ANA2025

150th ANNUAL MEETING

Long-term Sustained Improvement of Neurological Symptoms in Wilson Disease Patients on Tiomolybdate Choline

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Disclosures

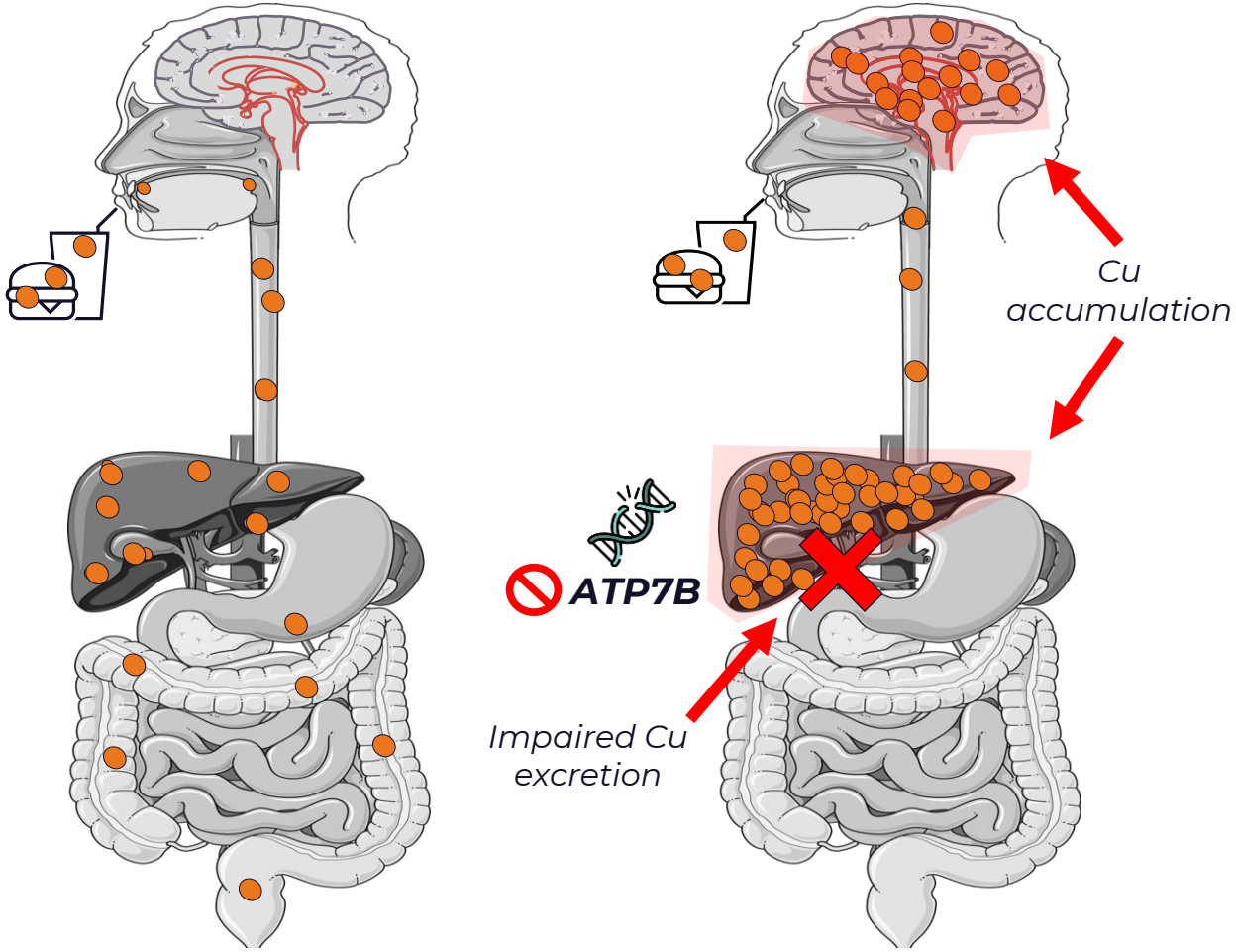
- Travel expenses to attend and present at ANA 2025 were paid for by Monopar Therapeutics

- No additional conflicts of interest to disclose

Wilson Disease

Wilson disease (WD) is a genetic disorder of impaired copper (Cu) transport

Cu accumulates in the **liver** and **brain**, causing hepatic damage and Parkinson-like symptoms



Unmet Need

Current standard of care (SoC) therapies have numerous limitations:

- May cause **paradoxical neurological worsening** (up to 30%)[1]

- Complex, multiple-per-day dosing results in **poor adherence** (up to 50%)[2]

- Risk of **severe side effects** (up to 31%)[3]

- **Slow onset of action**[4]

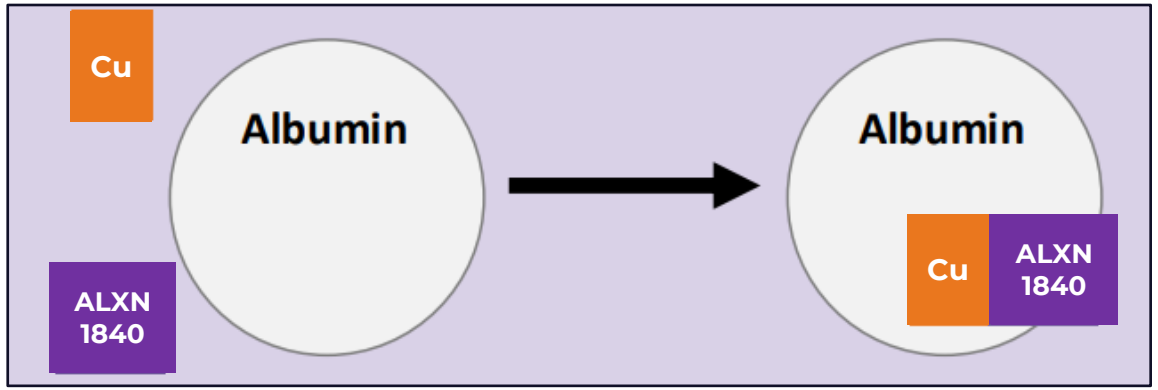
1. Ala A *et al. Lancet.* 2007;369(9559):397-408. 2. Maselbas W *et al. Neurol Neurochir Pol.* 2010;44(3):260-263; 3. Merle U *et al. Gut.* 2007;56(1):115-120; 4. Di Dato F *et al. EMJ.* 2024;9(2):84-95.

Tiomolybdate Choline (ALXN1840)

ALXN1840 is an investigational, once-daily, oral small molecule that binds Cu with high affinity[1]

ALXN1840 forms a tripartite complex with Cu and albumin, **mobilizing and sequestering** toxic Cu[2,3]

Tripartite Complex

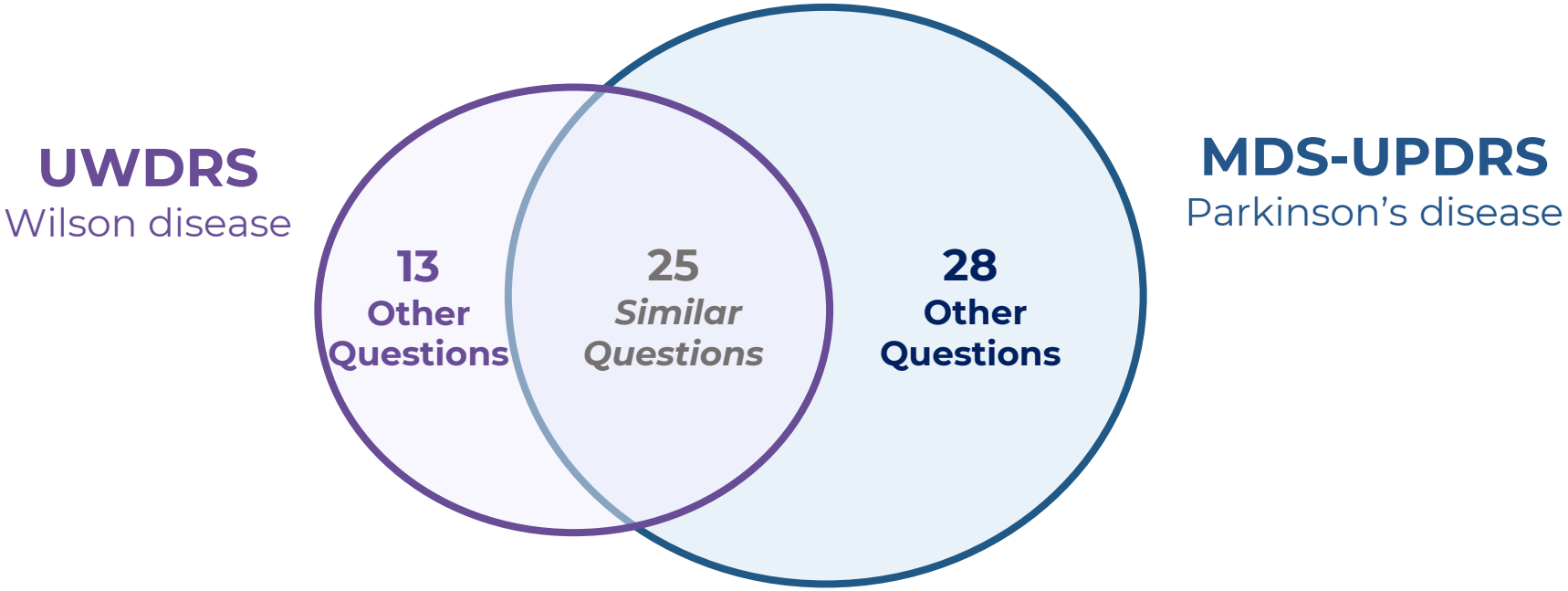


1. Smirnova J *et al*. *Sci Rep*. 2018;8(1):1463; 2. Zhang L *et al*. *Biochemistry*. 2009;48(5):891-897; 3. Kim P *et al*. *Biomedicines*. 2021;9(12):1861.

Unified Wilson Disease Rating Scale (UWDRS)

UWDRS is a validated tool for assessment of neurological symptoms in WD patients[1-3]

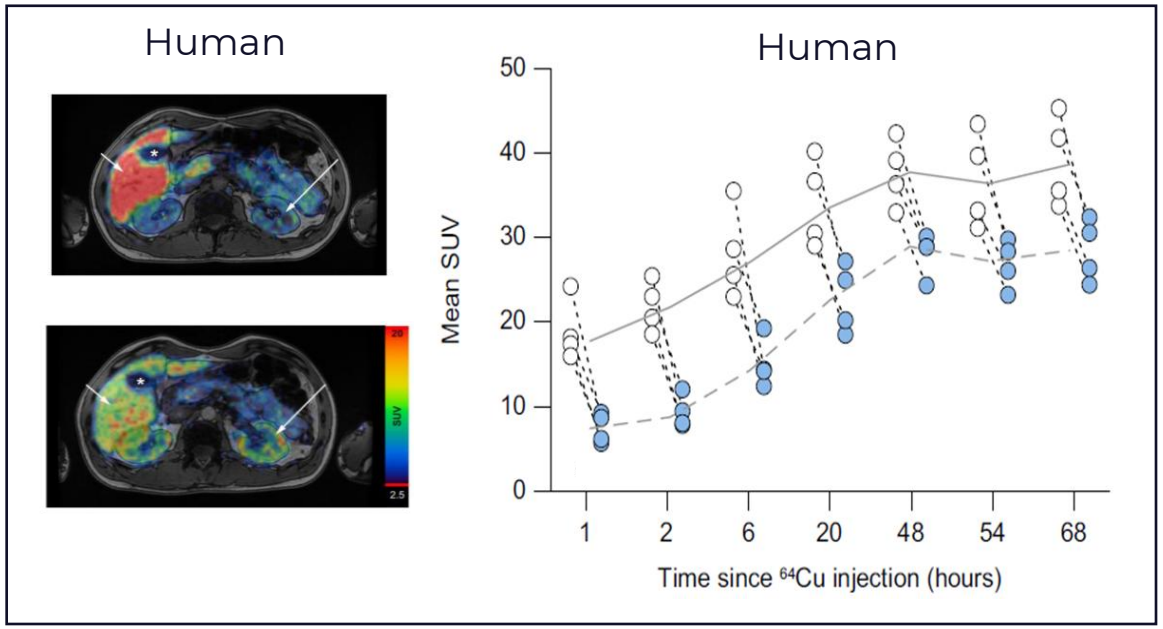
Significant overlap with the Unified Parkinson's Disease Rating Scale (MDS-UPDRS)



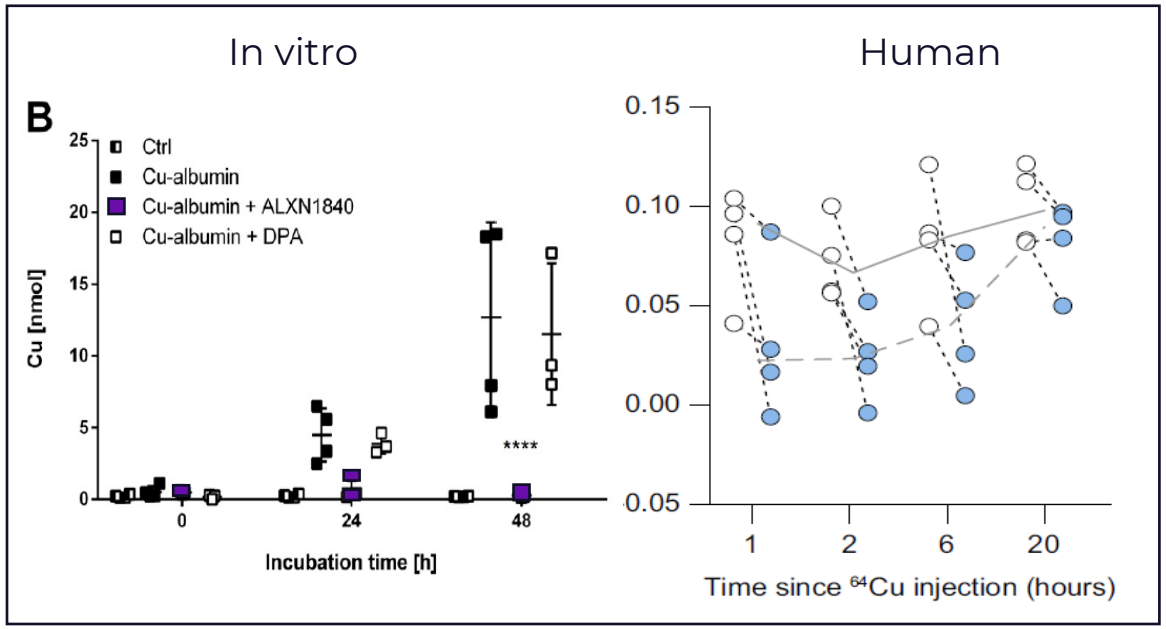
1. Czlonkowska A *et al*. *Neurol Neurochir Pol*. 2007;41(1):1-12; 2. Leinweber B *et al*. *Mov Disord*. 2008;23(1):54–62; 3. Karantzoulis S *et al*. *Adv Ther*. 2024;41(5):2070-2082.

ALXN1840 Prevents Toxic Copper Build-up in the Liver and Brain

Liver



Brain



Before treatment

After treatment

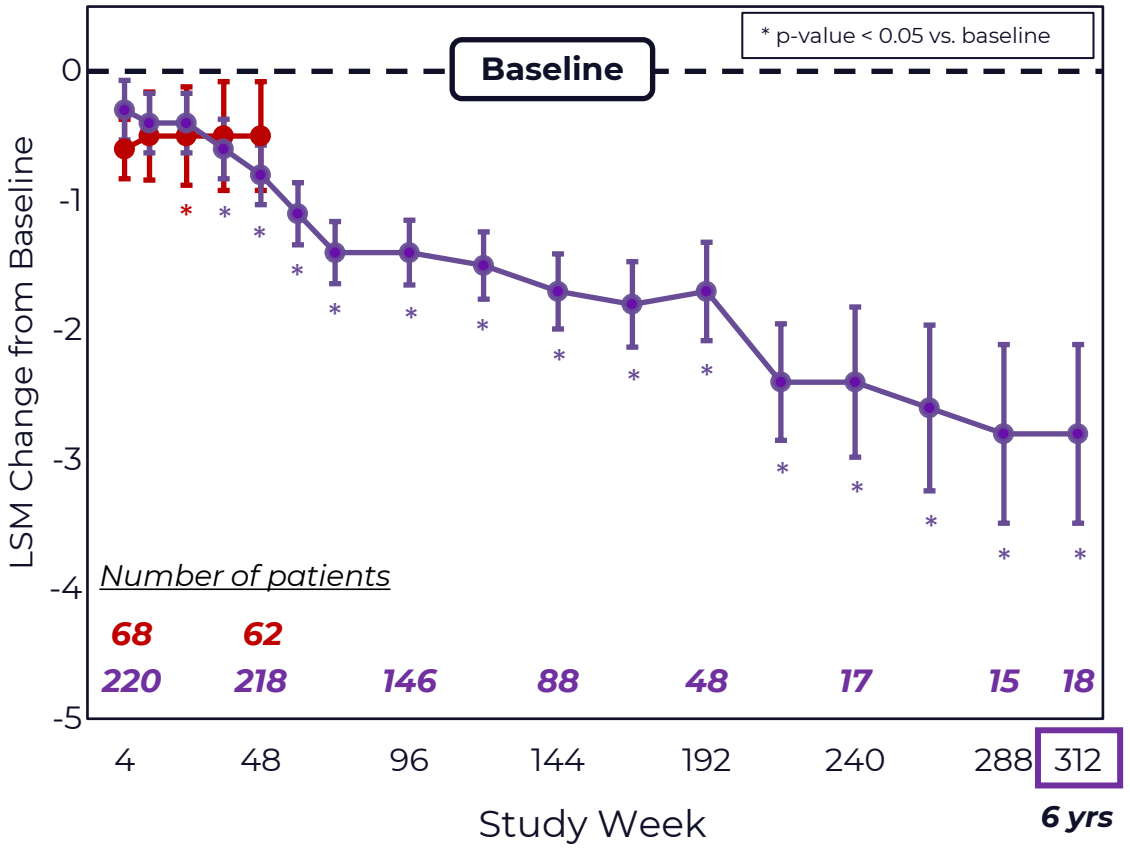
Before treatment (median)

After treatment (median)

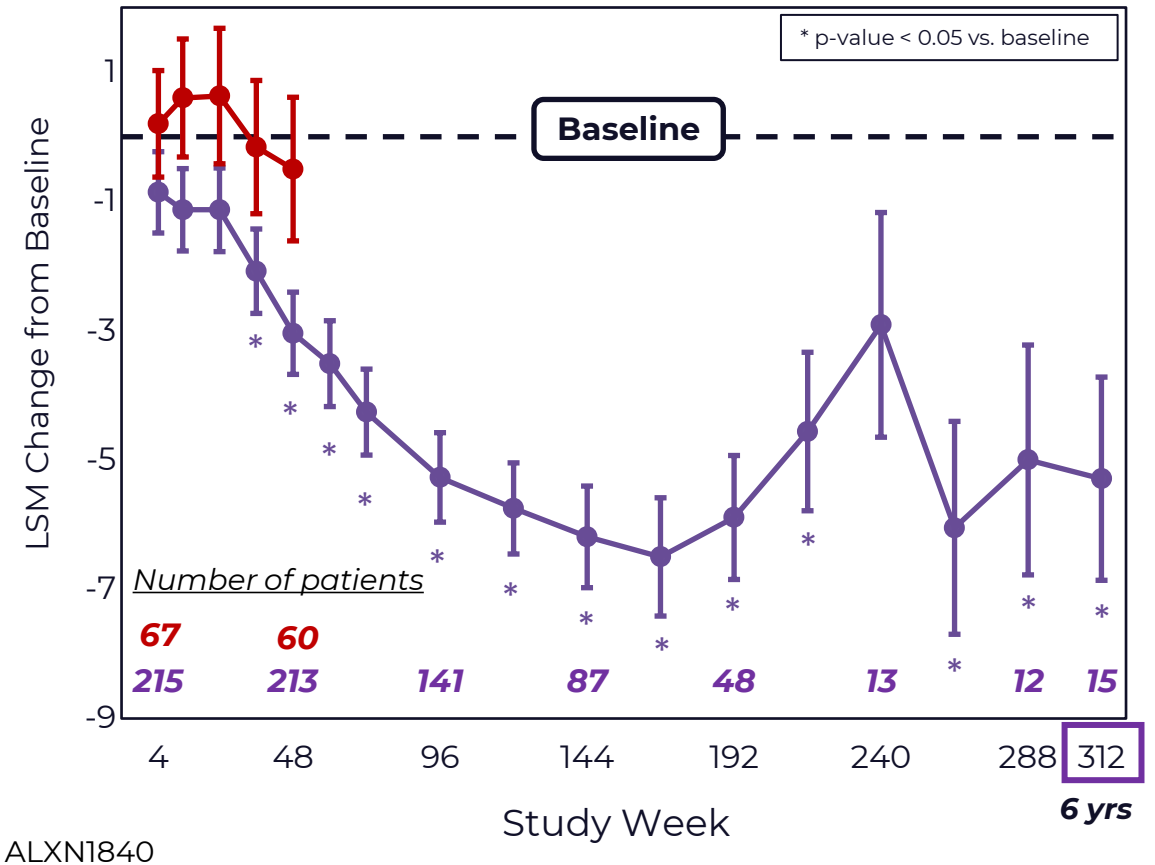
Figures adapted from Kirk FT *et al. J Hepatol*. 2024;80(4):586-595; Borchard S *et al. Life Sci Alliance*. 2021 Dec 2;5(3):e202101164.

Sustained Neurologic Improvement Over 6 Years

UWDRS Part II (Patient-reported)
Least squares mean (LSM) ± standard error – Ph2 & Ph3



UWDRS Part III (Physician-assessed)
Least squares mean (LSM) ± standard error – Ph2 & Ph3



ALXN1840
Standard of Care

Neurological Benefit Reproduced Across Independent Studies

UWDRS Minimum Clinically Important Difference (**MCID**)

- Previous studies have reported a Part II MCID of **1 pt**[1,2] and a Part III MCID of **4 - 6.9 pts**[1-3]
- Calculated UWDRS Part III MCID from Ph2 & Ph3 (n=255) – Part II: **1.84 pts**; Part III: **4.69 pts**

UWDRS Part III (Physician-assessed)

MCID responder rate (Change from baseline to Week 48) – Ph2 & Ph3

	ALXN1840			SoC	
Study ID *(n enrolled)*	**201** (n=29)	**205** (n=31)	**301‡** (n=137)	**ISE** (n=255)	**301‡** (n=70)
Improved† *(%)*	**94**	**57**	**45**	**50**	**32**
Worsened *(%)*	**5**	**4**	**8**	**7**	**13**

More improvement and ***less worsening*** on **ALXN1840** vs **SoC**

Abbreviations: ISE, integrated summary of efficacy; SoC, standard of care

† *Calculated from patients eligible to improve (baseline score ≥ MCID)*

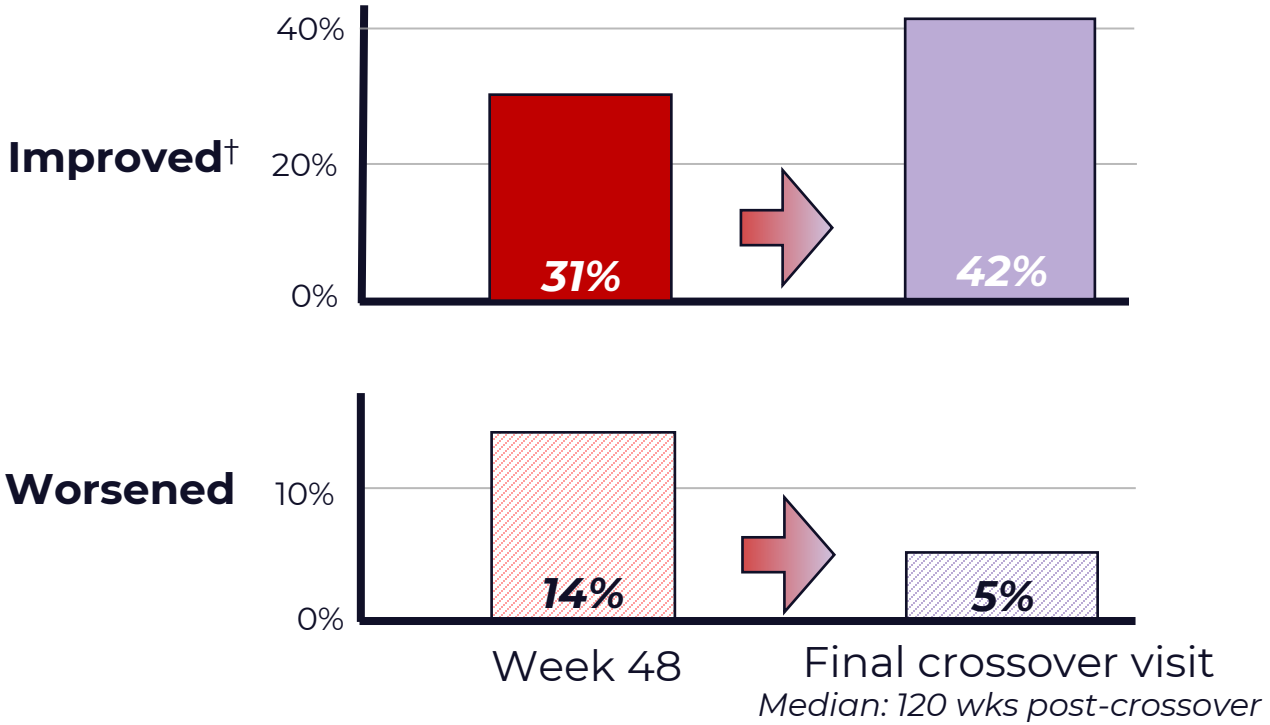
‡ *Physician rater-blinded*

1. Litwin T *et al. J Neurol Sci*. 2015;355(1-2):162-167; 2. Litwin T *et al. Mov Disord*. 2023; 38 (suppl 1); 3. Członkowska A *et al. BMC Neurol*. 2018;18:34.

Patients Further Improve After Crossover from SoC to ALXN1840

UWDRS Part III

MCID responder rate – Ph3



SoC-Crossover patients (n=56)
All changes vs. Wk 0 (baseline)

SoC

Crossover SoC to ALXN1840 @ Week 48

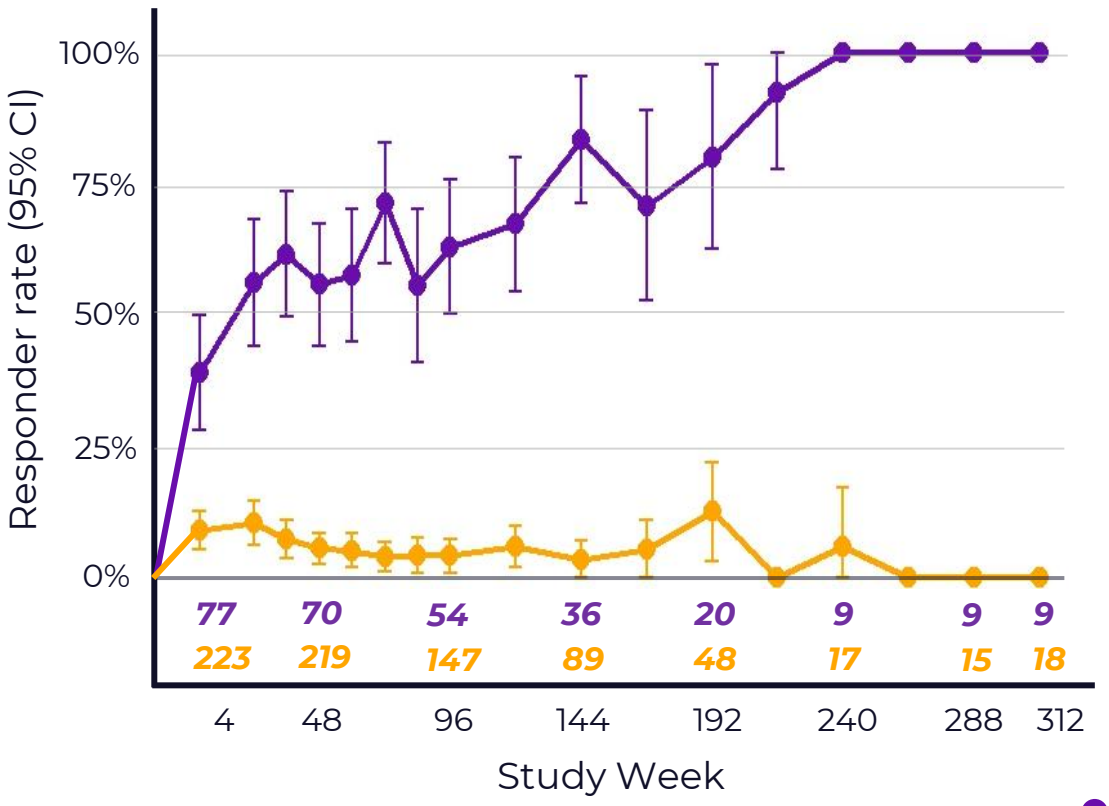
Mean Δ from Wk 0†: ***-1.9 pts*** → ***-4.8 pts***

† *Calculated from patients eligible to improve (baseline score ≥ MCID)*

Neurologic Benefit Increases Over Time

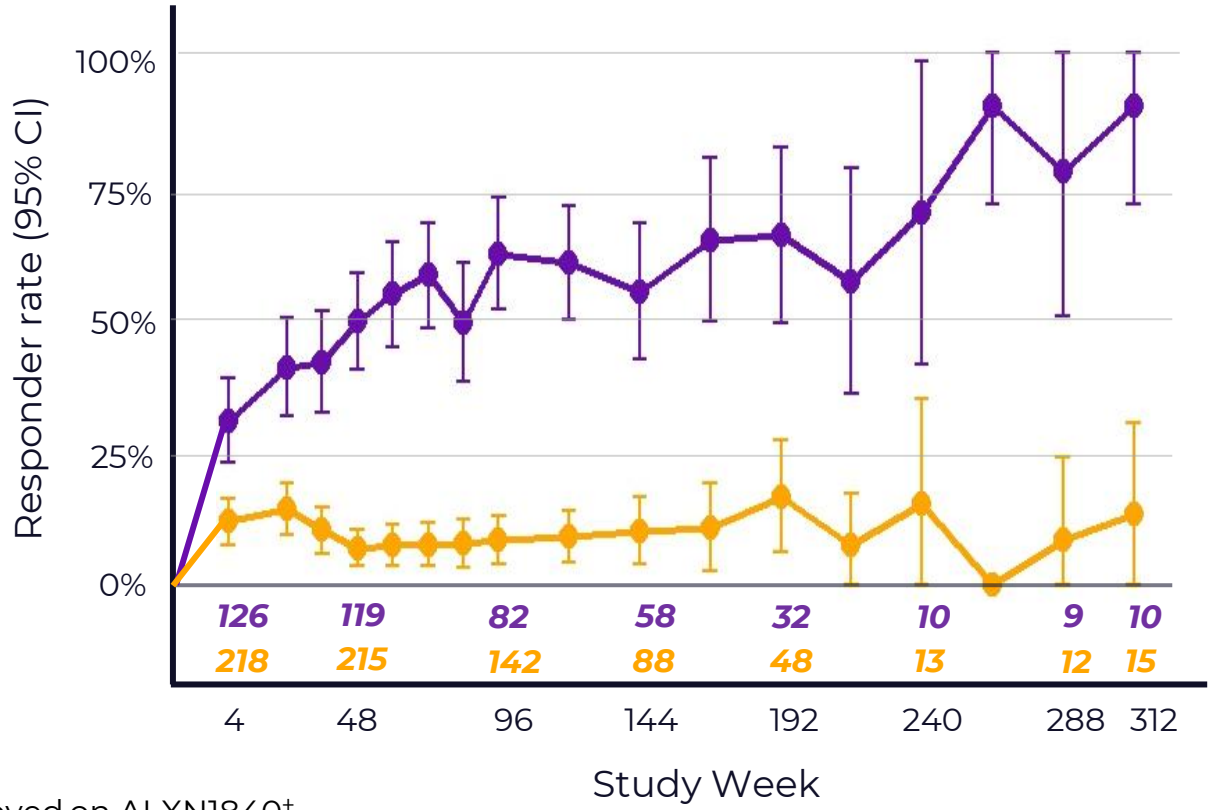
UWDRS Part II (Patient-reported)

MCID responder rate (1.84 pts) – Ph2 & Ph3



UWDRS Part III (Physician-assessed)

MCID responder rate (4.69 pts) – Ph2 & Ph3



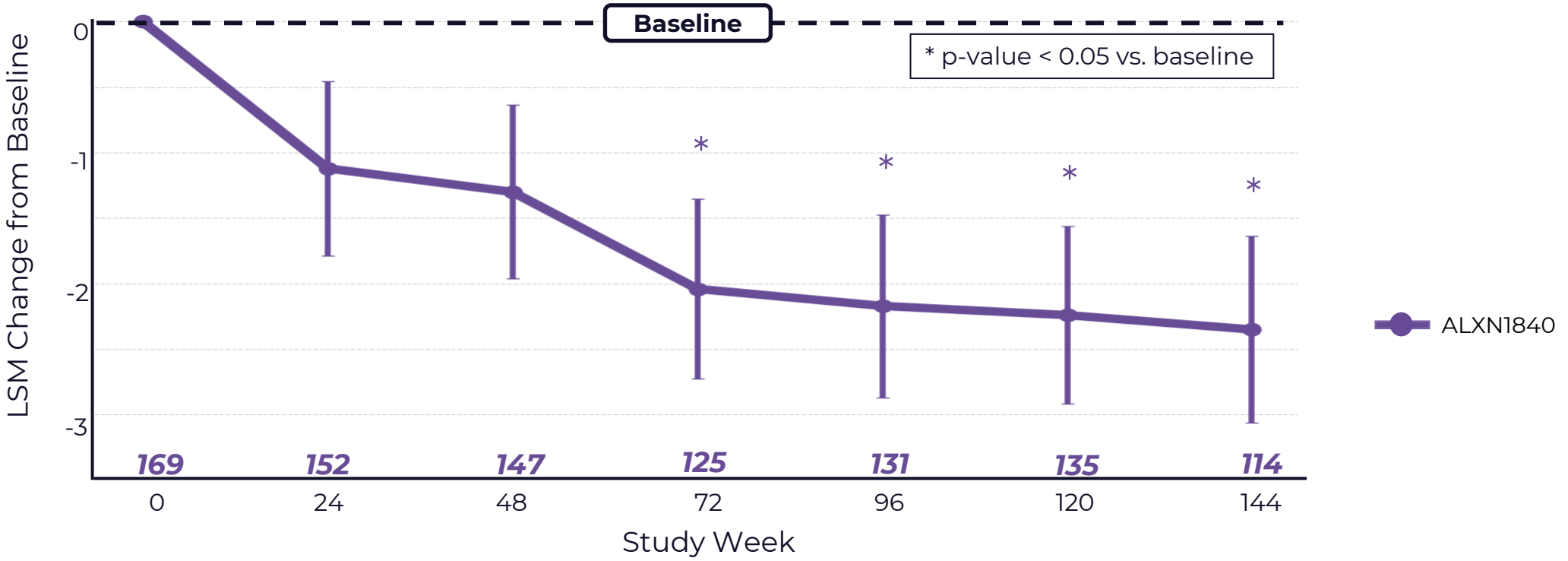
Improved on ALXN1840†

Worsened on ALXN1840

† *Calculated from patients eligible to improve (baseline score ≥ MCID)*

Sustained Improvement in Psychiatric Symptoms

Brief Psychiatric Rating Scale (BPRS) (Clinician-assessed)
Least squares mean (LSM) ± standard error – Ph3



ALXN1840 Has a Favorable Safety Profile

Long-term Safety

Serious Adverse Events (SAEs) on ALXN1840	
Number of patients	266
Median time on treatment (years)	2.58
Total **patient-years** (PYs)	645.6
Patients with **any drug-related SAE**	13 (4.9%)
Neurologic	2 (0.8%)
Psychiatric	1 (0.4%)

No deaths occurred that were deemed related to ALXN1840.

Questions?