Alterity THERAPEUTICS

CEO’s presentation

Dr David Stamler

21 November 2025

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 THERAPEUTICS

Investment highlights

Positive Phase 2 data in Multiple system atrophy (MSA), an aggressive Parkinsonian disorder

Robust efficacy on functional endpoint in double-blind study

Large market potential in neurodegenerative diseases

ATH434 has Orphan Drug designation for MSA treatment

Potential to treat Parkinson's disease and related disorders

Oral administration preferred over competition

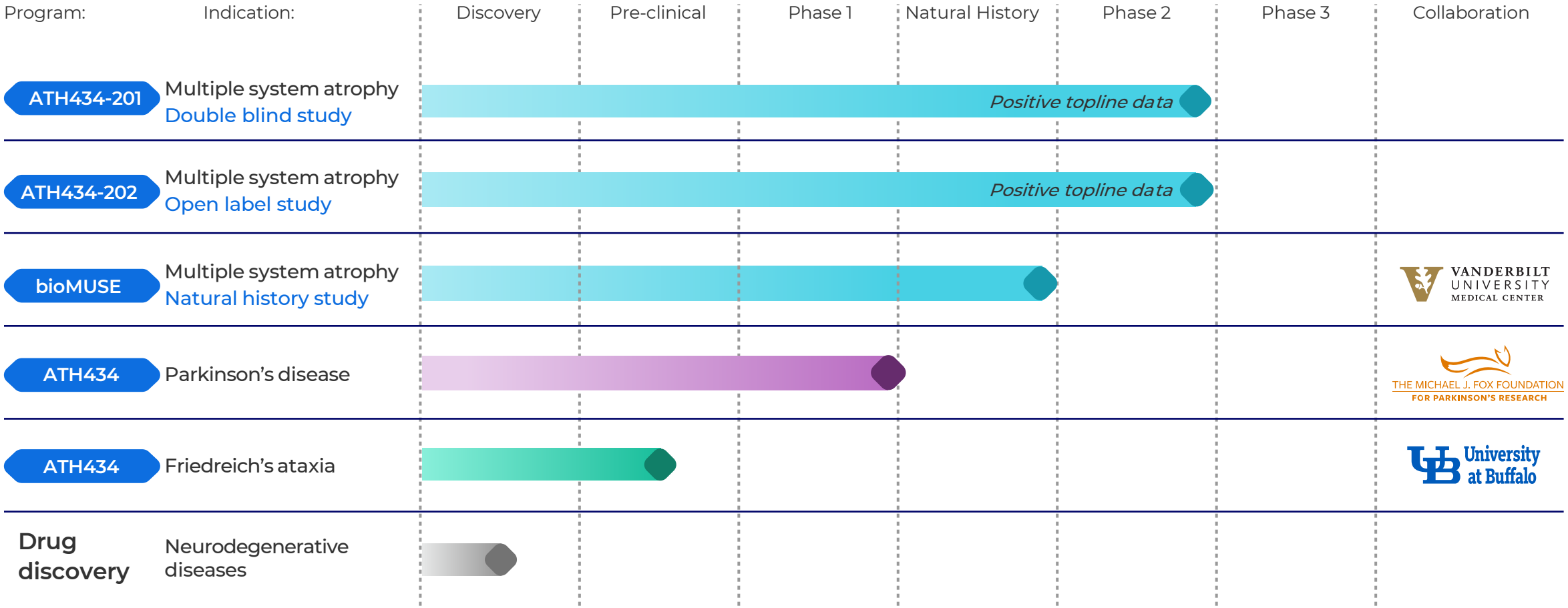
Patient friendly administration

Highly experienced leadership team in movement disorders

Three FDA approvals in neurology

Alterity THERAPEUTICS

Promising portfolio in neurodegenerative diseases



Alterity THERAPEUTICS

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

Rapidly progressive
Highly debilitating

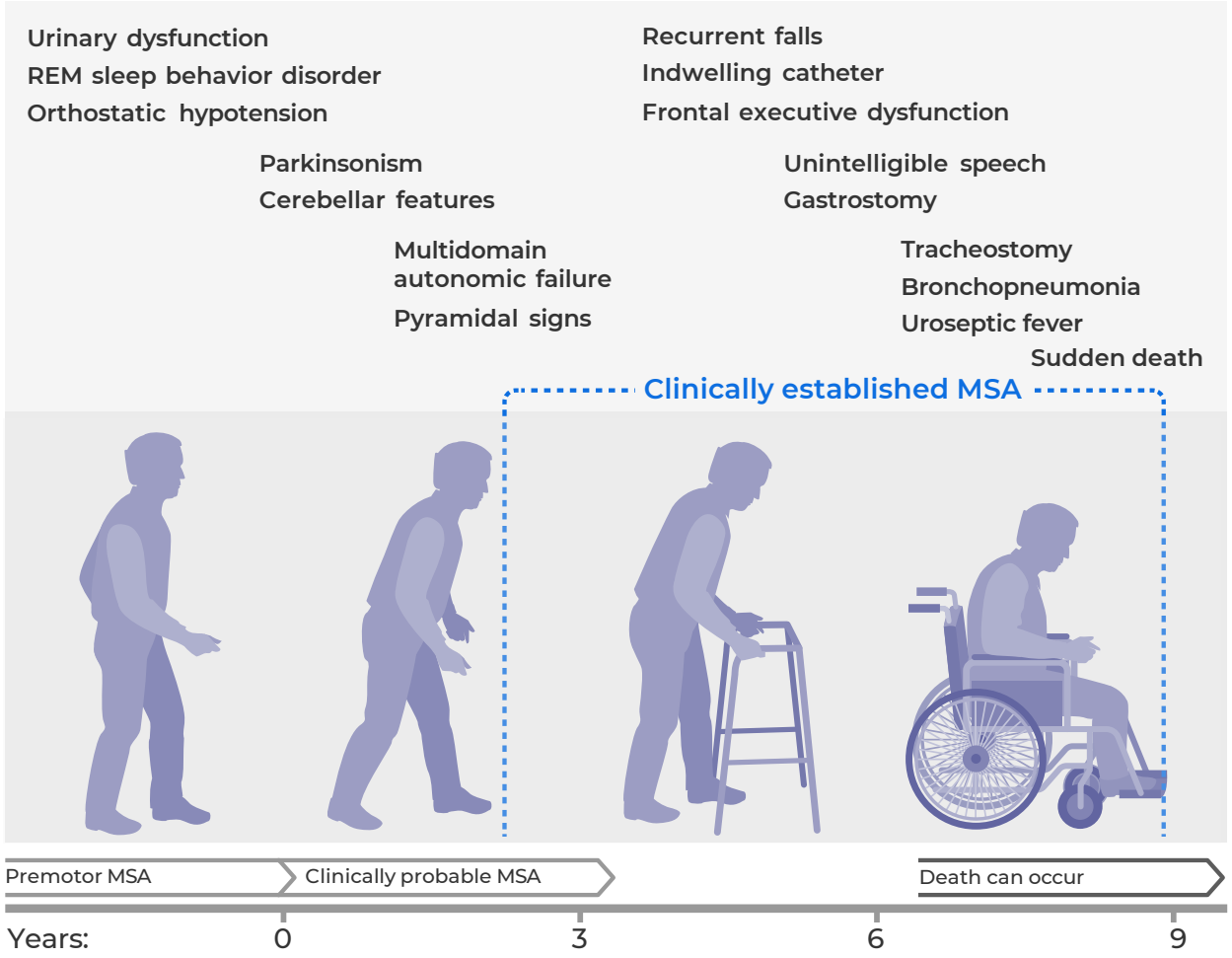
Up to 50,000
patients in U.S.

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

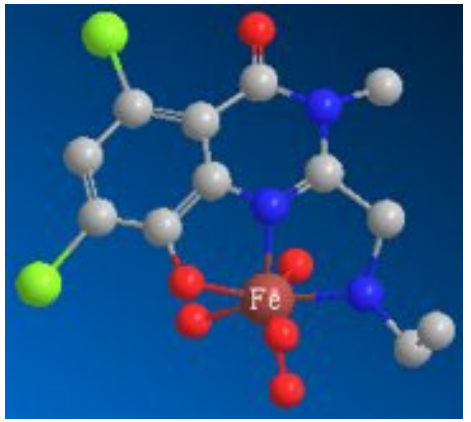


Sources: Fanciulli, Wenning. NEJM 2015 | Wenning, et al. Mov Disorders 2022 | Coon, et al. Brain 2015 | Multiple System Atrophy: National Institute of Neurological Disorders and Stroke (nih.gov)

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
Efficacy in animal models of disease	Efficacy shown in animals with experimental Parkinson's disease and MSA
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

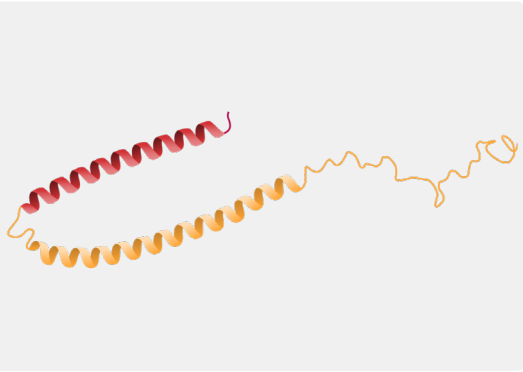


Alterity THERAPEUTICS

Targeting the pathology of MSA

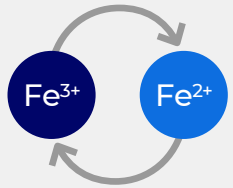
Alterity THERAPEUTICS

Key players in MSA pathology



α-Synuclein protein:

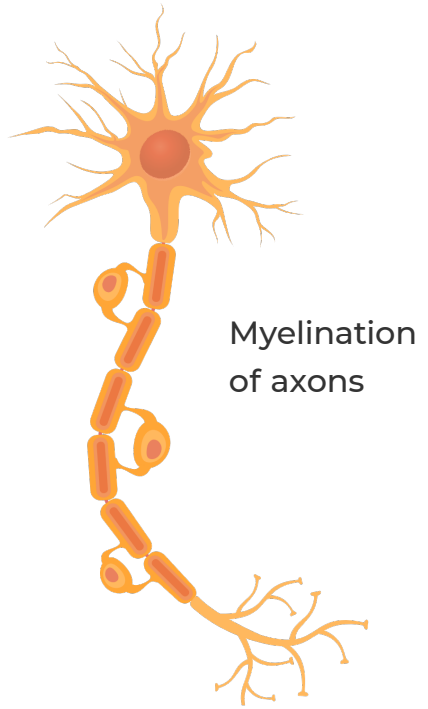
- Present in all neurons
- Regulates neurotransmitter release
- Facilitates neuronal communication



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



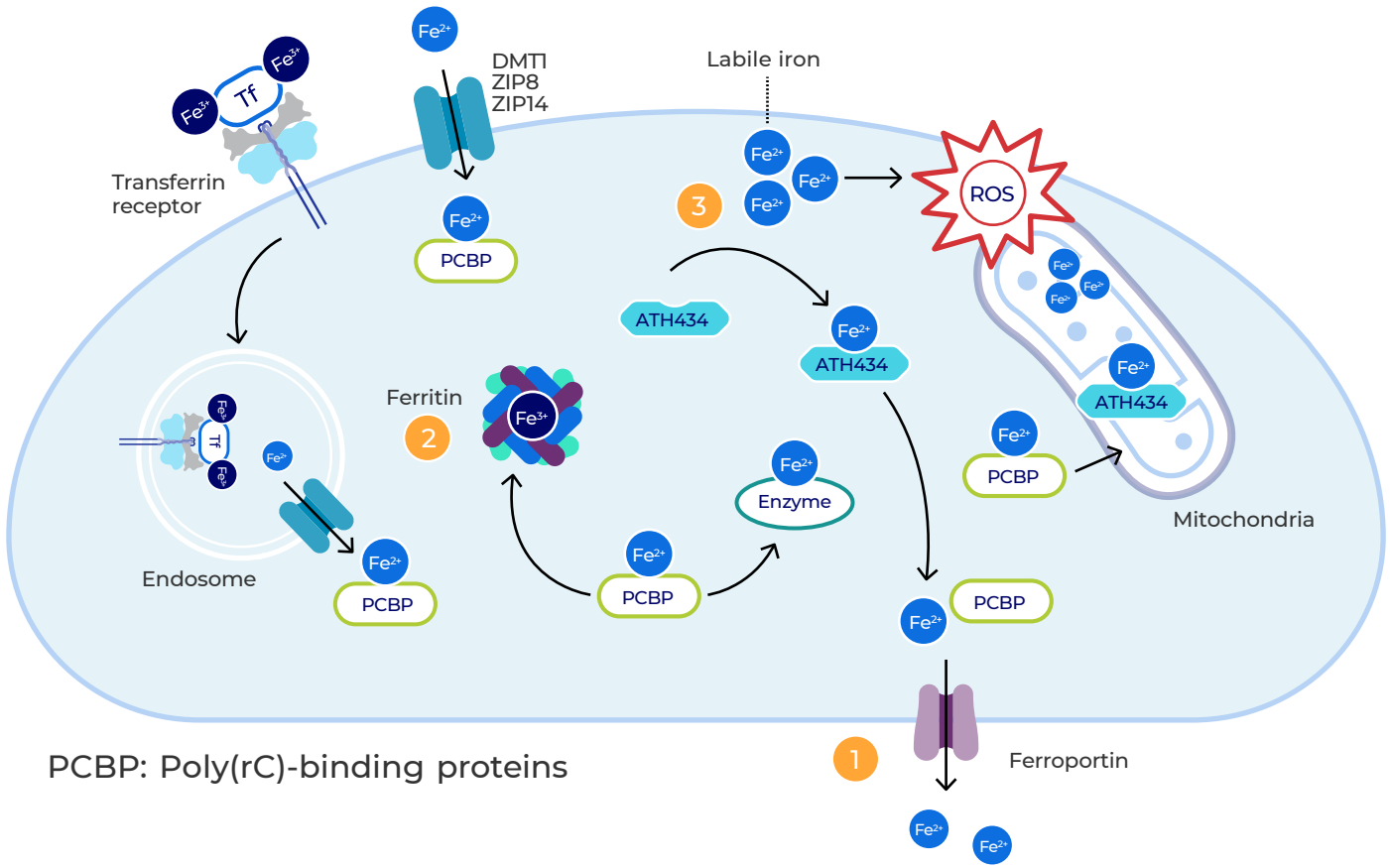
Myelination of axons

Alpha-synuclein and iron balance vital for normal CNS function

Alterity THERAPEUTICS

ATH434 mechanism of action: Iron chaperone

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



PCBP: Poly(rC)-binding proteins

Fe^{2+} Reactive

Fe^{3+} Stable

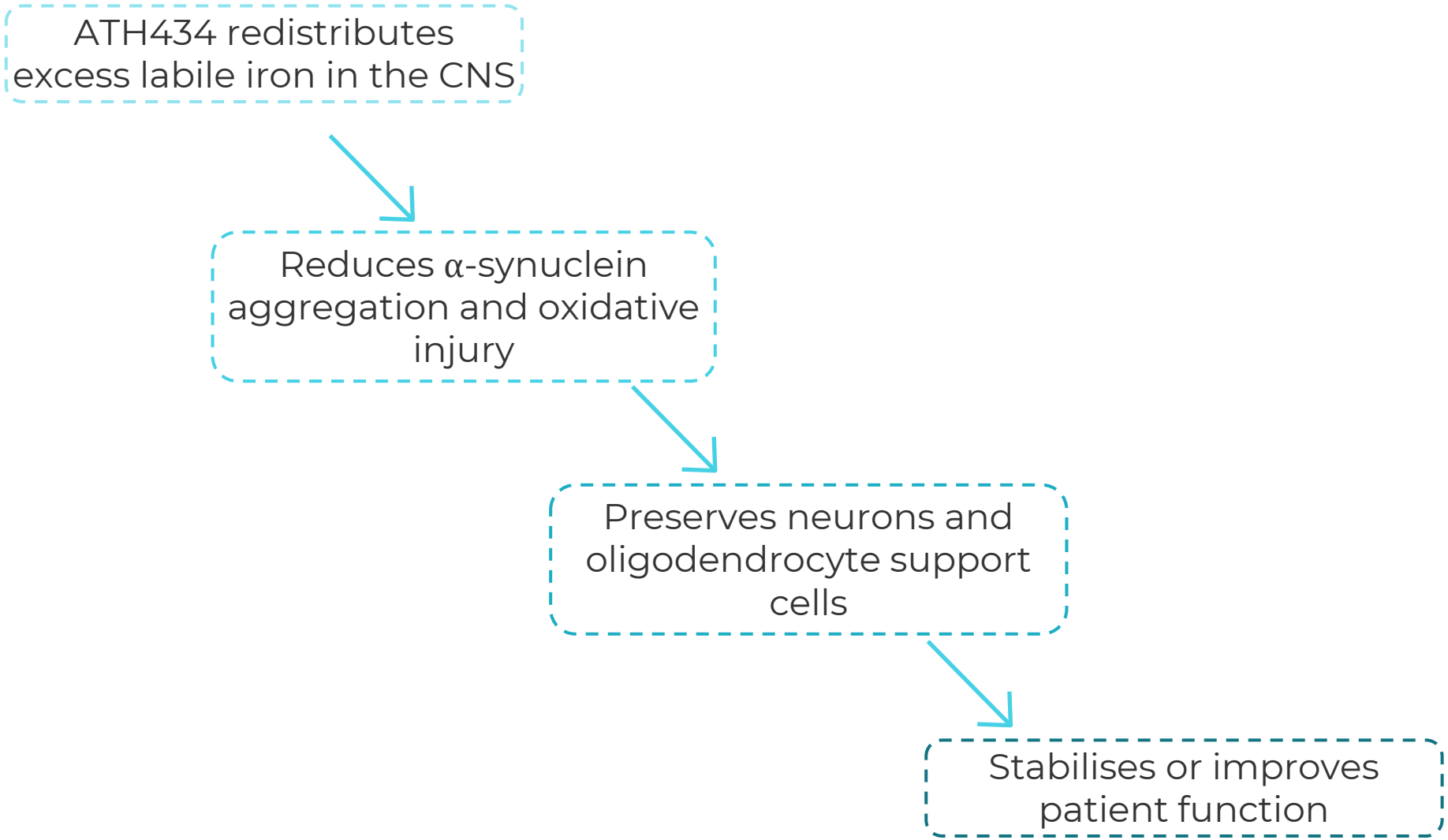
Redistribution mechanisms:

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

Alterity THERAPEUTICS

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 its mechanism of action, ATH434 is a potential disease modifying therapy

Alterity THERAPEUTICS

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

Alterity THERAPEUTICS

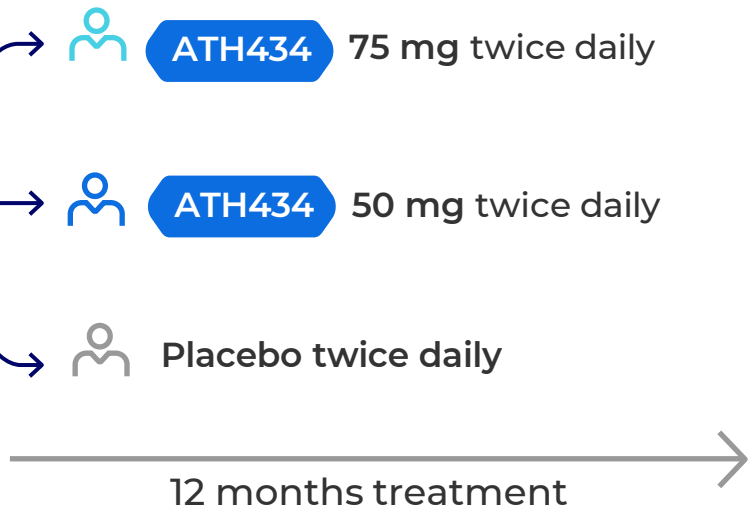
ATH434-201: Randomized, double-blind, placebo-controlled study

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

Alterity THERAPEUTICS

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

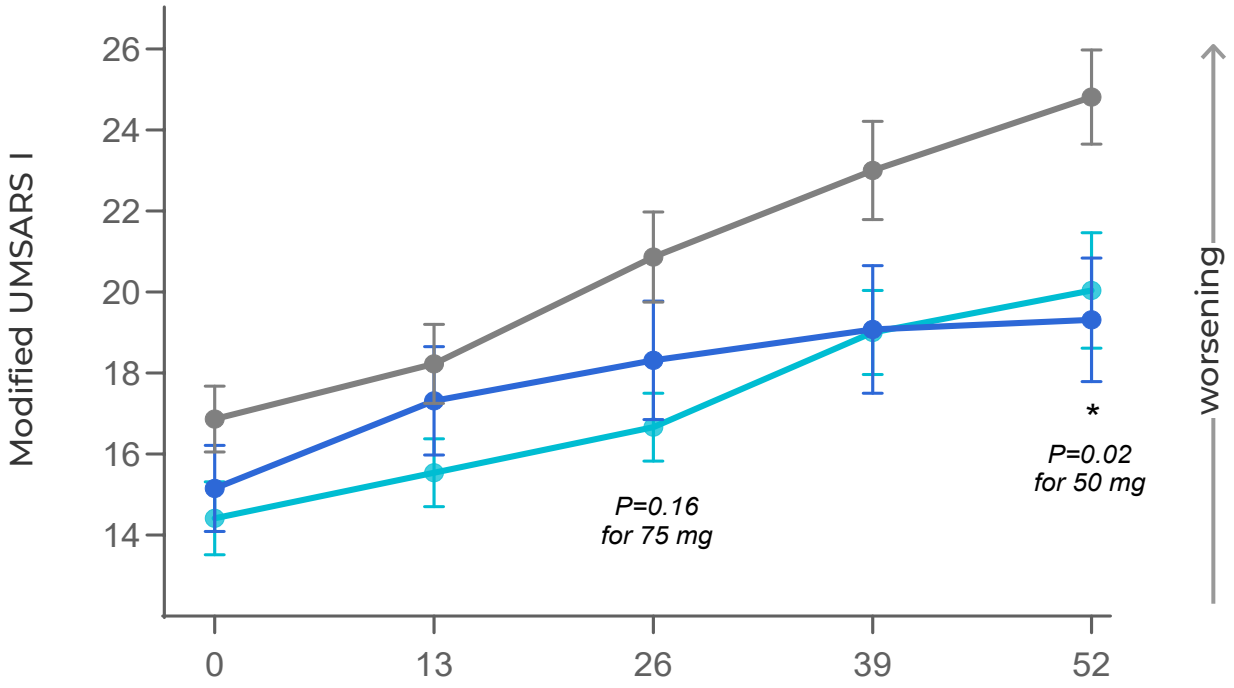
Validated rating scale to assess MSA disease severity

Rates functional impairment in domains affected in MSA

Alterity THERAPEUTICS

^ Modified version of UMSARS I excludes sexual function item

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 75 mg strengthens when correcting for important Baseline differences*

** Baseline ortho SBP change as covariate given imbalance of severe OH at baseline*

Relative Treatment Effect

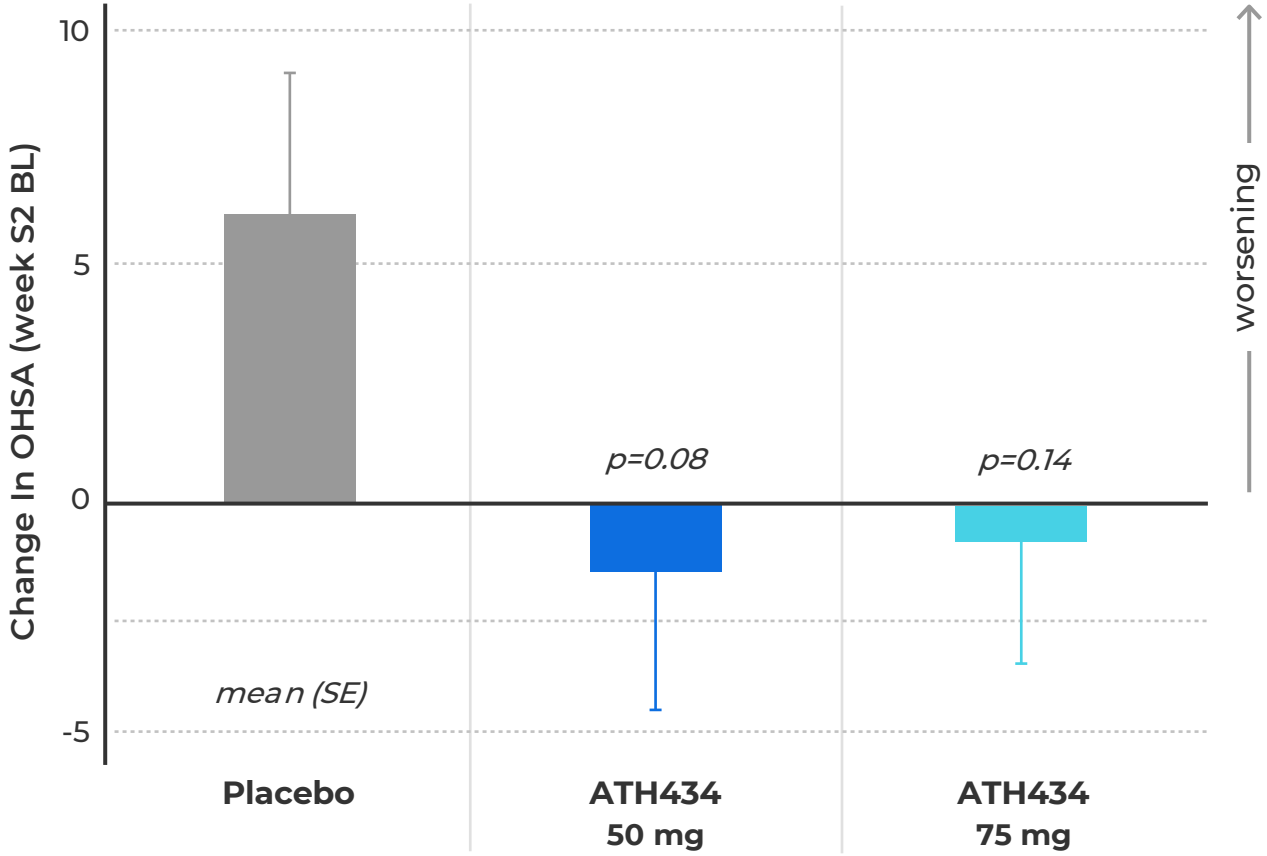
$$\frac{\text{Change}_{\text{ATH434}} - \text{Change}_{\text{Placebo}}}{\text{Change}_{\text{Placebo}}}$$

Alterity THERAPEUTICS

Clinical Analysis Population

Orthostatic Hypotension Symptom Assessment (OHSA)

Change from baseline to week 52



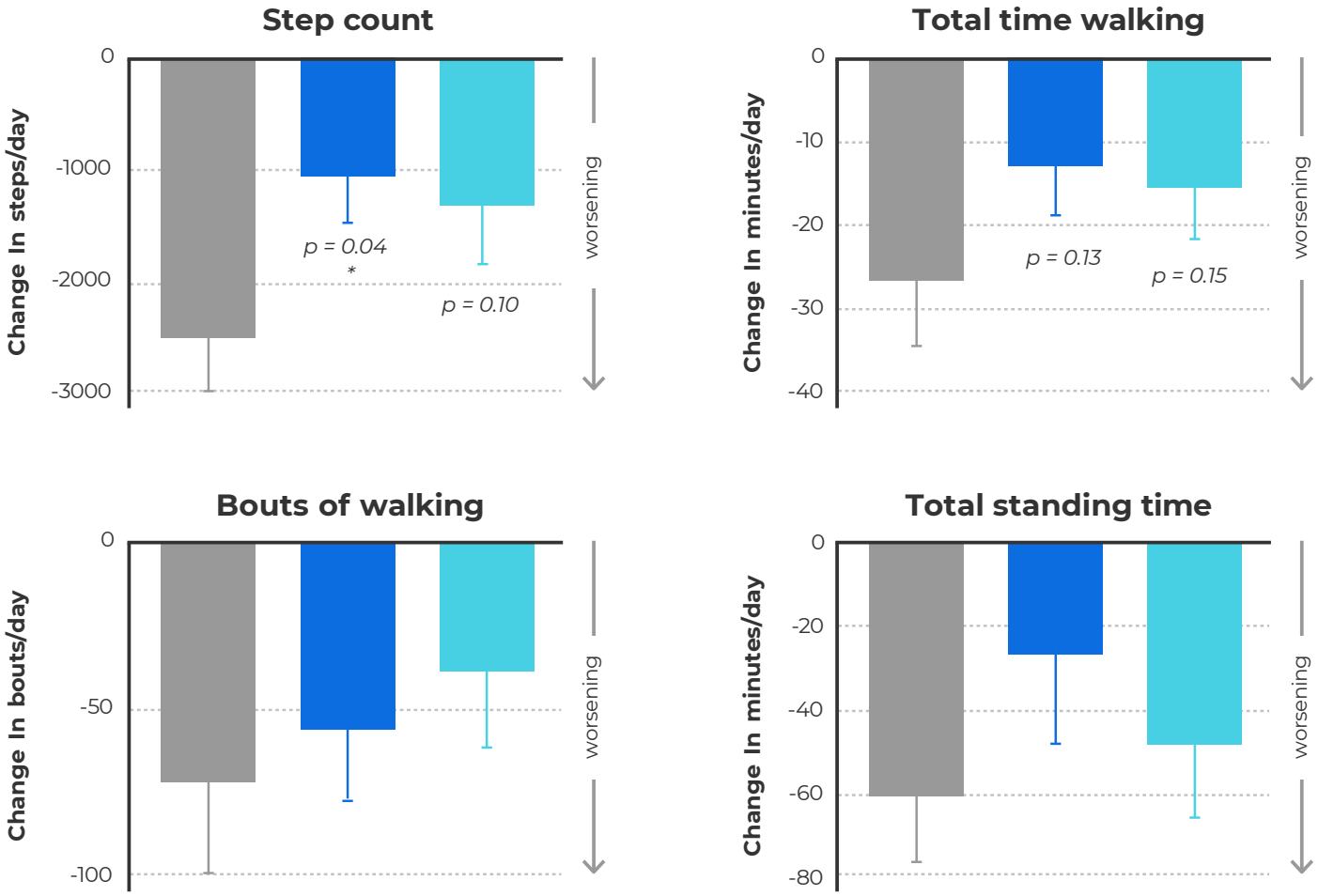
- Assesses symptoms of low blood pressure when going from sitting to standing (e.g., dizziness / feeling faint / lightheadedness)
- Patient reported outcome

Alterity THERAPEUTICS

Clinical Analysis Population

Kaufmann, et al. Clin Auton Res 2012..

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

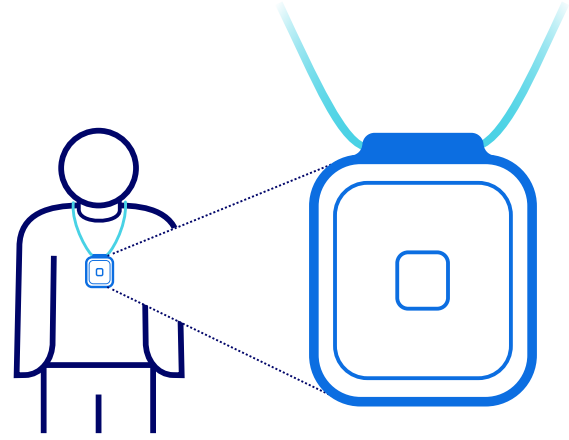


Placebo

ATH434-201
50 mg

ATH434-201
75 mg

Pendant
Wearable movement sensor



Alterity THERAPEUTICS

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**

Alterity THERAPEUTICS

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

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

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

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

Alterity THERAPEUTICS

Commercial opportunity in MSA
Key attributes of ATH434 drive significant value

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

Strong Intent to Prescribe

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

USD $2.4 Billion

Potential worldwide annual peak sales for ATH434 in MSA

Alterity THERAPEUTICS

^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

2025: Strengthening the Foundation for the Future

1. Robust efficacy in Phase 2 double-blind trial on key FDA endpoint
2. Open label trial confirms ATH434's safety and efficacy profile
3. Lead indication MSA is an Orphan Disease with no approved treatment
4. Accomplished team with multiple FDA approvals in neurology
5. Cash Balance:

   A $54.5M as of 30 September

Key Data Readouts, FDA Interactions & Medical Community Engagement

- ATH434-201 Positive Topline Data
- FDA Fast Track Designation in MSA
- ATH434-202 Positive Topline Data
- Phase 3 Trial Planning Ongoing with FDA End-of-Phase 2 expected in mid-2026

Data presentations and publications:

- ✓ *Annals of Clinical and Translational Neurology:* Publication on MSA Atrophy Index
- ✓ American Academy of Neurology (Platform Presentation)
- ✓ American Autonomic Society (Oral Presentation)
- ✓ American Neurological Association
- ✓ International Congress of Parkinson's Disease & Movement Disorders (Platform presentation)
- ✓ International MSA Congress (Oral Presentation)
- ✓ MSA Trust Symposium (Oral Presentation)

Alterity THERAPEUTICS

ASX: ATH
NASDAQ: ATHE

Alterity
THERAPEUTICS