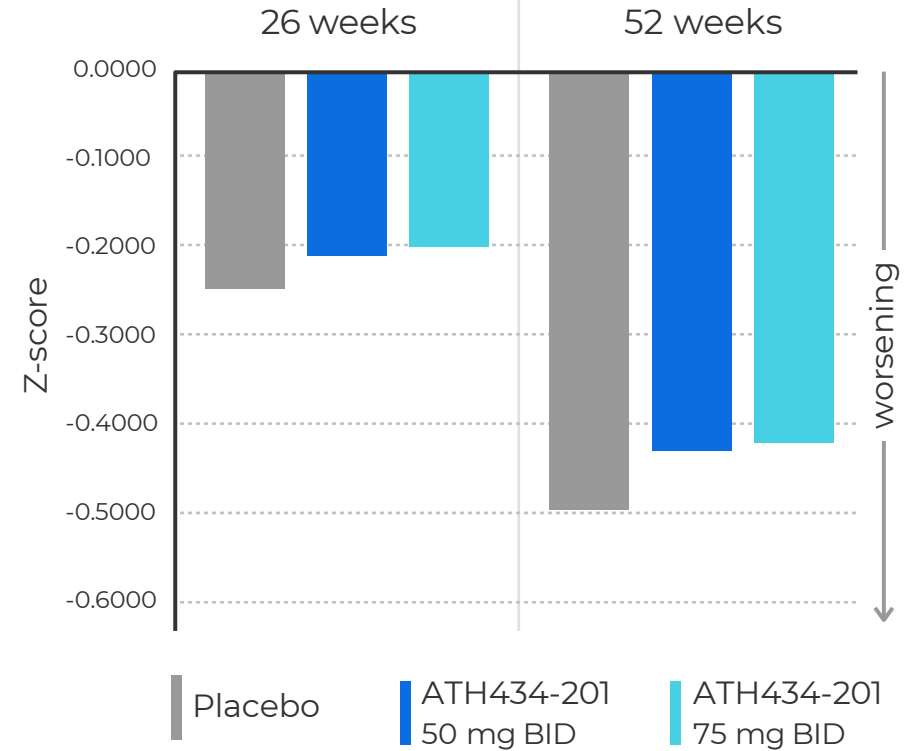
## Summary: ATH434 Interrupts the Pathologic Process in MSA

- Iron accumulates in the basal ganglia of MSA patients, most prominently in the globus pallidus and putamen
- QSM allows quantitation of total brain iron but does not distinguish between reactive (toxic in excess) and stable forms of iron
- In placebo-treated patients, change in iron **strongly** correlates with change in disease severity
- In ATH434-treated patients, change in iron **weakly** correlates with change in disease severity
  - ATH434 leads to a **decoupling** of iron accumulation and clinical worsening as assessed by UMSARS I

# Measuring Brain Volume in MSA Regions of Interest



## 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

# Successful End-of-Phase 2 meeting with FDA

## Alignment on key elements of the Phase 3 design

- ✓ **Primary endpoint:** 11-Item UMSARS Part I
- ✓ **Population :** ~200 patients with clinical and biomarker evidence of MSA
- ✓ **Dosing regimen:** 50 mg dose administered twice-daily for 12 months
- ✓ **Key secondary endpoints:** Swallowing Disturbance Questionnaire (SDQ), Orthostatic Hypotension Symptom Assessment (OHSA), and the Clinical Global Impression of Severity (CGIS)
- ✓ **Statistics:** Methods for analyzing primary and secondary efficacy endpoints acceptable
- ✓ **Safety database:** Anticipated safety database at the conclusion of Phase 3 reasonable

# FDA Alignment on Phase 3 trial Design

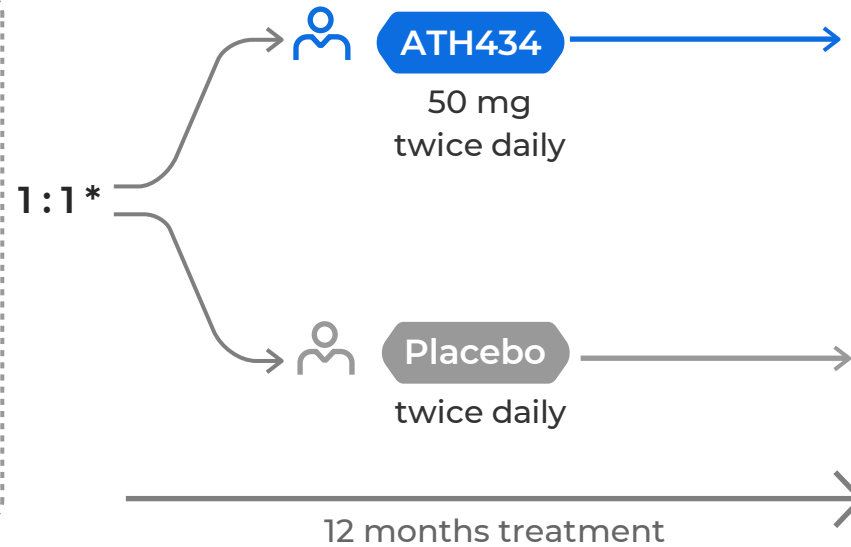
## Patient criteria:



N = ~200

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

## Study design:



\* Randomization stratified by screening plasma NfL

## Efficacy Endpoints:



### Primary endpoint

11 Item UMSARS Part I  
FDA endorsed clinical endpoint



### Key Secondary endpoints

SDQ, OHSA, CGIS



### Efficacy Analysis

Includes baseline CSF NfL as covariate

Expect to initiate trial activities by YE 2026

The background is a solid blue color with a repeating pattern of white, rounded, diamond-shaped outlines. The pattern is arranged in a grid-like fashion, with the shapes slightly offset from each other.

# 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

# Well Positioned for 2026 Catalysts

## Finalize Regulatory Strategy - Align with U.S. FDA on Phase 3 clinical trial

- ✓ Reached alignment in Type C meeting related to clinical pharmacology and non-clinical elements
- ✓ Reached alignment in Type C meeting related to Chemistry Manufacturing & Controls (CMC)
- ✓ Agreement with FDA on Phase 3 study design at End-of-Phase 2 meeting

## Phase 3 Readiness activities

- Clinical site identification and qualification
- Manufacture and package of clinical drug supply
- Initiate start-up activities for the trial by year end

## Build for Scalable Growth

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

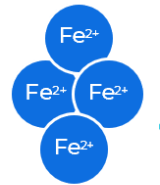
ASX: ATH  
NASDAQ: ATHE





# 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  
Journal of Alzheimer's Disease (2018) DOI 10.3233/JAD-170601

**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.

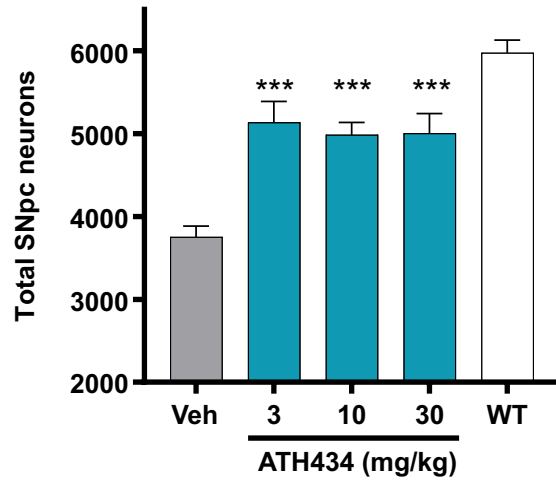
## Cellular iron deposition patterns predict clinical subtypes of multiple system atrophy

Seojin Lee, Ivan Martinez-Valbuena, Anthony E. Lang, Gabor G. Kovacs  
Neurobiology of Disease. 2024. <https://doi.org/10.1016/j.nbd.2024.106535>

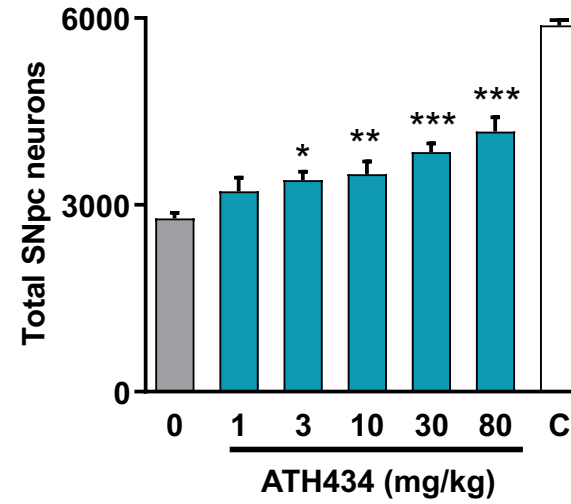
**Importantly, extensive evidence suggests a molecular relationship between iron accumulation and  $\alpha$ -syn pathology.**

# Animal data supporting Phase 2 dose selection

## PLP- $\alpha$ -syn Mouse model



## MPTP Mouse model



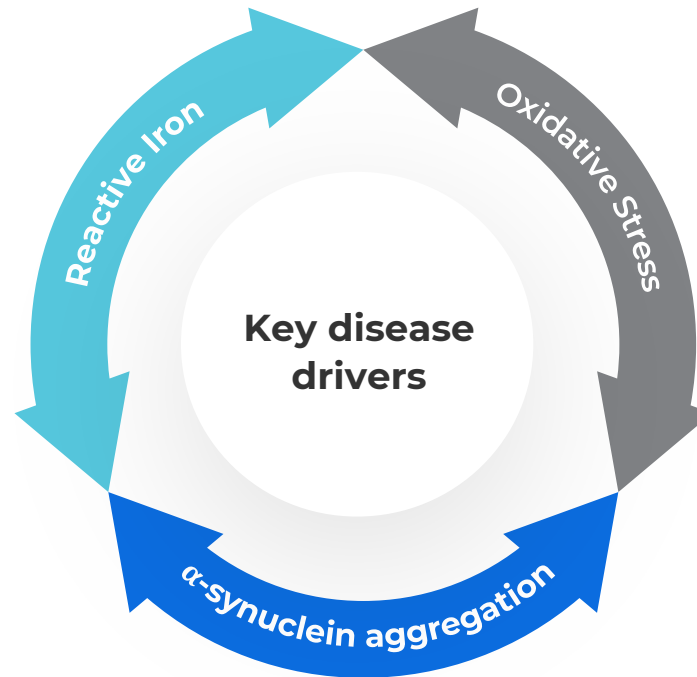
# Iron is a key driver of the MSA Pathology

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

## MSA Pathology Cycle

### 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

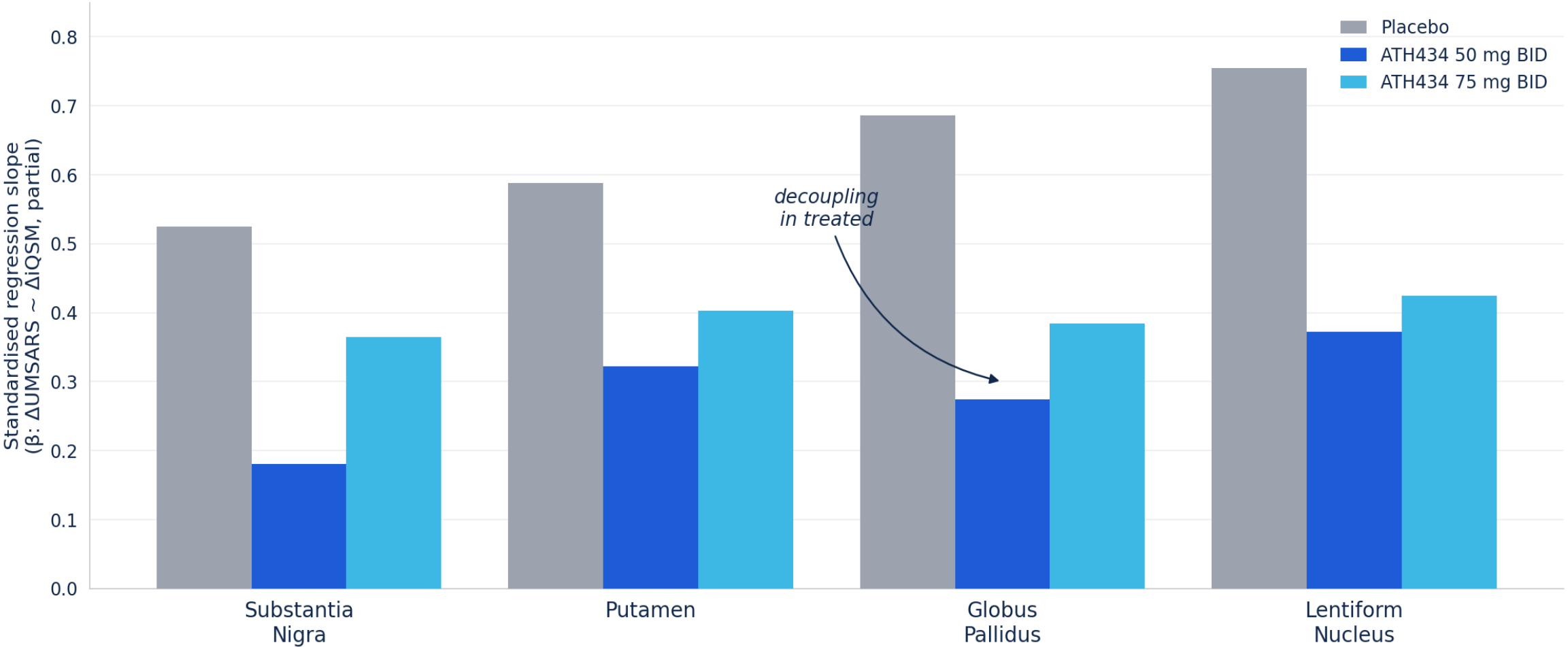
Disrupts multiple cellular functions  
Promotes  $\alpha$ -synuclein aggregation

### $\alpha$ -synuclein aggregation

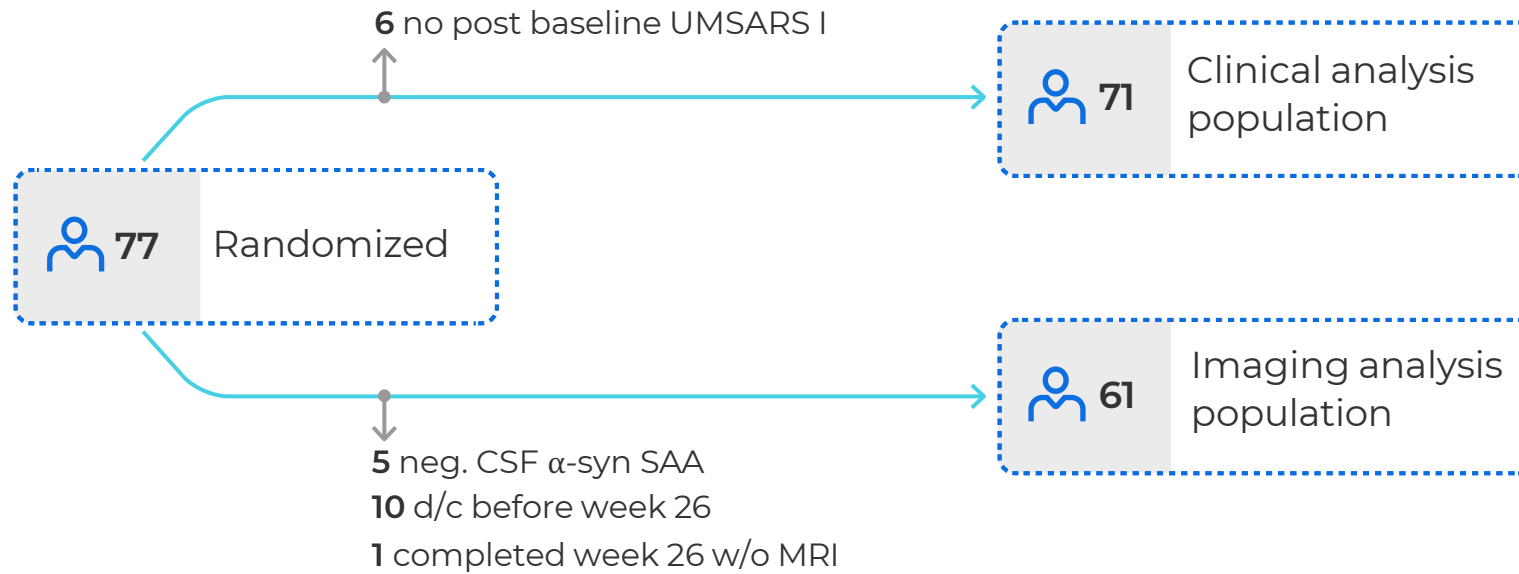
Neuronal toxicity  
Impaired myelin production

# Correlation Between Change in Iron and Change in UMSARS I Score at Week 52

*ATH434 decouples iron accumulation from clinical worsening*





Controlling for Sex, Age, Baseline CSF NfL, Baseline QSM



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

# ATH434-202: Open label study in advanced MSA

ATH434-202

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 <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