RESTORE-FA data update

May 18 2026

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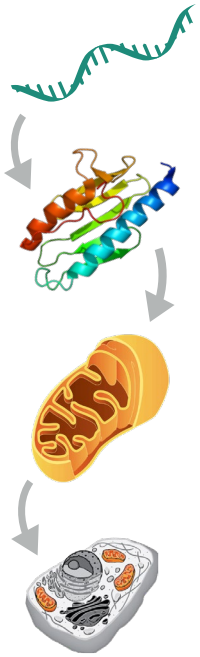
Data support advancing DT-216P2 towards registration

- **Four-week data readout for RESTORE-FA - a multiple ascending dose study in patients with Friedreich Ataxia**
  - Results are from 4 weeks of IV DT-216P2 dosed once weekly at 4 dose levels (0.1, 0.3, 0.6 and 1 mpk) with a total of 16 patients
  - DT-216P2 (also known as DT-216 for injection) generally well-tolerated
- **Comprehensive endogenous FXN biomarker activity**
  - Significant increases in production of endogenous natural frataxin mRNA and protein
  - Biomarker activity observed in both blood and muscle
- **Dose-dependent improvements in multiple clinical measures**
  - Measured by well accepted clinical endpoints such as mFARS, Upright Stability Score and supported by patient reported measures of fatigue
- **Data support a potentially best-in-disease profile for DT-216P2**
  - We are now planning to pursue a registrational path and expect to provide an update on these plans in the fourth quarter of this year

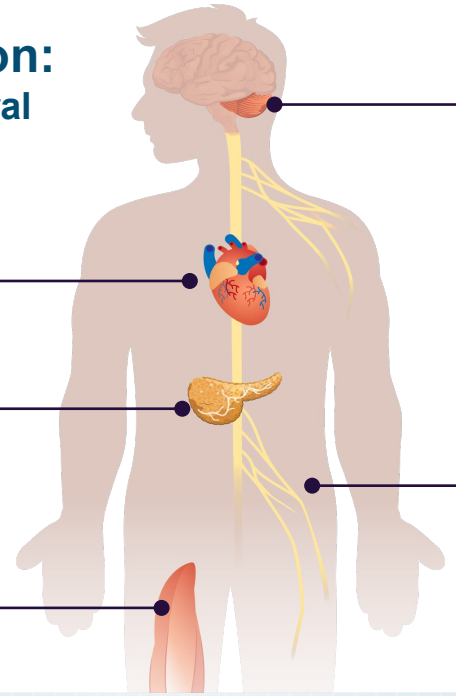
FA: Debilitating disease with limited treatment options today

Monogenic disease caused by GAA-repeat expansion in 1st intron of frataxin (FXN) gene

Mutation leads to reduced FXN transcription, which is necessary for mitochondrial and cellular function



Multi-organ dysfunction:
muscle, central and peripheral nervous systems, heart, and pancreas



HEART
cardiomyopathy, arrhythmias

PANCREAS
diabetes

SKELETAL MUSCLE
stiffness, weakness

CENTRAL NERVOUS SYSTEM
ataxia, loss of coordination, slurred speech

PERIPHERAL NERVOUS SYSTEM
neuropathy

Unmet need in FA remains significant

Biogen

REATA PHARMACEUTICALS

- Skyclarys® (Omaveloxolone) does not address the genetic root cause of FA or change FXN level
- Skyclarys® slows disease progression on neurological end point (mFARS) but large unmet remains
- Estimated peak sales of $1.6B/yr

Larimar Therapeutics

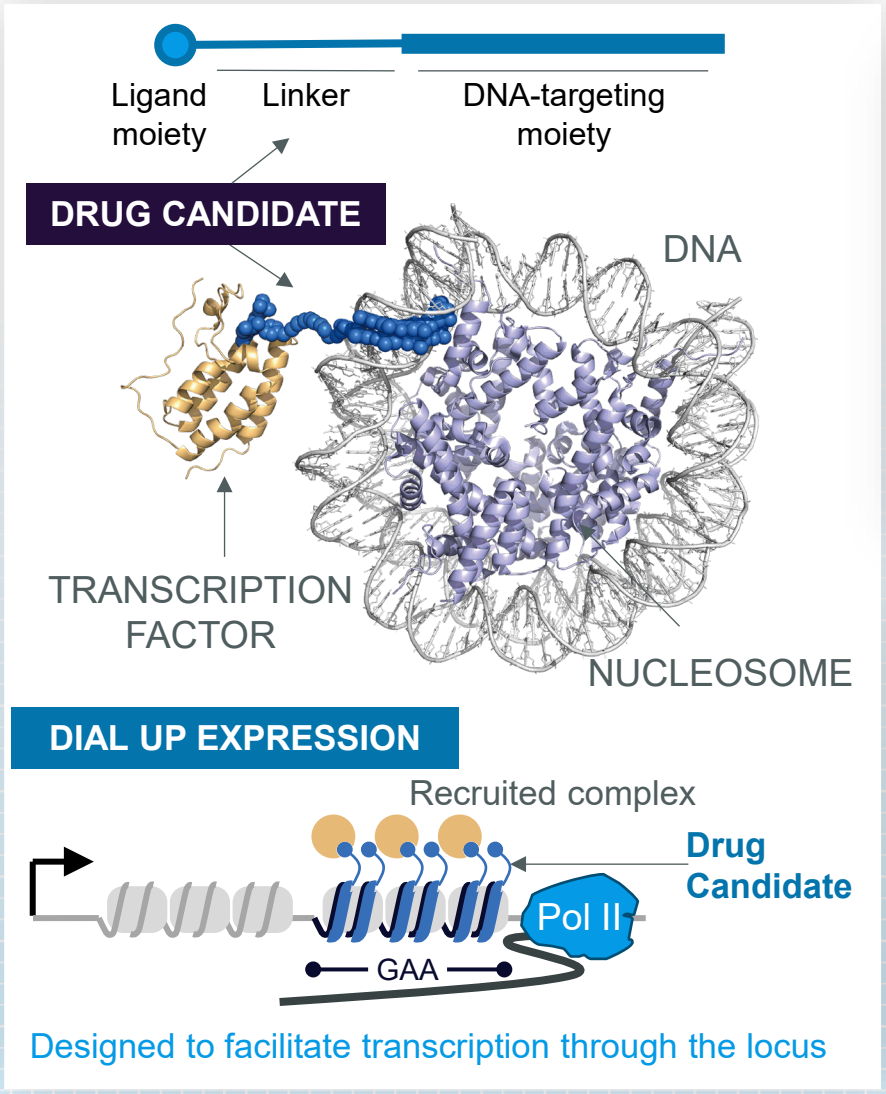
HIV-TAT-FXN protein

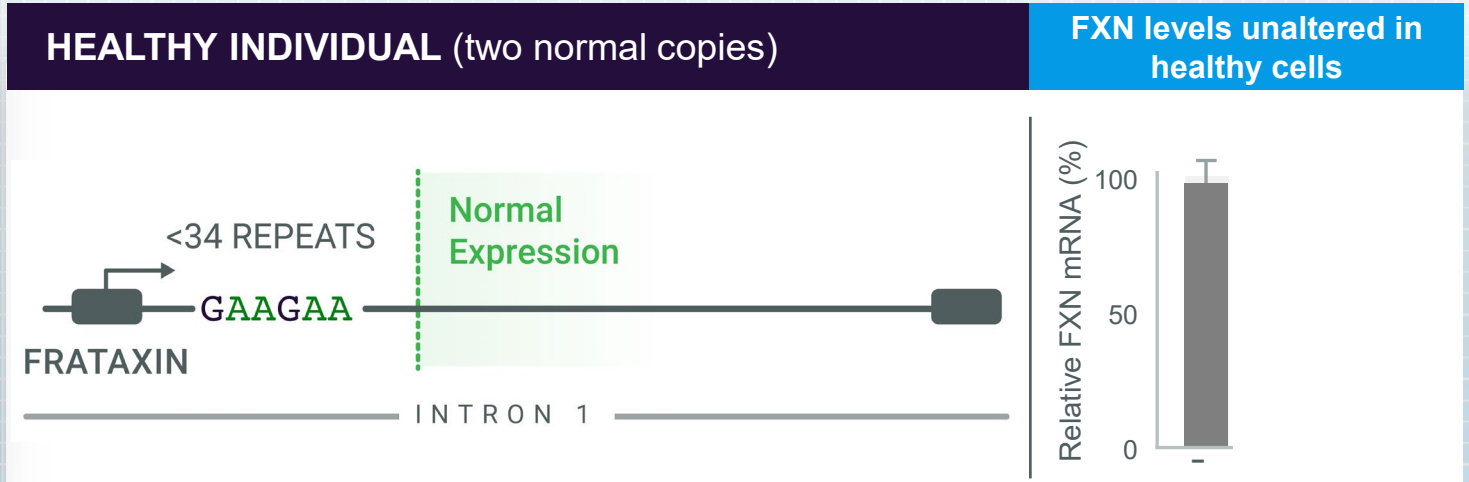
LEXEO therapeutics

AAV gene therapy targeting cardiac tissue

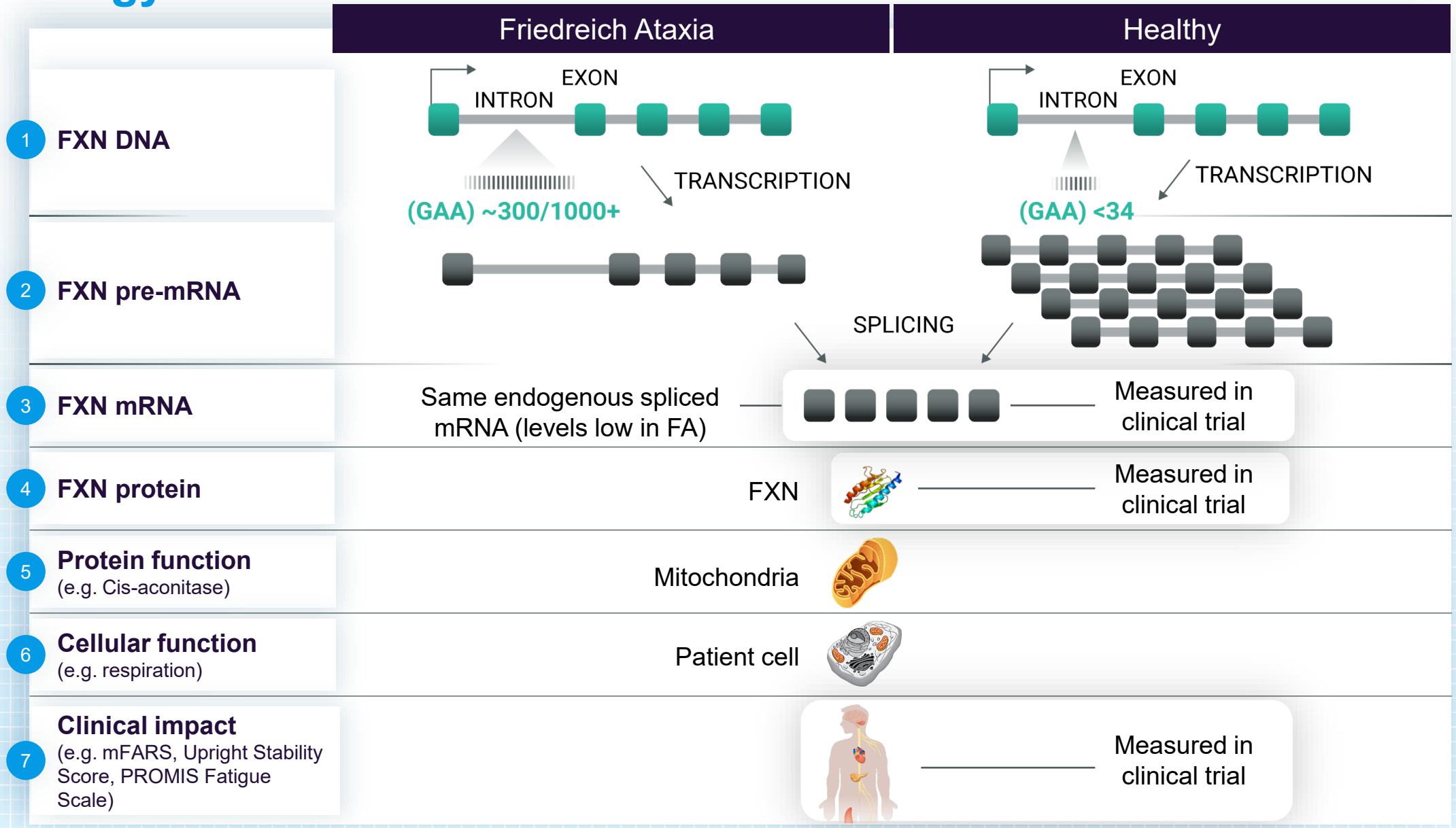
- Other drug candidates in clinical development that aim to address the root cause of FA involve complex modalities
- None of these change endogenous FXN

FA GeneTAC® molecules normalized FXN levels in FA patient cells but did not alter FXN levels in healthy cells





Pathogenic Cascade in Friedreich Ataxia and Clinical Biomarker Strategy



RESTORE-FA MAD study in FA patients: Dosing design

Dosing duration	Weekly IV infusion (target cohort size ≥ 4)	SC infusion	Biomarker endpoints Endogenous FXN biomarkers	Exploratory clinical endpoints
4 weeks *Data presented from 4-week IV cohorts*	0.1 mpk (5-8 mg) 0.3 mpk (15-24 mg) 0.6 mpk (30-48 mg) 1 mpk (50-80 mg)	Dosing cohort details TBD	1. Whole blood mRNA and protein 2. Muscle biopsy mRNA and protein	1. mFARS[2] 2. Upright Stability Score (USS) 3. PROMIS Fatigue Scale 4. Various other exploratory endpoints
12 weeks	1 mpk (50-80 mg) TBD mpk[1] (Maybe multiple cohorts)			

Note:1. PK projections support multiple additional cohorts within nonclinical safety exposures. 2. modified Friedreich Ataxia Rating Scale

Observations in mFARS across FA landscape
(modified Friedreich Ataxia Rating Scale)

- The mFARS is a clinician-administered tool to measure neurologic dysfunction and disease progression in FA
- Omaveloxolone (SKYCLARYS™) pivotal trial (MOXIE study) used mFARS as the primary endpoint
- Omaveloxolone is now using Upright Stability Score (USS), a component of mFARS, in the ongoing pediatric study (BRAVE study); USS is considered the most objective, least variable component of mFARS

Biogen
Omaveloxolone
NRF2 activator

1.56 improvement over baseline (N=34) at 48 weeks

LEXEO therapeutics
AAV gene therapy targeting cardiac tissue

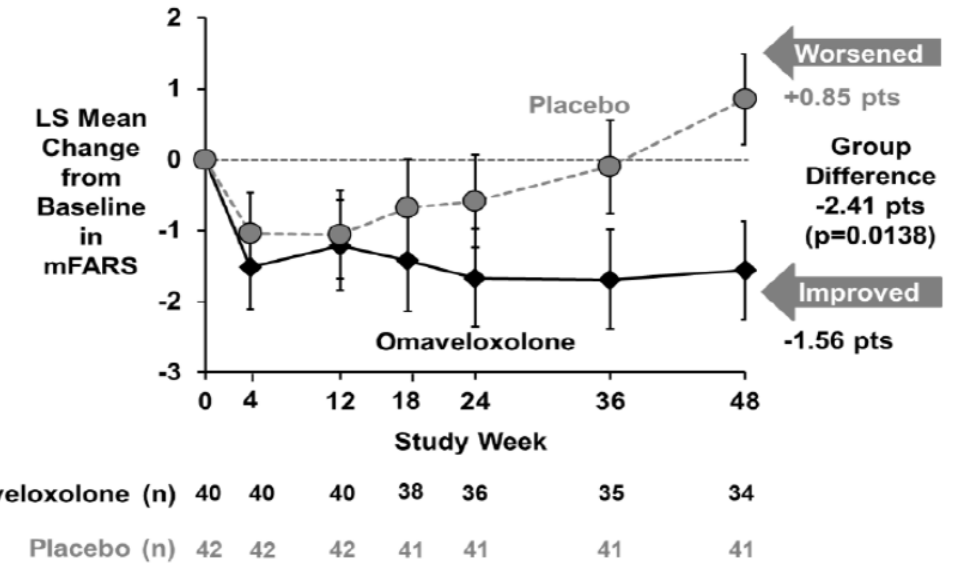
2-point improvement over baseline (n=16) at 6 months

Larimar Therapeutics
Nomlabafusp
HIV-TAT-FXN protein

2.25-point improvement over baseline (n=8) at 1 year

Omaveloxolone pivotal trial results (MOXIE study)

Figure 6 mFARS Change from Baseline by Visit (FAS Population)



Source: Omaveloxolone summary basis of approval; Lexeo and Larimar corporate communications; Lexeo data at 6 months, Larimar data at 12 months

How much FXN do we believe is enough?

Therapeutic level	Readout questions	Biomarker data
Any significant increase	Does DT216P2 increase FXN mRNA? (either blood or muscle)	✓
Natural history: *"FRATAXIN LEVELS directly correlate with all major clinical outcomes in FA [patients] … such as age of onset and disease severity… loss of ambulation and long-term progression slopes of mFARS and USS…Peripheral frataxin quantification provides biologically grounded measure of the pathophysiology and disease progression."* [1]	Does DT-216P2 increase FXN protein? (either blood or muscle)	✓
Regulatory commentary: In Feb 2025, Lexeo announced FDA *"alignment on the accelerated development pathway with frataxin expression co-primary endpoint to be evaluated for any increase from baseline rather than numerical threshold."* [2]	Activity in both blood and muscle? (either mRNA or Protein)	✓
	Biomarkers and clinical data	✓

Note: 1. Rummey C, et al. Peripheral frataxin levels govern long-term clinical progression in Friedreich ataxia. BMJ Neurology Open. 2026; 2. Lexeo Therapeutics, Inc., 2026 Form 10-K (FY2025); Design will wait to seek regulatory alignment on FA registration path after data support such discussions

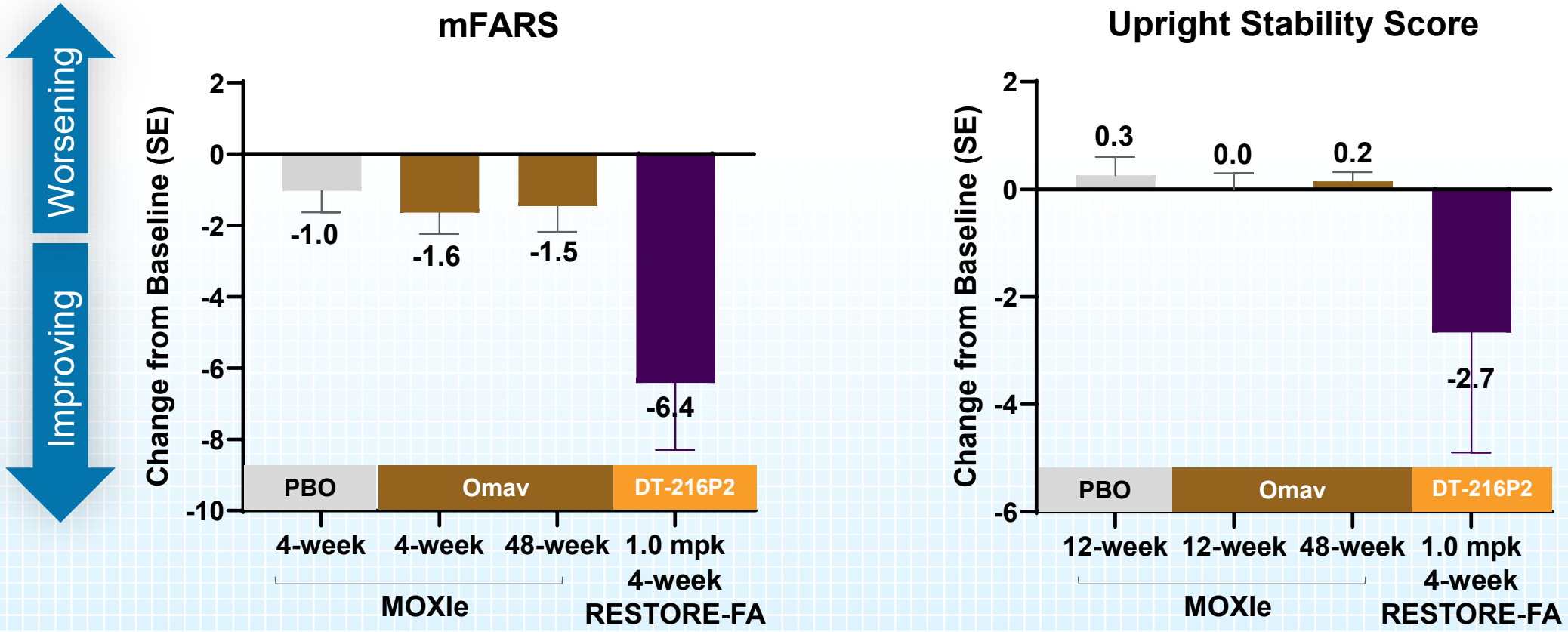
Baseline characteristics

	Cohort 1 0.1 mg/kg IV (n = 4)	**Cohort 2** 0.3 mg/kg IV (n = 4)	**Cohort 3** 0.6 mg/kg IV (n = 4)	**Cohort 4** 1.0 mg/kg IV (n = 4)	**Total** (N = 16)
Age (years), Mean (SD)	43.5 (16.8)	39.5 (5.3)	26.75 (6.7)	34.75 (10.3)	36.125 (11.6)
Age at onset (years), Mean (SD)	26.5 (19.9)	18.75 (7.4)	14.75 (4.8)	18.5 (4.7)	19.625 (10.9)
Female, n (%)	4 (100%)	1 (25%)	3 (75%)	2 (50%)	10 (62.5%)
Functional Staging for Ataxia, Mean (SD)	3.9 (0.9)	4.4 (1.3)	4 (1.7)	3.9 (1.4)	4 (1.2)
GAA1 repeat length, Mean (SD)	368 (192)	377 (94)	696 (268)	303 (165)	436 (232)

10 of 16 patients on stable Omaveloxolone for an average of > 5 years

Note: Data analysis as of May 17 2026; GAA1 is the GAA repeat length of the shorter allele

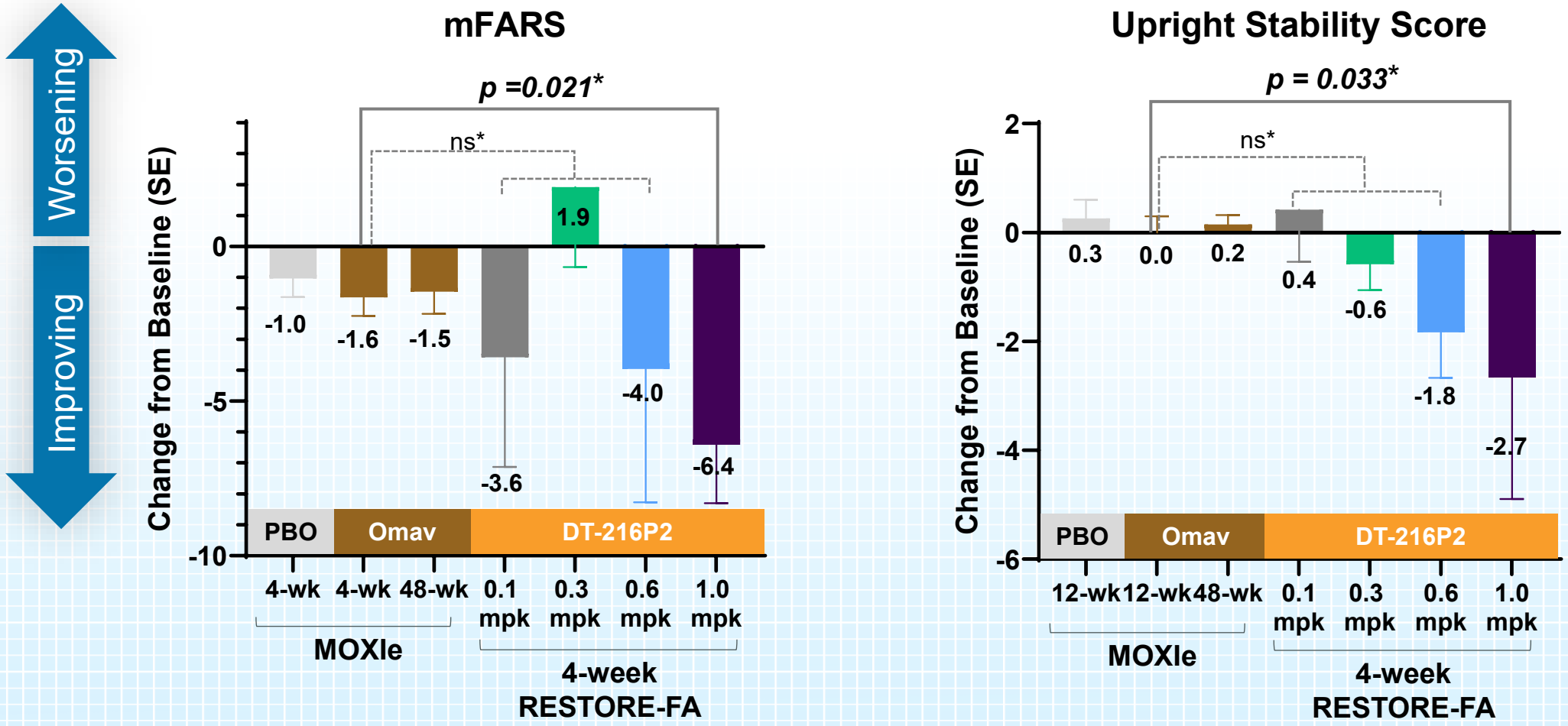
Ataxia measurement: mFARS and upright stability score improvement observed



Note: Data analysis as of May 17 2026; Bars are standard error. All DT-216P2 cohort data n=4, MOXIe placebo n= 42, MOXIe Omaveloxolone 4/12-week n=40, 48-week n=34. Placebo and Omaveloxolone data are from the MOXIe study; U.S. Food and Drug Administration (2022) *Clinical Reviews* (216718Orig1s000); Lynch, et. al., Annals of Neurology 2021

Exploratory statistical analysis (two-sided) comparing 1mpk DT-216P2 4-week RESTORE-FA to MOXIe study placebo arm 4-week mFARS *(nominal p=0.012)* and 12-week USS *(nominal p=0.027)*, no formal hypothesis testing for any endpoint was prespecified. Comparison between trials for illustrative purposes only; no head-to head trial has been conducted comparing DT-216P2 to omaveloxolone; differences exist between study designs, patient characteristics and other factors and caution should be exercised when comparing against unrelated studies.

Ataxia measurement: mFARS and upright stability score improvement observed



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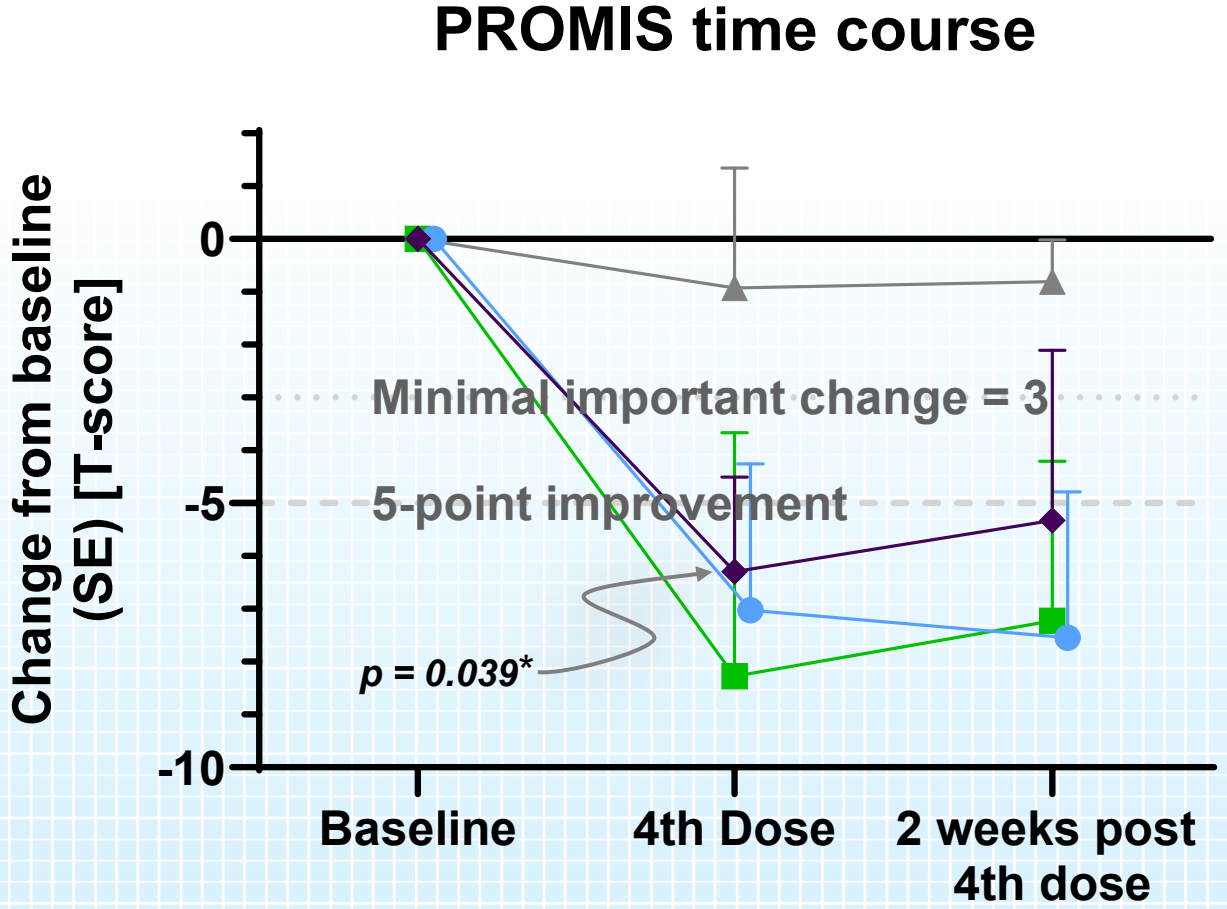
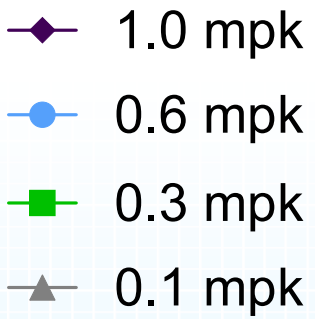
Fatigue: Change from baseline in PROMIS fatigue scale (T-score)





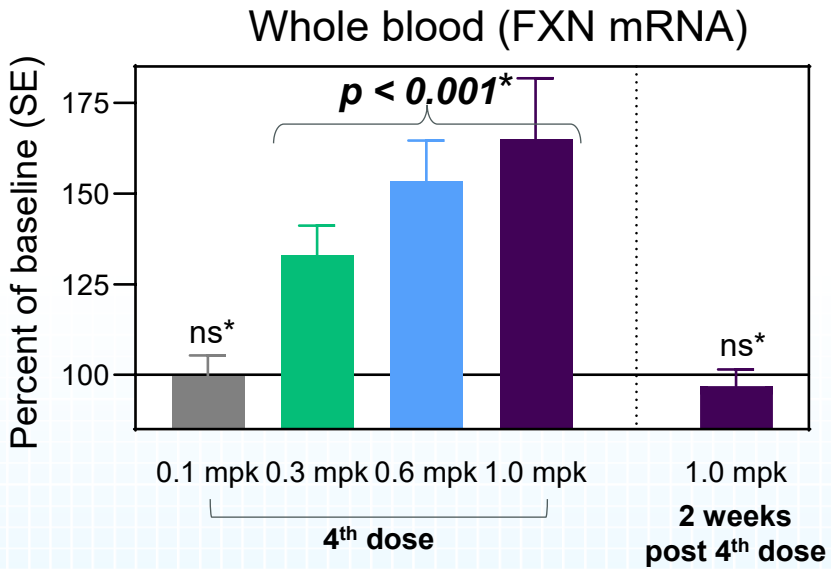
5-point improvement responders (post 4th dose)

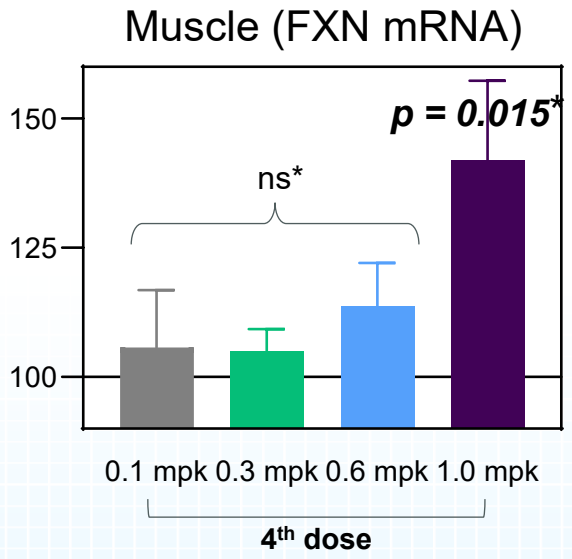
1.0 mpk	3/4
0.6 mpk	2/4
0.3 mpk	1/4
0.1 mpk	0/4

Note: Data analysis as of May 17 2026; Bars are standard error; All DT-216P2 cohort data n=4; Minimal important mean change; Terwee et. al. Minimal important change (MIC): a conceptual clarification and systematic review of MIC estimates of PROMIS measures. Qual Life Res. 2021; * Exploratory statistical analysis (two-sided) compared to baseline, no formal hypothesis testing for any endpoint was prespecified.

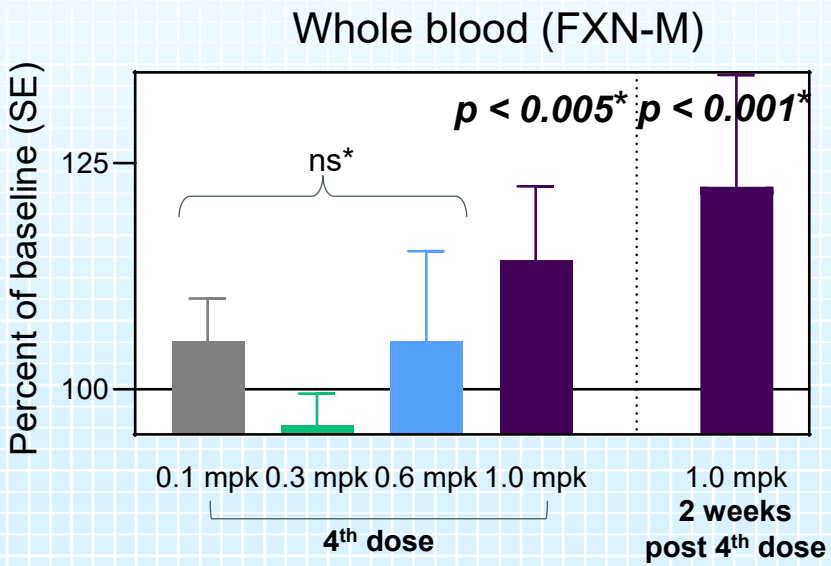
Clinical improvement observations supported by comprehensive biomarker activity at 1.0 mpk

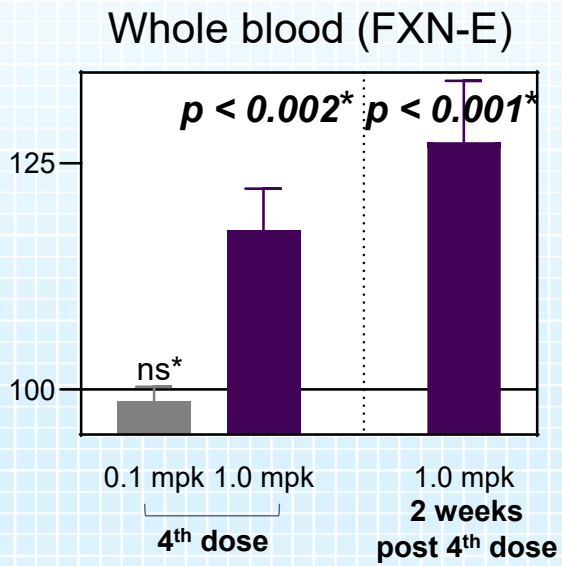
FXN mRNA





FXN Protein





Readout questions

- Does DT216P2 increase FXN mRNA? (either blood or muscle) ✓
- Does DT-216P2 increase FXN protein? (either blood or muscle) ✓
- Activity in both blood and muscle? (either mRNA or Protein) ✓
- Biomarkers and clinical improvement ✓

Note: Data analysis as of May 17 2026; Data is shown as percent of baseline pre-dose FXN level; * Exploratory statistical analysis (two-sided) compared to untreated individuals (data not shown), no formal hypothesis testing for any endpoint was prespecified. FXN-E was not measured for 0.3 and 0.6mpk cohorts

Safety data

- DT-216P2 was generally well-tolerated
  - No serious adverse events
  - No study discontinuations
  - All adverse events were mild to moderate

- Adverse events possibly or probably considered related to DT-216P2 occurring in more than one patient:
  - Three patients experienced transient asymptomatic ALT elevations (mild to moderate, <5x ULN) with no bilirubin increases – all three were on background omaveloxolone

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Leerink research report[1]: *"One KOL noted that LFT increases with Skyclarys appeared to correlate with response in the clinical trial and may reflect an on-target metabolic effect rather than liver toxicity… …The broader implication is that AST/ALT elevations could potentially appear with other agents that restore frataxin in the liver, though the clinical meaning and relationship to efficacy would still need to be assessed drug by drug."*

Note: Data analysis as of May 17 2026; [1]Leerink Partners, *Neuro in Focus: Takeaways from Our Friedreich's Ataxia MEDACorp Pulse Call,* 2026.

Next steps: Advancing DT-216P2 towards registrational development

- Based on this data we believe we have identified a suitable dose and route of administration at 1mpk IV weekly to advance toward registration
- The timing and venue of future data updates is TBD because of the shift in focus to registrational planning
- We anticipate providing an update on registrational plans in Q4 2026

Note: Along the course of development, we plan to explore potential future regimens (for example less frequent dosing intervals and subcutaneous administration)