



DESIGNING A NOVEL CLASS OF GENOMIC MEDICINES FOR GENETIC DISORDERS

Disclaimers

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to projections from early-stage programs, preclinical data and early-stage clinical data; the therapeutic potential of DT-216P2, DT-168 and DT-818; the initiation and progression of studies and clinical trials for DT-216P2, DT-168, DT-818 and the timing thereof; the expected timing for data readouts; the potential benefits of restoring FXN in FA patients; clinical outcomes and potential benefits of DT-216P2 for Friedreich ataxia; historical placebo effect on mFARS and USS as a predictor of future placebo effect; the ability to advance 1 mg/kg intravenous (IV) weekly toward a potential registration path; the design, timing, duration, dose levels, enrollment, completion and expected results of ongoing and future studies of DT-216P2; potential regulatory pathways for FA; Design’s plans to shift focus toward studies to support the potential future registration of DT-216P2, prioritize the IV route of administration, and obtain further clarity on development plans in the fourth quarter of 2026; Design’s FECD GeneTAC® program and its potential therapeutic benefits and advantages; the impact of Design’s FECD observational study on a clinical program for FECD; the potential utility of corneal endothelium biomarkers in clinical development; Design’s DM1 GeneTAC® program and its potential therapeutic benefits and advantages; the benefit of a reduction in toxic foci in human myotubes as a predictor of restoring clinical splicing in DM1; DT-818’s potential to be a best-in-disease treatment for DM1; Design’s HD GeneTAC® candidates and their potential therapeutic benefits and advantages; the anticipated or implied market opportunities for Design’s GeneTAC® programs; milestones, next steps, and Design’s ability to deliver on its short- and long-term goals; the design and capabilities of Design’s GeneTAC® platform; establishing clinical proof of concept for any product candidate, including through biomarker measurements; Design’s estimated cash runway and the sufficiency of Design’s resources to enable its programs and platform and support its planned operations; and the capabilities and potential advantages of Design’s pipeline of GeneTAC® molecules. 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Challenging the status quo of genomic medicines with small molecules (GeneTAC[®] molecules) that dial up or dial down transcription...

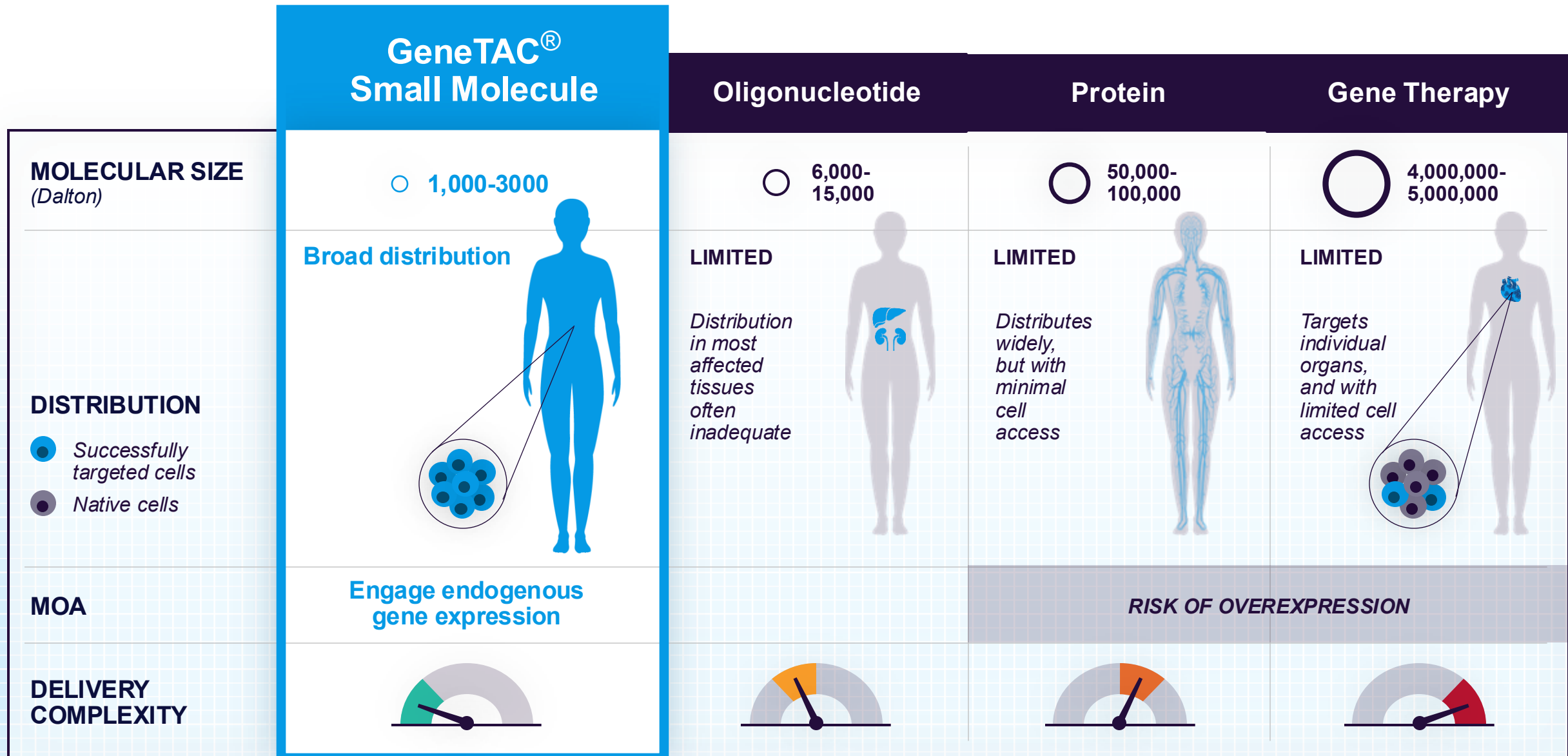
...to treat significant monogenic disorders

BECAUSE WE BELIEVE YOUR FATE DOESN'T
HAVE TO BE WRITTEN IN YOUR GENES

Advancing four GeneTAC[®] molecule programs

	Gene	Monogenic disease	Differentiated profile	Status	Market Overview	
CLINICAL	Friedreich Ataxia	FRATAXIN (FXN)	GAA repeat expansion leads to reduced transcription	Restoration of endogenous frataxin with broad tissue distribution	Robust biomarker + clinical effects w/ 4-week IV data; update on registrational plans anticipated 4Q 26	\$7.3B Biogen acquired Skyclarys [®] (REATA) in 2023
	FECD	TCF4	CTG repeat expansion causes corneal endothelial cell dysfunction	Allele-selective reduction of mutant transcript (TCF4) with an eye drop	Ph2 biomarker trial in pts ongoing; data expected 2H 26	Over 1 million TCF4 expansion pts in US (multi-billion \$ opp)
	DM1	DMPK	CTG repeat expansion causes nuclear foci & cellular dysfunction	Allele-selective reduction of mutant DMPK leads to foci resolution & splicing correction	DT-818 pt dosing expected 1H 26	Est. >70K cases in US (multi-billion \$ opp)
PRECLINICAL	Huntington's Disease	HUNTINGTIN (HTT)	CAG repeat expansion leads to toxic mRNA & protein product	Allele-selective reduction of mutant HTT	Next step: Select DC	~40,000 affected by HD in US (multi-billion \$ opp)

GeneTAC[®] molecules can distribute widely, overcoming a central challenge for traditional genomic medicines

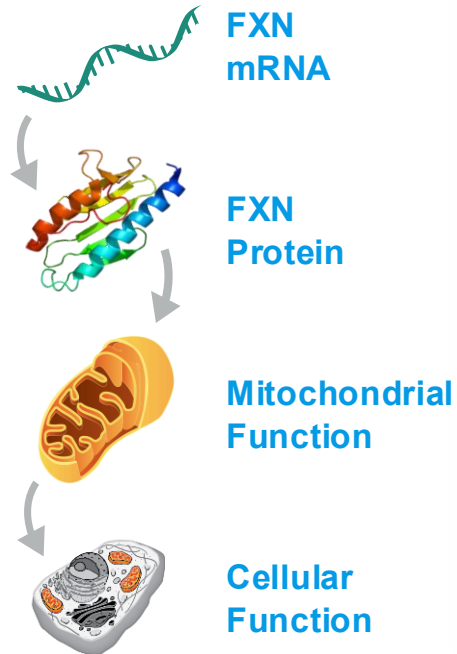


DT-216P2 for Friedreich Ataxia

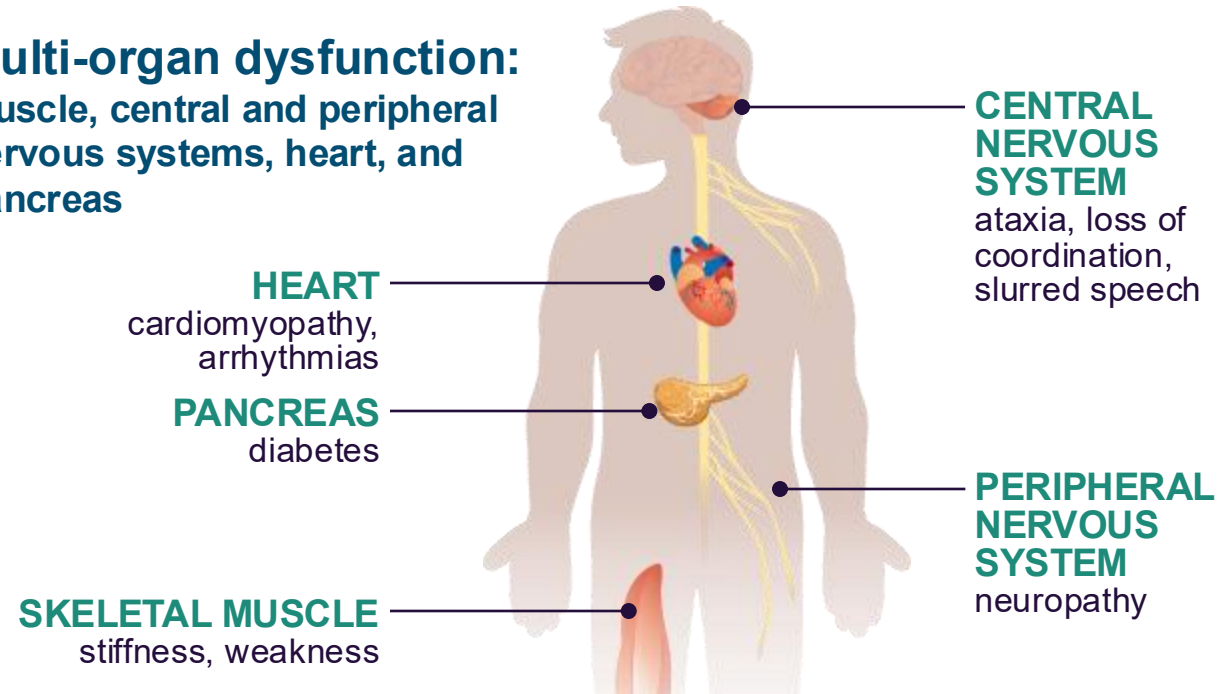
FA: Debilitating disease with limited treatment options today

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



Unmet need in FA remains significant



- Skyclarys[®] does not address the genetic root cause of FA or change FXN level
- Skyclarys[®] slows disease progression on neurological end point (mFARS) but only during the 1st year
- Estimated peak sales of \$1.6B/yr



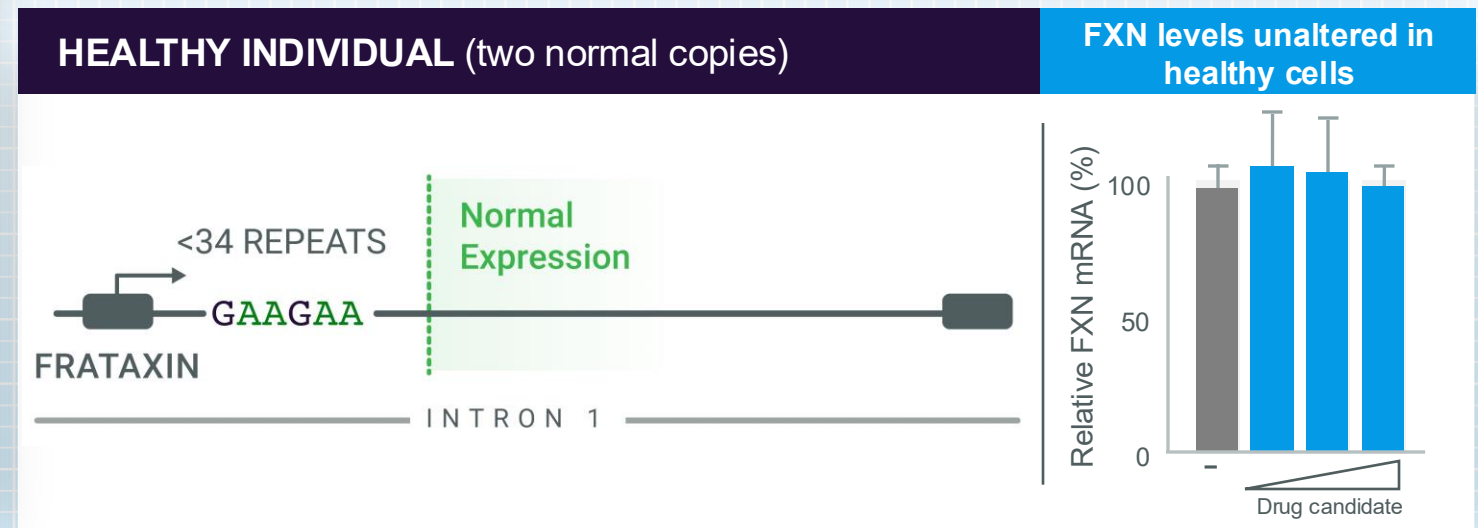
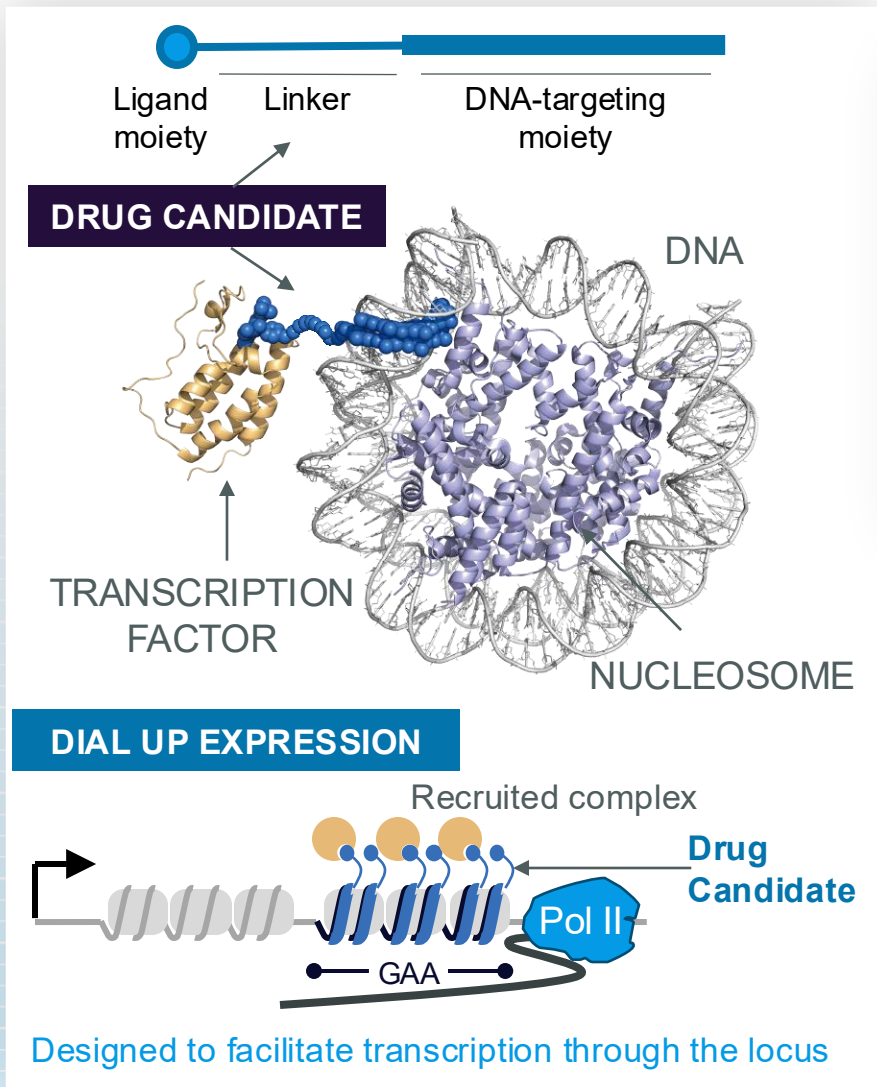
HIV-TAT-FXN protein



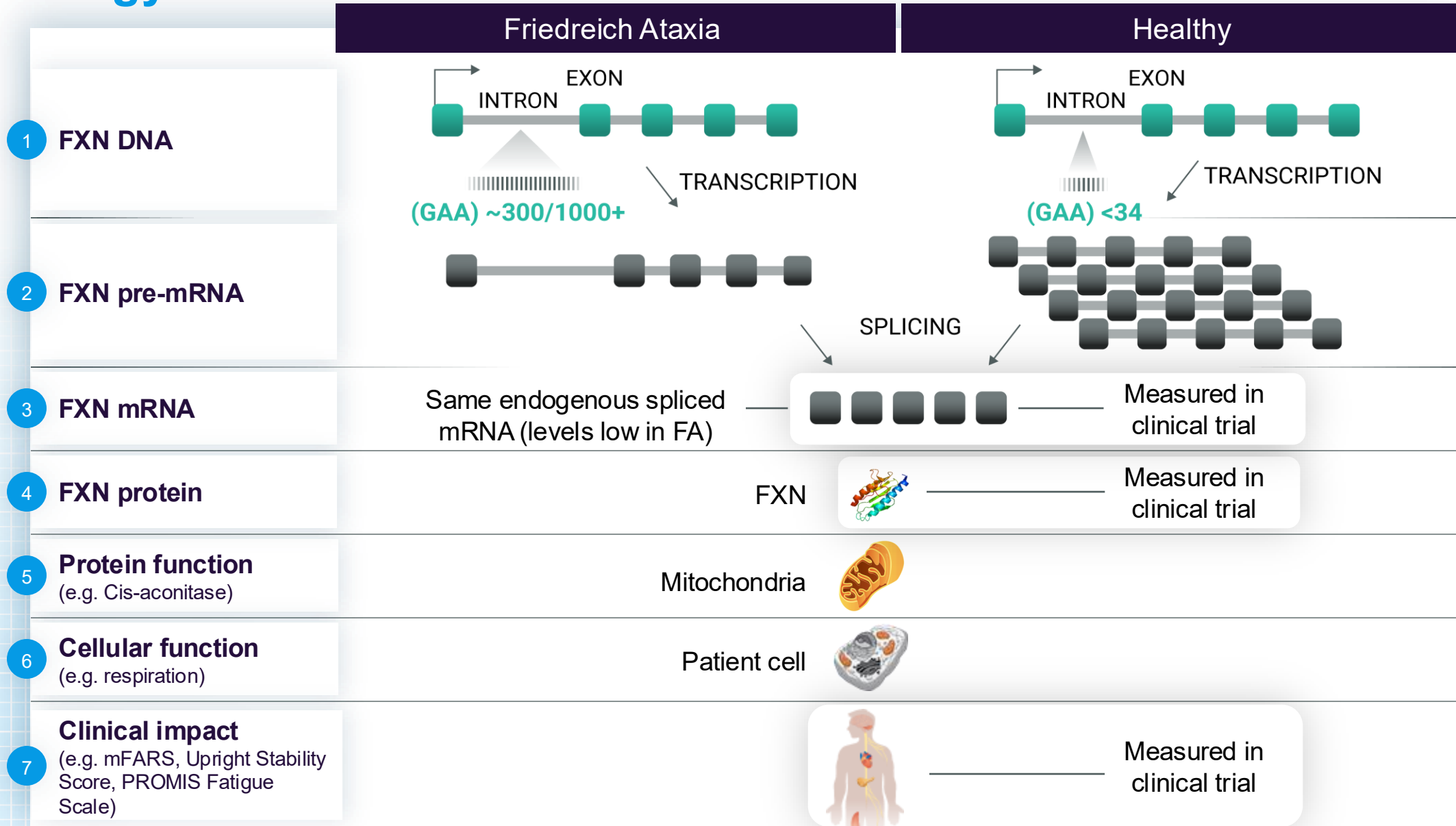
AAV gene therapy targeting cardiac tissue

- 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	0.1 mpk (5-8 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
	0.3 mpk (15-24 mg)			
	0.6 mpk (30-48 mg)			
	1 mpk (50-80 mg)			
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)

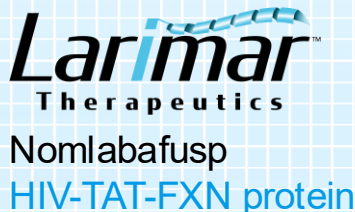
- The mFARS is a clinician-administered tool to measure neurologic dysfunction and disease progression in FA
- Omaveloxolone (SKYCLARYS™) pivotal trial (MOXIE study) used mFARS as the primary endpoint
- Omaveloxolone is now using Upright Stability Score (USS), a component of mFARS, in the ongoing pediatric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



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



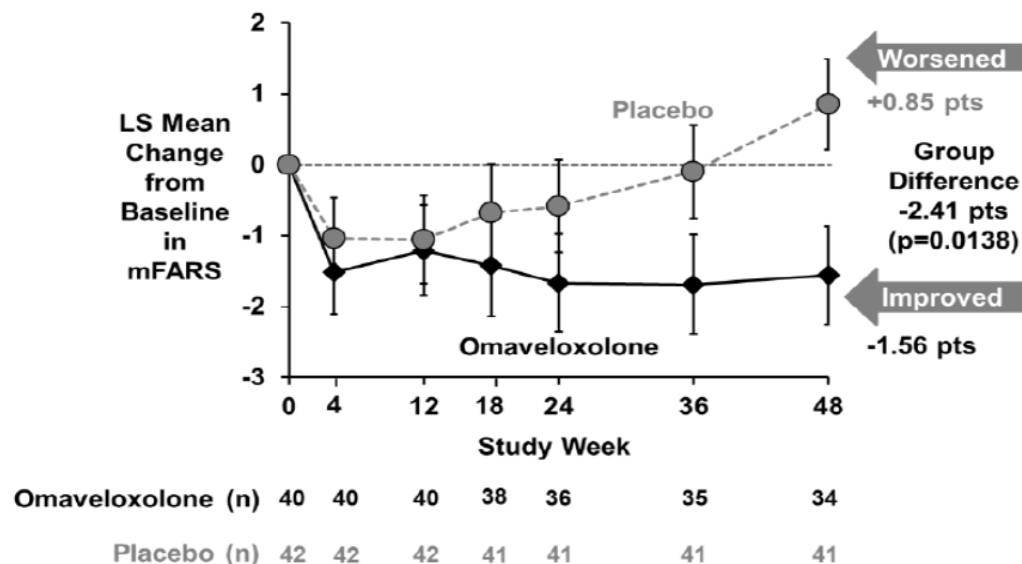
2-point improvement over baseline (n=16) at 6 months



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

Any significant increase

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

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

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 data

Biomarker data



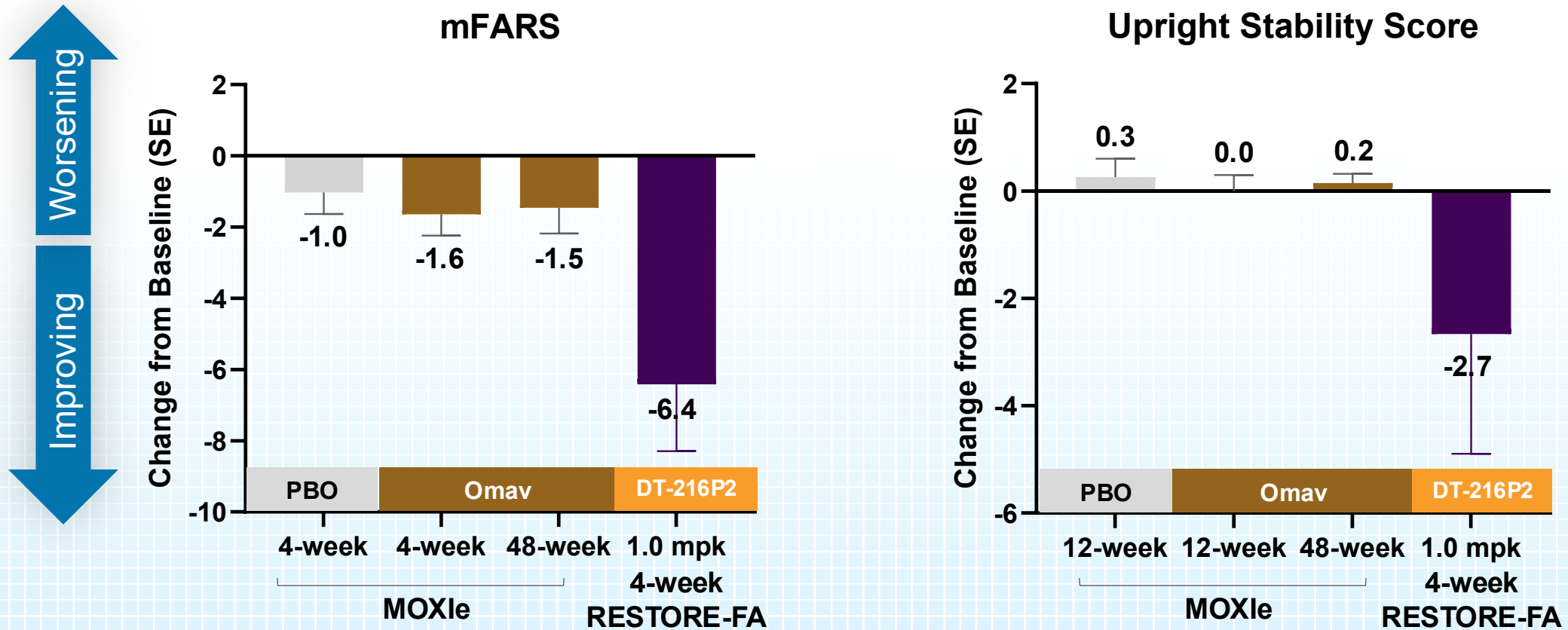
Baseline characteristics

	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, MOXle placebo n= 42, MOXle Omaveloxolone 4/12-week n=40, 48-week n=34. Placebo and Omaveloxolone data are from the MOXle study; U.S. Food and Drug Administration (2022) *Clinical Reviews* (216718Orig1s000); Lynch, et. al., *Annals of Neurology* 2021; Mean baseline mFARS: RESTORE-FA DT-216P2 0.1 mpk 41.7, 0.3 mpk 48.7, 0.6 mpk 48.3, 1 mpk 42.7; MOXle Omav 41.0; Placebo 38.8

Exploratory statistical analysis (two-sided) comparing 1mpk DT-216P2 4-week RESTORE-FA to MOXle 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.

Historical placebo effect on mFARS and USS

Peak mean mFARS placebo cohort effects observed is 3 points

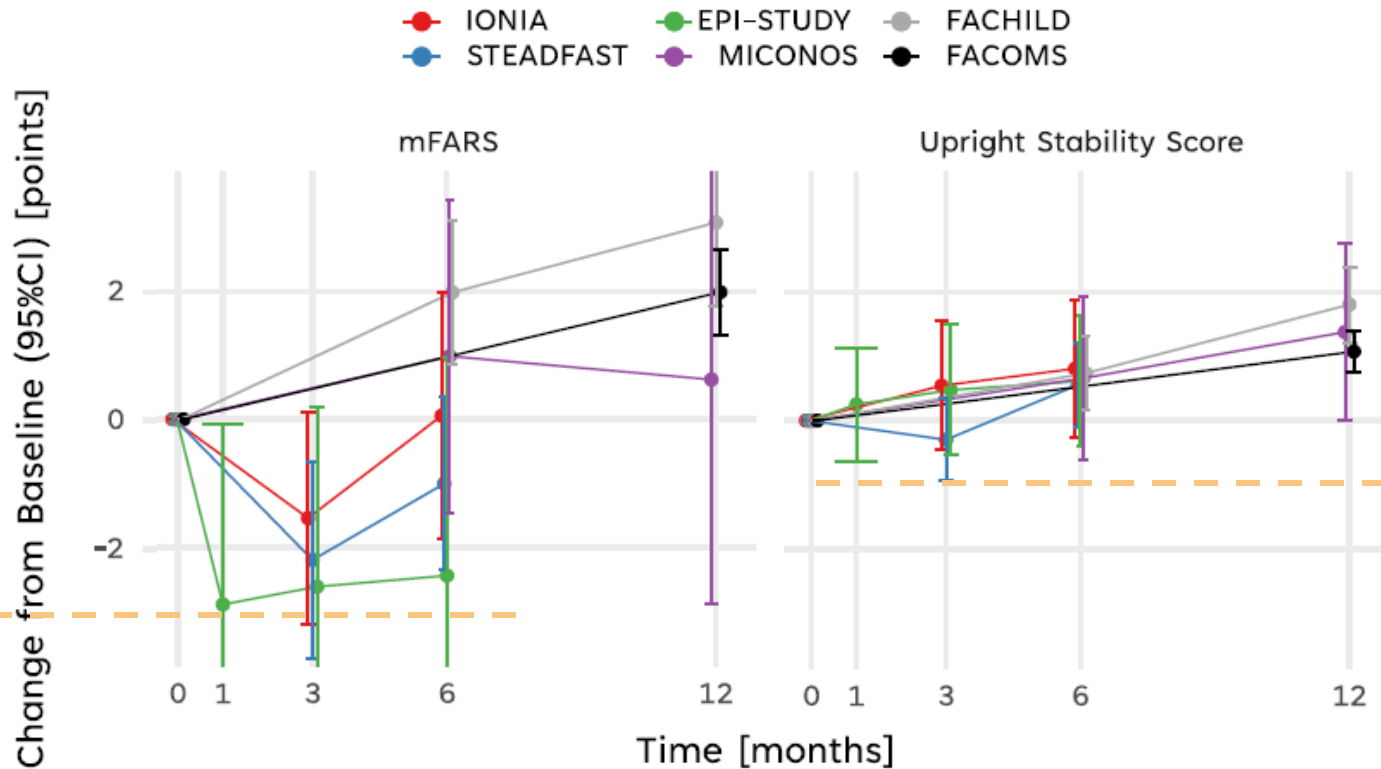
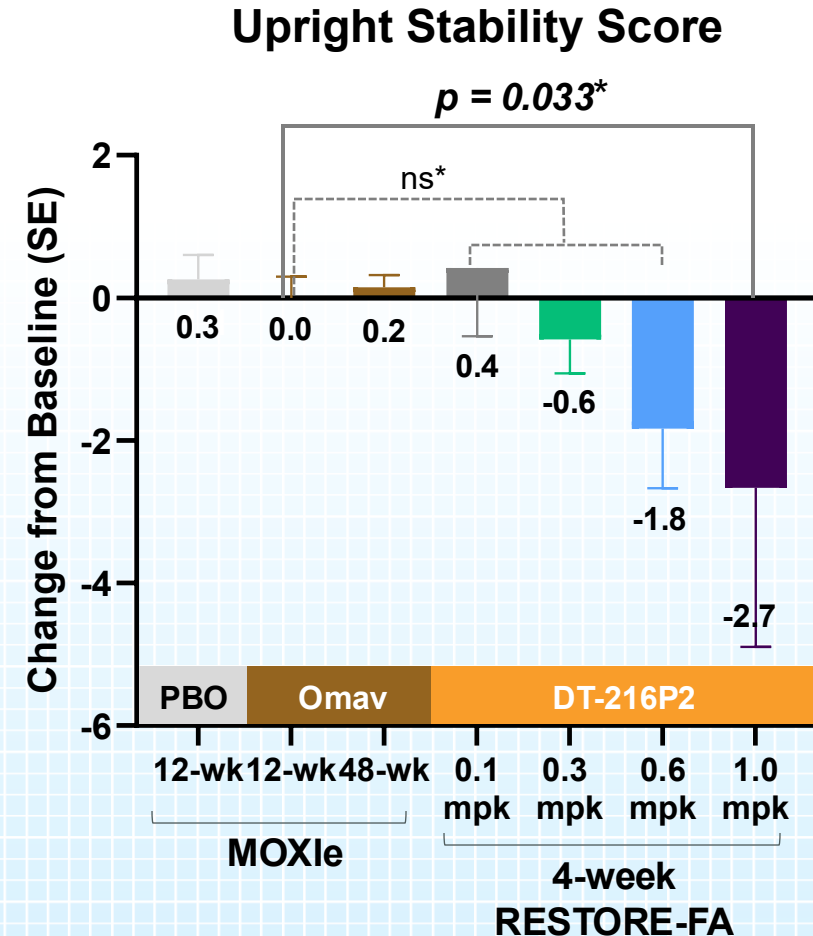
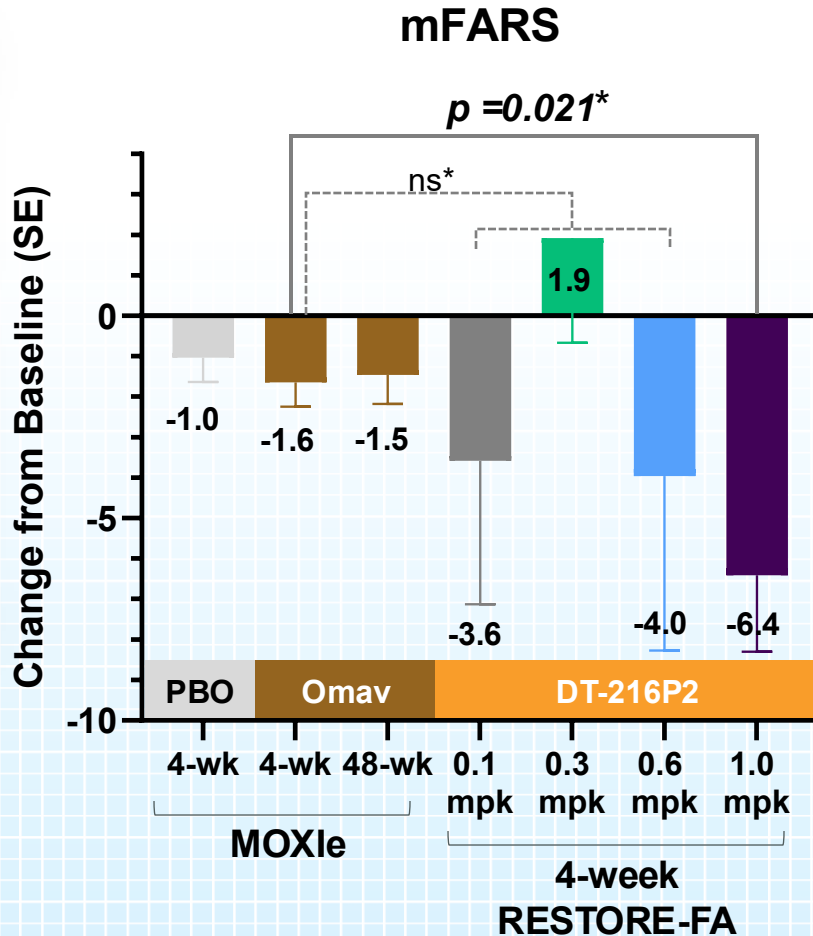


FIGURE 2 | Change from baseline by study, and timepoint (mean, 95% CI). RCTs are shown in color, Natural History Studies in Gray/Black.

USS shows the least variability and is resistant to placebo effects

1 point improvement is beyond 95% confidence interval in previous placebo groups

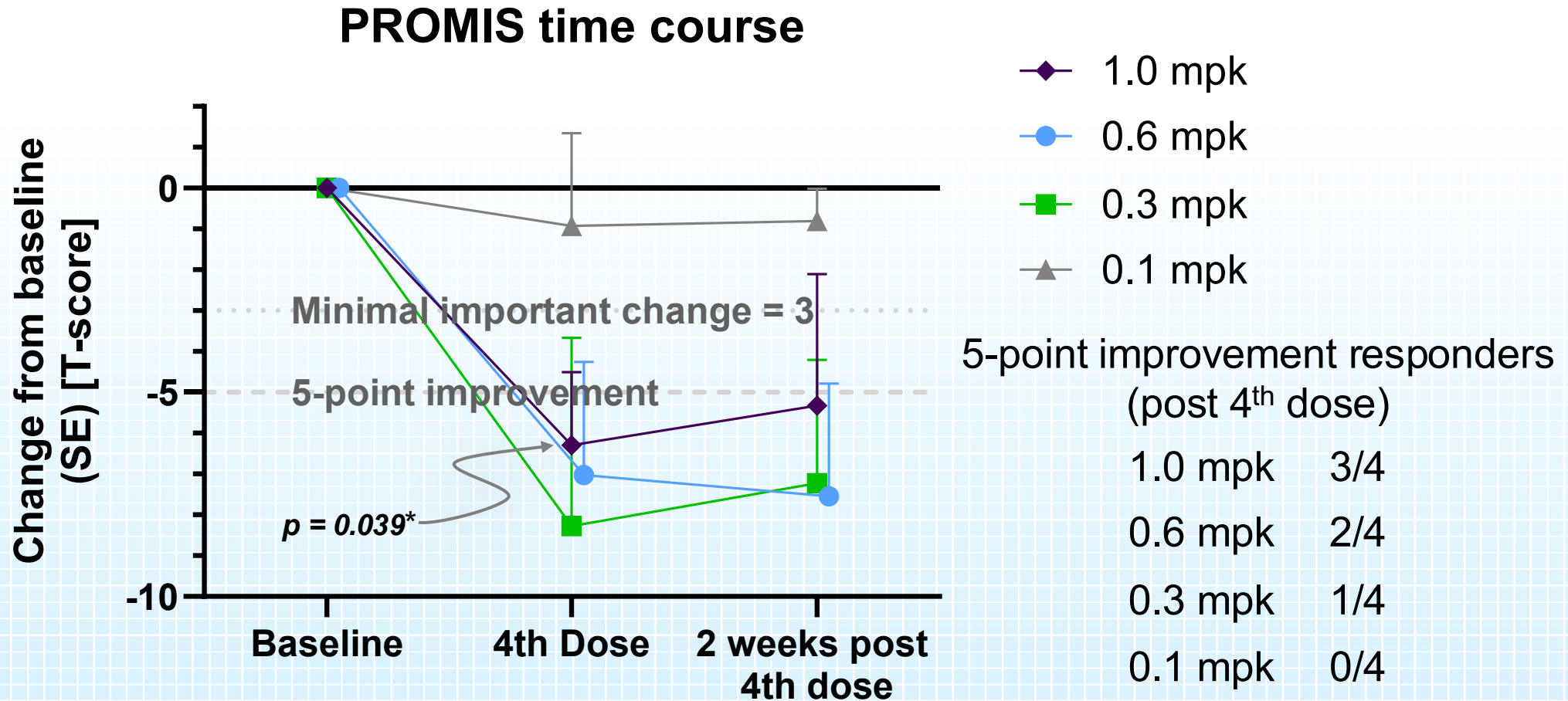
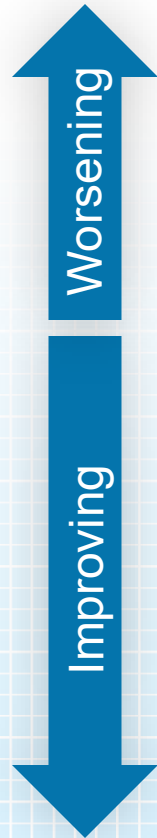
Ataxia measurement: mFARS and upright stability score improvement observed



Note: Data analysis as of May 17 2026; Bars are standard error. All DT-216P2 cohort data n=4, MOXle placebo n= 42, MOXle Omaveloxolone 4/12-week n=40, 48-week n=34. Placebo and Omaveloxolone data are from the MOXle study; U.S. Food and Drug Administration (2022) *Clinical Reviews* (216718Orig1s000); Lynch, et. al., *Annals of Neurology* 2021; Mean baseline mFARS: RESTORE-FA DT-216P2 0.1 mpk 41.7, 0.3 mpk 48.7, 0.6 mpk 48.3, 1 mpk 42.7; MOXle Omav 41.0; Placebo 38.8

*Exploratory statistical analysis (two-sided) compared to MOXle study omaveloxolone arm 4-week mFARS and 12-week USS, 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.

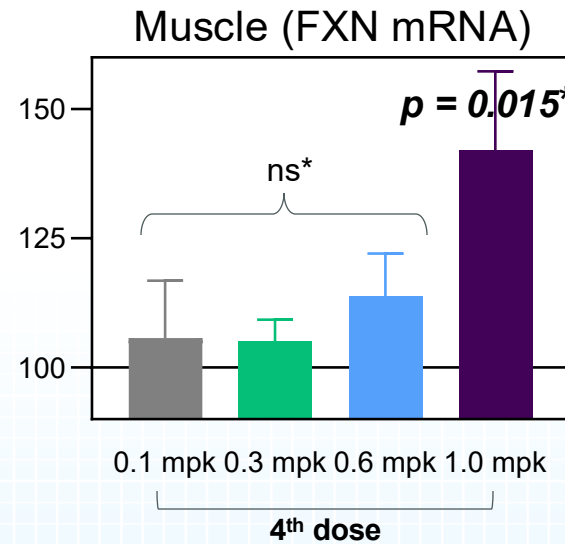
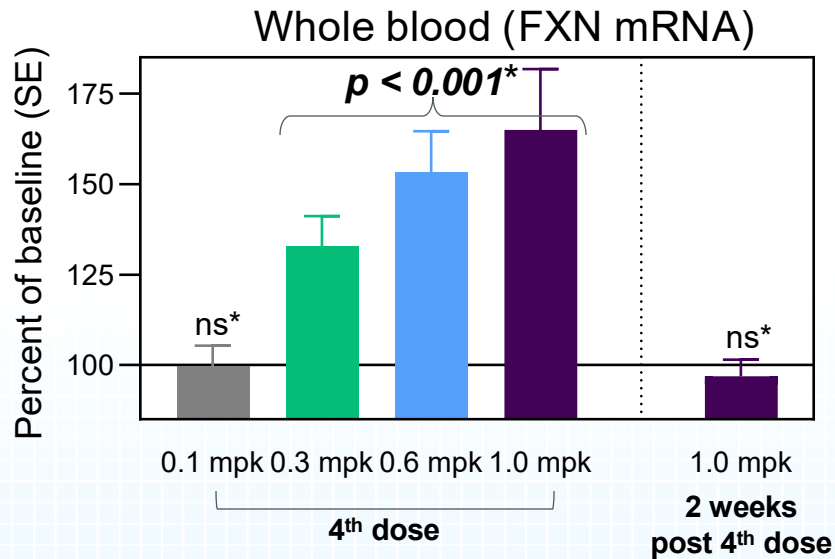
Fatigue: Change from baseline in PROMIS fatigue scale (T-score)



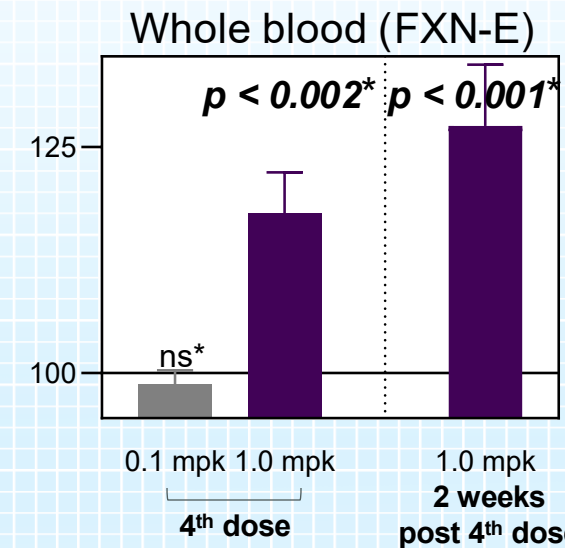
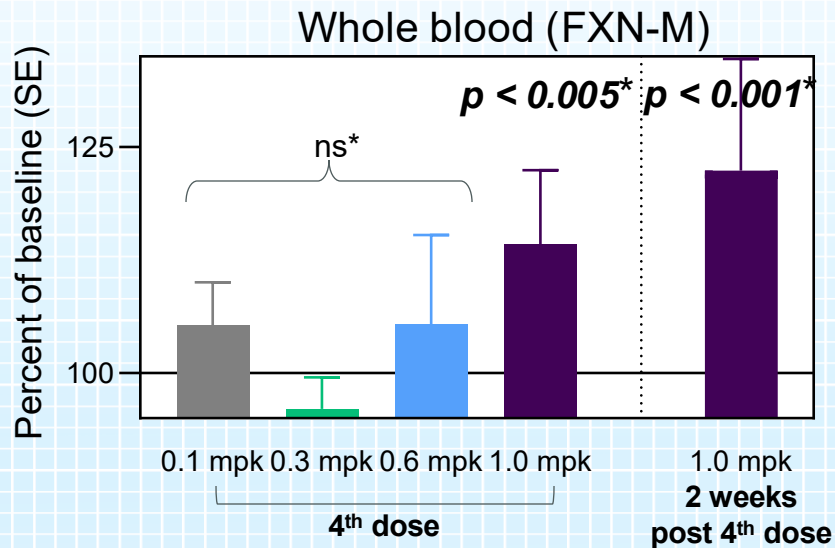
Note: Data analysis as of May 17 2026; Bars are standard error; All DT-216P2 cohort data n=4; Minimal important mean change; Terwee et. al. Minimal important change (MIC): a conceptual clarification and systematic review of MIC estimates of PROMIS measures. Qual Life Res. 2021; * Exploratory statistical 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; Whole blood mRNA: in data from untreated individuals, the 90th percentile of FA patients is 24% above the FA patient average while the carrier range begins at 46% higher than FA patient average. * 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

Leerink research report¹: *“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.”*

RESTORE FA results intended to support clinical POC and inform probability of future approval

Potential approval frameworks based on	
Accelerated	Traditional
<p>Initial approval based on surrogate marker reasonably likely to predict clinical benefit Followed by clinical confirmatory study</p>	<p>Approval based on clinical efficacy</p>
<p>FXN endpoint is primary</p>	<p>Clinical endpoint is primary</p>
<p>Clinical endpoint(s) supportive</p>	<p>FXN endpoint(s) supportive</p>

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

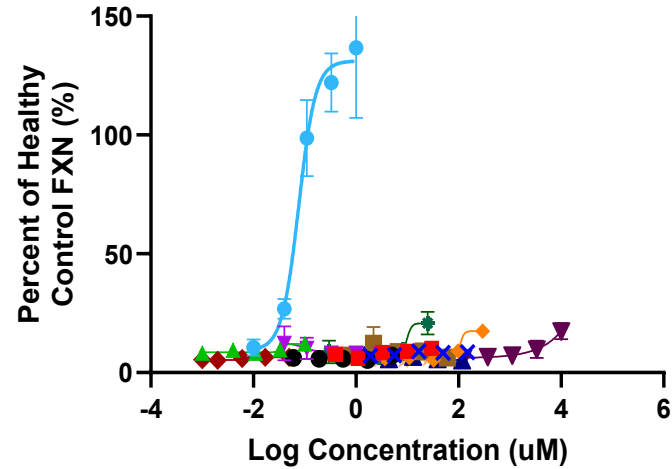
- The timing and venue of future data updates is TBD because of the shift in focus to registrational planning

- 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)

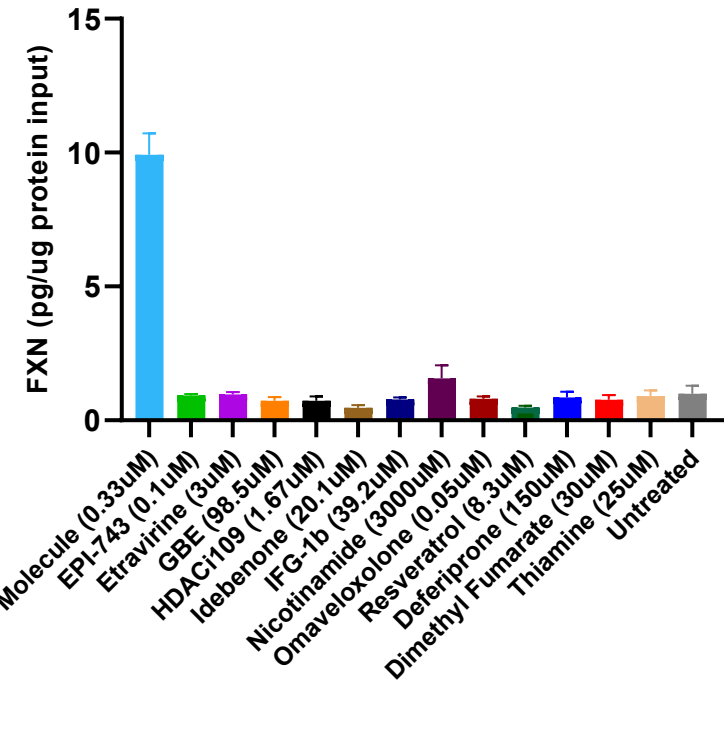
Activity of FA GeneTAC™ molecules compared with other compounds that have purportedly increased frataxin

FXN mRNA (1 day)



- FA GeneTAC™ Molecule
- ◆ Gingko Biloba Extract
- ◆ Omaveloxolone
- ✕ Deferiprone
- HDACi109
- ◆ Resveratrol
- Dimethyl Fumarate (DMF)
- Idebenone
- ◆ Thiamine
- ▲ EPI-743
- ▲ Interferon Gamma - 1b
- ▼ Etravirine
- ▼ Nicotinamide

FXN Protein (3 days)



Note: Molecules tested in FA patient lymphoblastoid cells. Bars represent standard error of the mean. Cells treated with DT-003 FA GeneTAC™ molecule. Concentrations selected based on published active ranges. Omaveloxolone is a NRF2 activator that was not purported to increase FXN.

DT-168 for Fuchs Endothelial Corneal Dystrophy

FECD is a progressive corneal disease caused by a single gene mutation in a majority of cases

Increasing Endothelial Cell Dysfunction — Loss of cells, pump function, corneal edema


 **Diagnosed by community optometrist**

~2M diagnosed patients (U.S.)¹



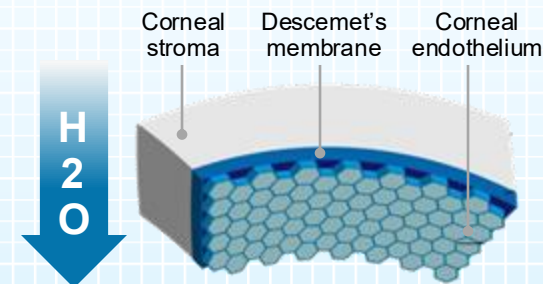
 **Loss of visual quality**



 **Patient can't stand symptoms**

 **Corneal transplant surgery**

Surgical Descemet membrane stripping or corneal transplant limited to 18–30k² per year (US)

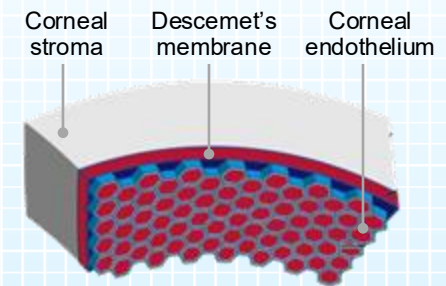
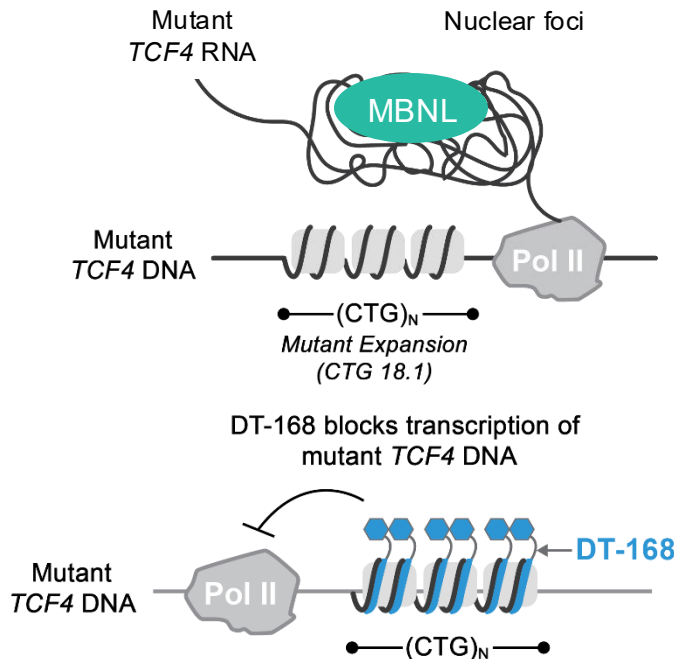


Corneal endothelial cells (CECs) pump water out of the stroma to prevent edema and maintain corneal transparency

Most cases are caused by a **CTG repeat expansion in the TCF4 gene (CTG 18.1)**

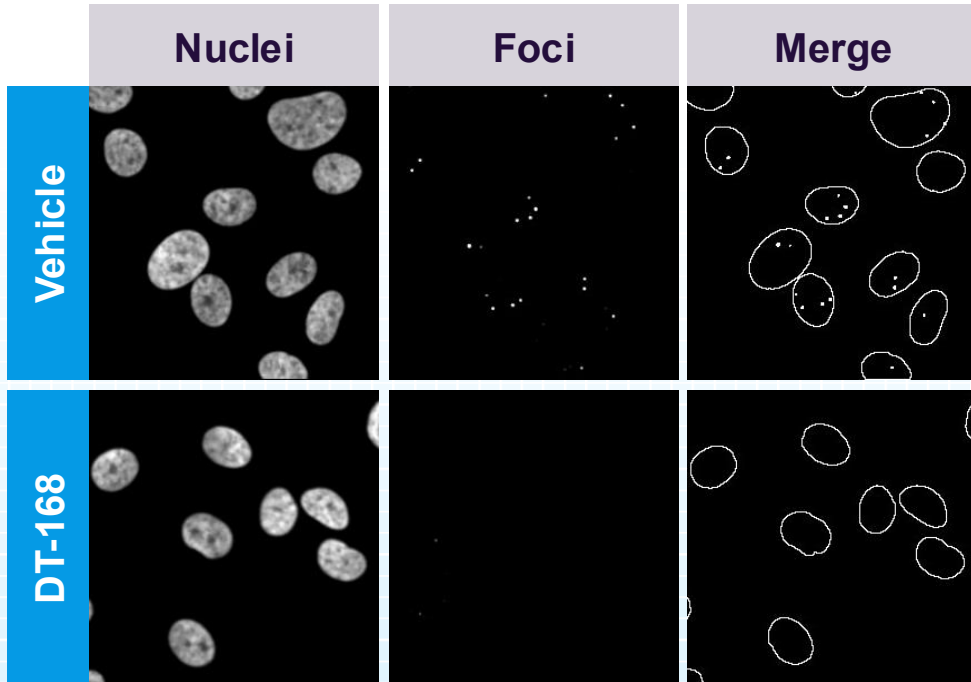
Expression of mutant TCF4 RNA leads to spliceopathy, CEC dysfunction and loss

DT-168 eye drops designed to block the expression of mutant **TCF4 RNA**



Tissues removed during surgery

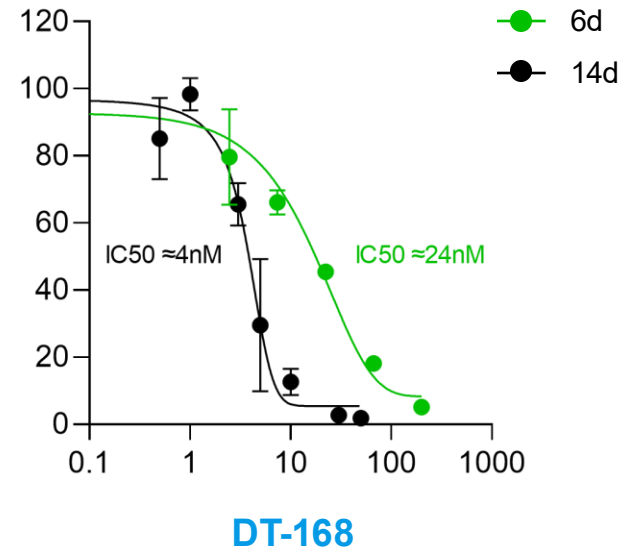
DT-168 reduction of nuclear foci observed in primary CECs isolated from patients with FECD with high potency (<5nM foci IC50)



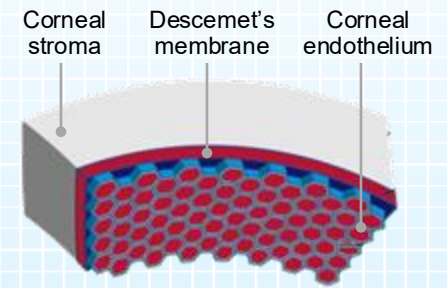
CECs treated daily for 6 or 14 days with DT-168

Foci per nucleus

Percent of untreated



Cells taken from discarded FECD corneal endothelium used to **evaluate efficacy across patients**

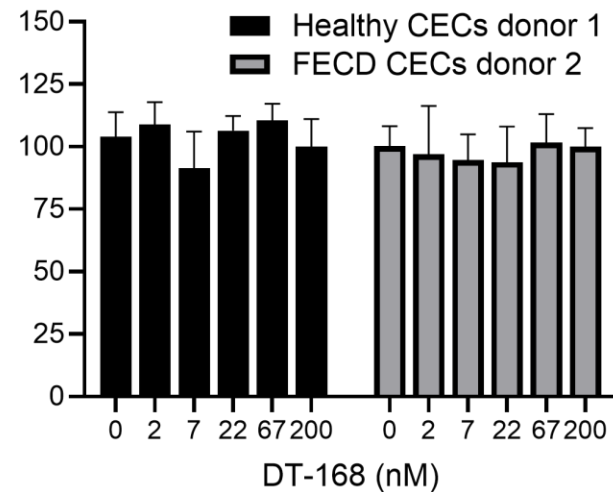


Tissues **removed during surgery**

Treatment with DT-168 left wild-type TCF4 transcripts unaffected in primary control and FECD CECs while improving spliceopathy

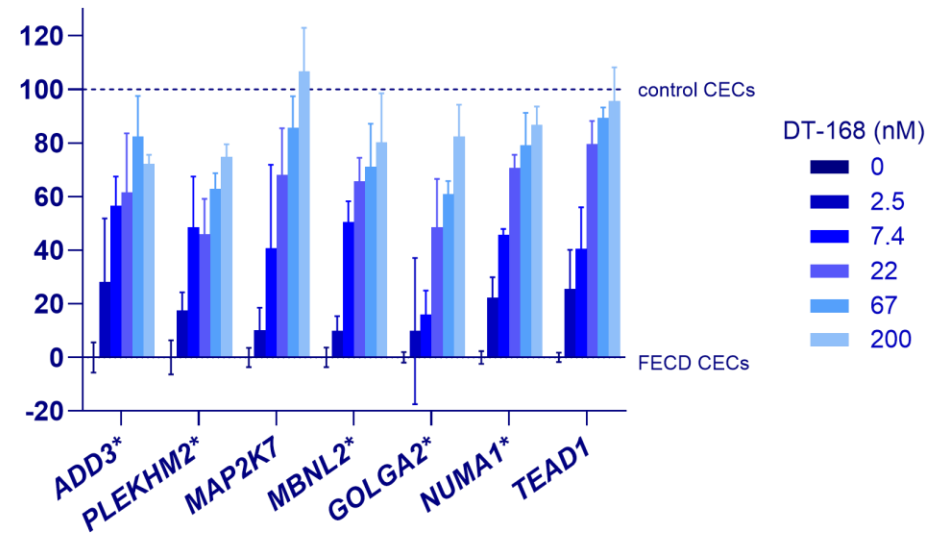
TCF4 mRNA

Percent of untreated

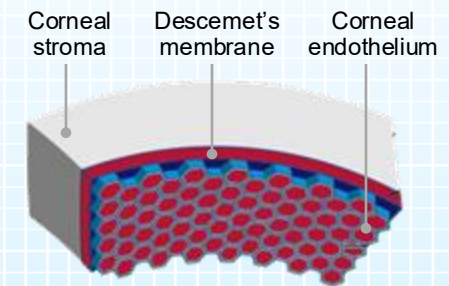


Patient-derived FECD CECs + DT-168

6d treatment; percent spliced



Cells taken from discarded FECD corneal endothelium used to **evaluate efficacy across patients**



Tissues **removed during surgery**

Notes: (LEFT FIGURE) Control CECs (Corneal endothelial cells) from donor 1 and patient-derived FECD CECs from donor 2 were incubated with DT-168 for 6 days, after which mRNA was purified and used to quantify wild-type TCF4 transcripts using a primer-probe set targeting exons 18/19. Data represent averages of N=3 replicates, and error bars represent standard deviation. Data source: DSGN-2023-DT168-1006.

* (RIGHT FIGURE) Previously reported as mis-spliced genes in primary FECD CECs (Fautsch et al., 2021) Bars represent standard deviation.

DT-168 Phase 1 SAD/MAD study in healthy participants assessed safety, tolerability, and systemic PK

- DT-168 eye drops were **well-tolerated in all subjects**

- There were **no serious adverse events**, no ocular adverse events, or participant discontinuations due to adverse events¹

- All observed adverse events were **non-ocular** and were considered **not related to drug product** by the investigator

- There were **no clinically significant findings observed in any safety assessments**

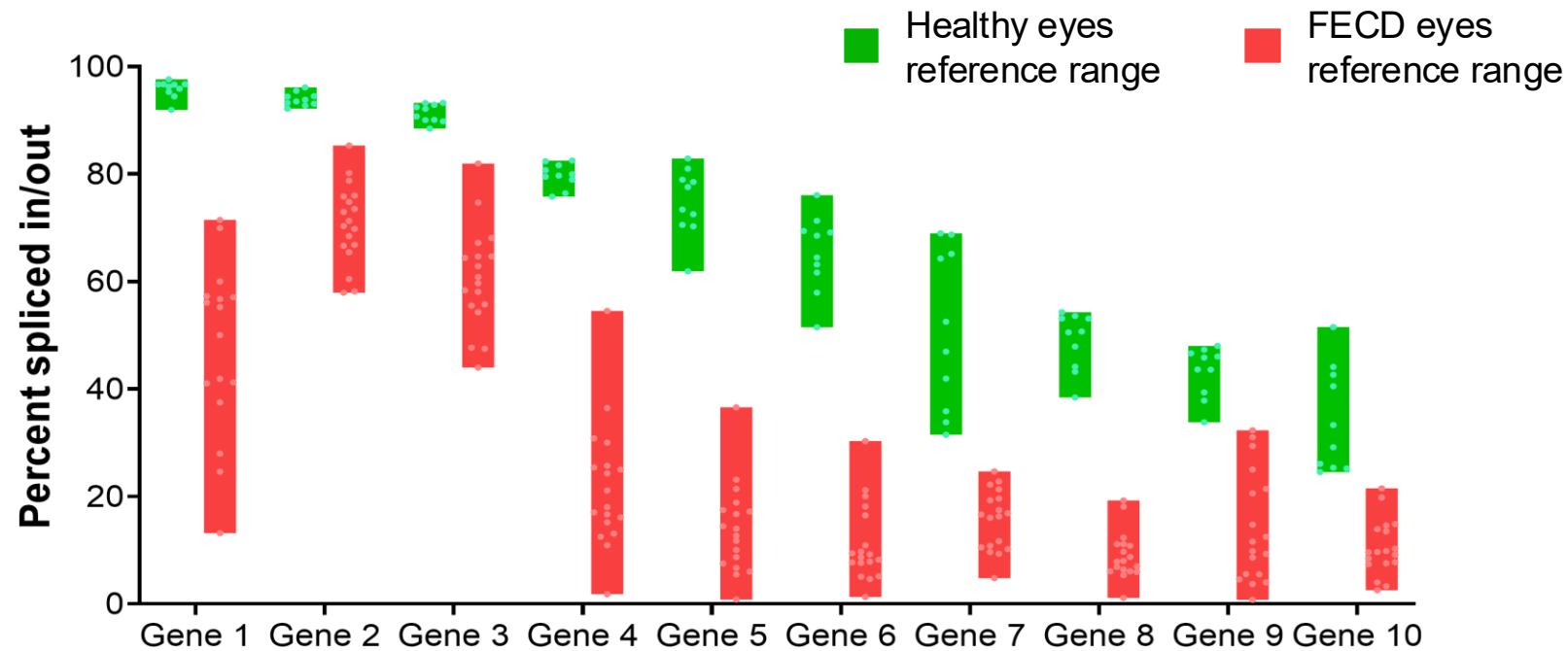
- **Pharmacokinetic analysis** demonstrated **systemic exposure below the limit of quantitation** following administration of DT-168 across all timepoints and all dose groups

1) One placebo participant discontinued from study treatment early on day 4 due to personal reasons; that participant completed all early termination events, follow-up events, and completed the study.

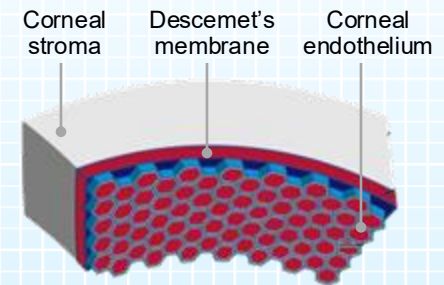
Splicing biomarker is measurable in surgically removed corneal endothelial cells

- Design conducted reference range studies showing **consistently different splicing** between unaffected eyes and mutant TCF4 FECD surgical samples
- Design has developed RNA biomarker measurements **potentially suitable for use as a clinical proof-of-concept measure of drug activity**

Splicing differences between TCF4 mutant FECD and unaffected eyes



Cells taken from discarded FECD corneal endothelium used to **evaluate efficacy across patients**



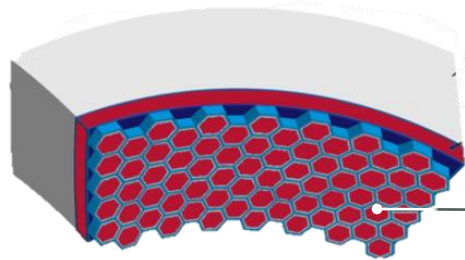
Tissues **removed during surgery**

DT-168 Phase 2 biomarker study with data in 2H 2026

Objectives: Safety and tolerability; corneal endothelial biomarkers

FECD corneal endothelium

*TCF4+ FECD patients
scheduled for surgery*



Corneal endothelium

Tissues removed during
corneal transplant surgery

**FECD UNTREATED
REFERENCE**



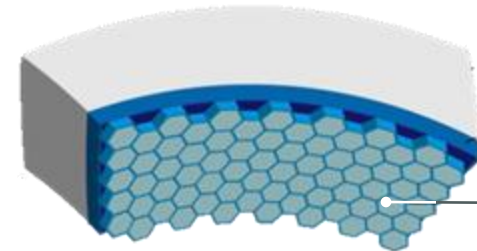
FECD TREATED

*0.5% DT-168 BID
for ~4 weeks or longer*

**FECD eye
reference range
biomarker result**

**Treated FECD
eye biomarker
result**

Unaffected corneal endothelium



Corneal endothelium

Tissue from
unaffected **eye donors**



**HEALTHY UNTREATED
REFERENCE**



**Unaffected eye
reference range
biomarker result**

Myotonic Dystrophy Type 1 (DM1)

DT-818 summary

Summary

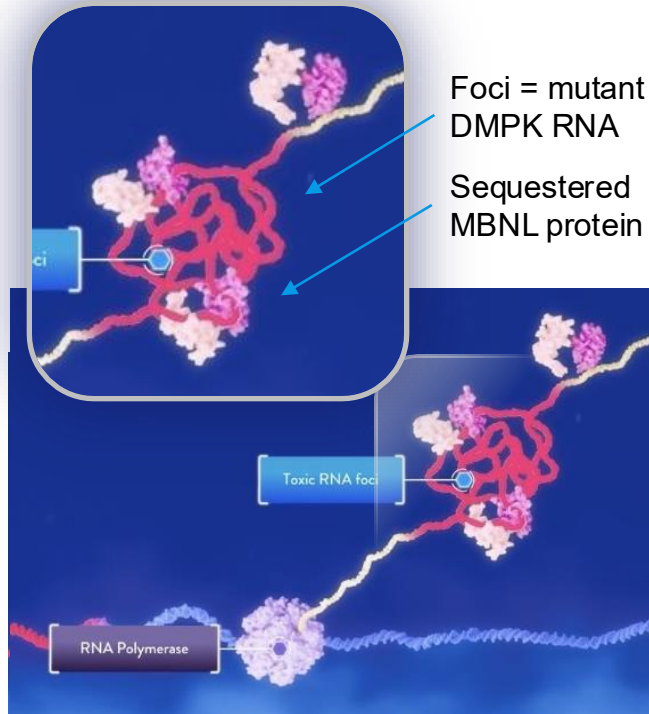
- DT-818 nominated as development candidate for the treatment of DM1 with potential best-in-disease profile; designed to selectively target mutant DMPK
- In preclinical studies, DT-818 has demonstrated a greater than 90% reduction in toxic RNA foci in DM1 patient cells, corresponding splicing correction and selective targeting of mutant DMPK
- Ex-US regulatory clearance obtained to initiate Phase 1 development

Phase 1

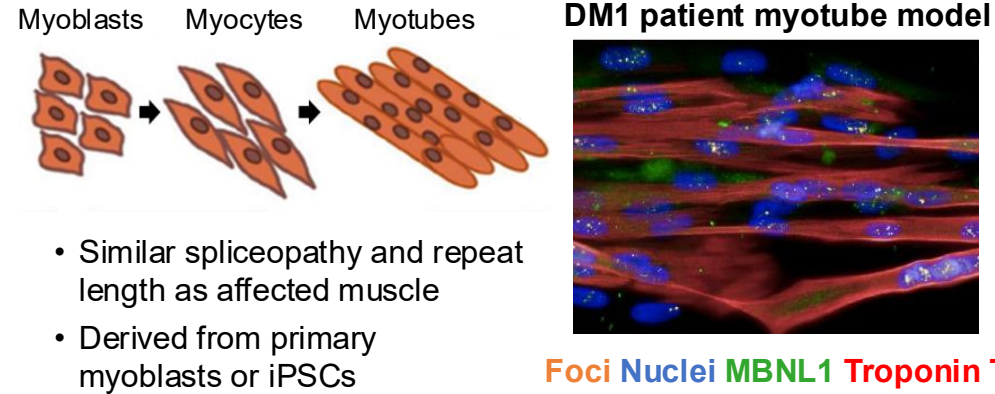
- Begin dosing DM1 patients in a Phase 1 MAD trial of DT-818 in Australia in 1H 2026
 - Injectable (initially once weekly IV, exploring subcutaneous route)
- Endpoints:
 - Safety
 - Correction of mis-splicing
- Results anticipated in 2027

DM1 (Myotonic dystrophy type 1)

1 Mechanism of disease



2 Preclinical human cells



3 Preclinical animal models



HSA^{LR} mouse model

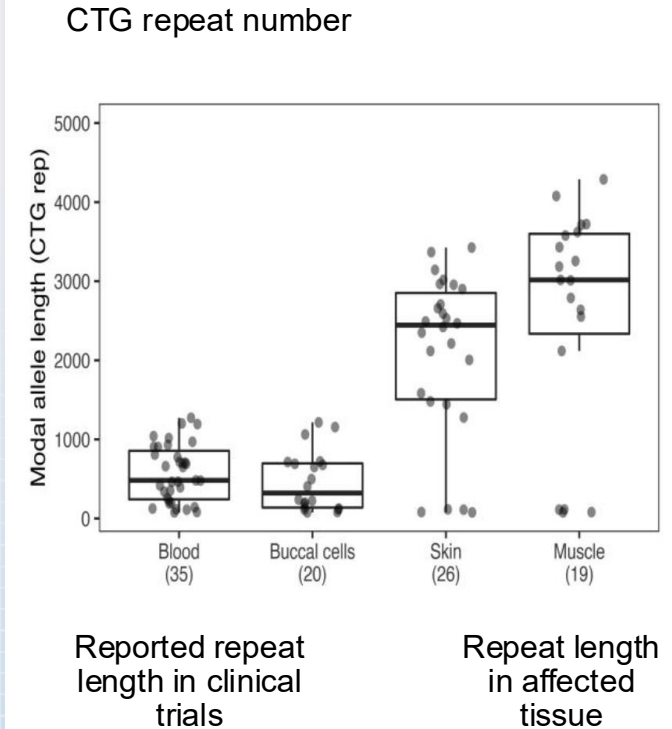
Actin transgene with CTG repeats
Used because DMPK expanded CTG repeat model has limited myotonia



Wild type NHP

Contain no CTG expansions
Suitable for testing oligonucleotides that target non-CTG DMPK sequences

4 Longer DMPK CTG repeats in affected tissues cause disease



5 Symptoms



intellectual impairment and excessive daytime sleepiness



cataracts



heart problems



digestive problems causing stomach pain



skeletal muscle weakness



muscle atrophy













myotonia


70,000+
individuals affected in the
U.S.

90,000+
individuals affected in
Europe

DM1 clinical stage programs

					
Approach ¹	 siRNA linked to transferrin receptor mAb >100kDa	 Degrading ASO linked to transferrin receptor Fab >50kDa	 Blocking ASO linked to peptide >10kDa	 Blocking ASO linked to cyclic peptide >10kDa	 RNAi linked to targeting ligand >10kDa
Stage of development	Registrational trials (vHOT primary)	Registrational trials (vHOT primary)	Phase 2	Phase 1/2	Phase 1/2
Distribution	Muscle, small intestine	Muscle	Muscle	Muscle	Muscle
Allele selectivity	Preferentially degrades cytoplasmic (wild type) DMPK	Non-selective	Selective	Selective	Non-selective
Clinical CASI-22 splicing	16% ²	25% ⁵	53.7% ⁷	Data not available	Data not available
Preclinical human myotube foci	~55% ³ reduction	~30% ⁶ reduction	54% ⁷ reduction	~55% ⁸ reduction	Data not available
Preclinical animal model	Nonhuman primate: >75% DMPK reduction (wild type) ⁴	HSA ^{LR} mouse: ~80 to >90% splicing improvement, near complete myotonia elimination ⁶	HSA ^{LR} mouse: near complete restoration of splicing and myotonia elimination ⁷	HSA ^{LR} mouse: ~67% foci reduction, near 100% restoration of splicing ⁸	TREDT960i/HSA-rTA mouse: >50% DMPK reduction, >50% restoration of splicing ⁹

Note: Patient cell data refers a DM1 patient cell line containing ~2600 repeats; Source: 1. Company materials, INN structures where available, Anand P, et, al, Metabolic Stability and Targeted Delivery of Oligonucleotides. J Med Chem. 2025; 2. Avidity Biosciences, Corporate Presentation, May 2023; 3. WMS 2023 Poster; 4. AAN 2021 Presentation; 5. Dyne Therapeutics, ACHIEVE Clinical Update, Jan 2025; 6. ASGCT 2021 Presentations; 7. PepGen, Corporate Presentation, Oct 2025; 8. Entrada Therapeutics, Myology Congress Poster, Sept 2022; 9. Arrowhead Pharmaceuticals, MDA 2024 Poster Mar 2024,



GeneTAC®
small molecule
1-3kDa

Designing a better DM1 approach

Design hypothesis

We believe reduction of toxic foci in human myotubes is a better predictor of clinical splicing biomarker observations

- Animal preclinical models (e.g. HSA-LR or wild-type NHPs) are supportive but have not been predictive of clinical splicing results

We believe that the limited clinical benefit for therapeutics in clinic are driven by

- Targeting muscle leaves many target organs untreated
- Reduced efficacy in cells with somatically expanded (longer) repeats
- Incomplete splicing improvement; toxic RNA tangles are refractory to degradation mechanisms
- Safety concerns about dosing higher

Features designed into DT-818

Greater than 90% reduction of toxic foci and restoration of splicing in human myotubes

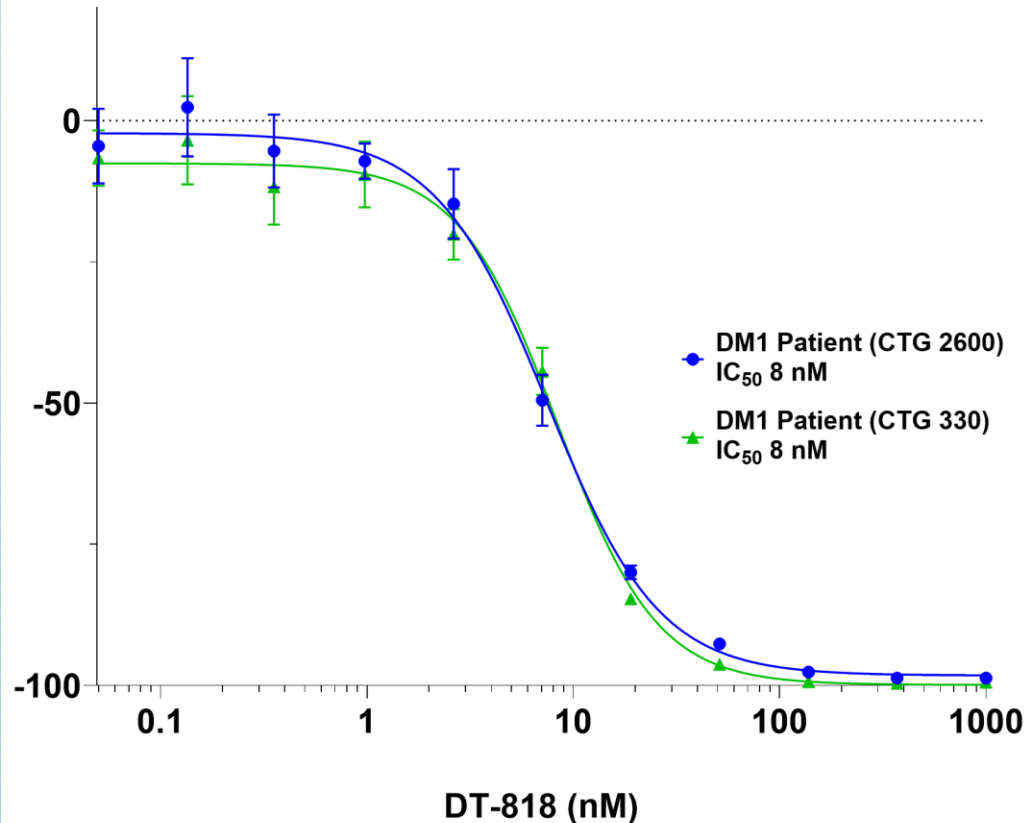
- Human genetic models seem to better correlate to what has been observed in the clinic so far
- Broad distribution to key affected tissues
- Efficacy in cells with somatically expanded repeats
- DT-818 mechanism works upstream of oligos resulting in greater than 90% restoration of splicing in human myotubes
- Maintain expression of wild-type DMPK

DT-818 treatment results in foci reduction, leads to improvement in splicing, regardless of repeat length or patient genetics

DT-818 reduces toxic RNA nuclear foci in DM1 myotubes

Foci per nucleus

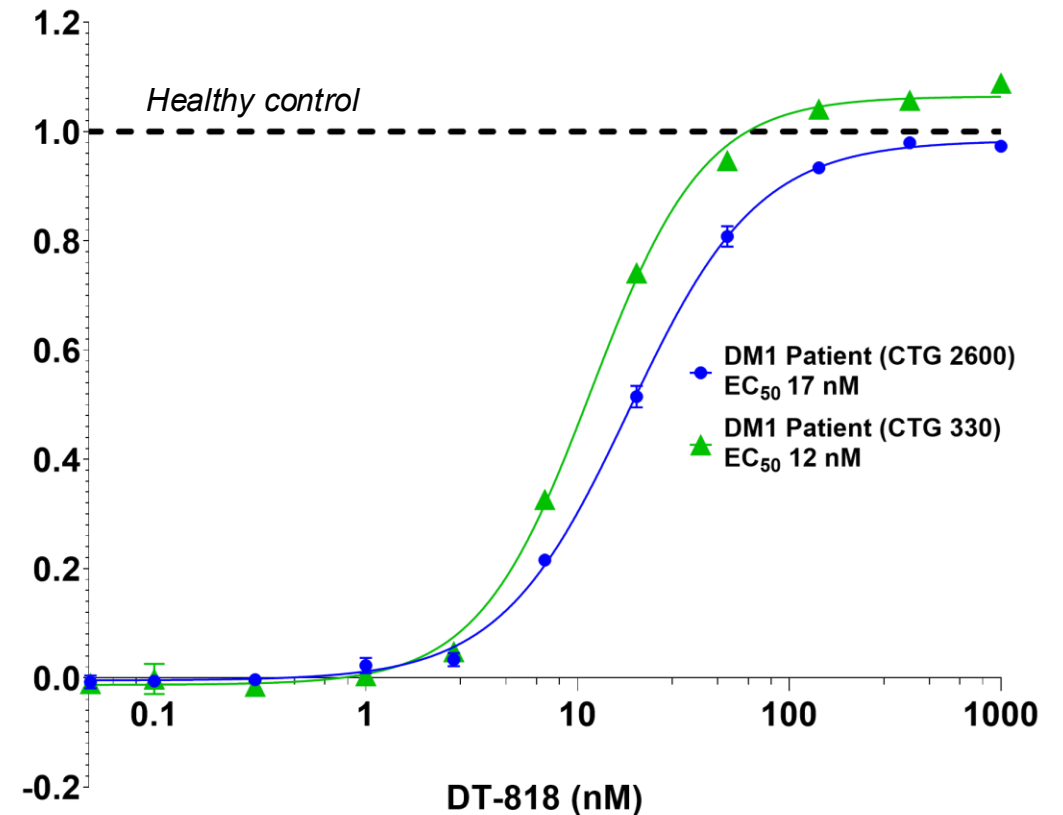
Percent change relative to untreated (FISH)



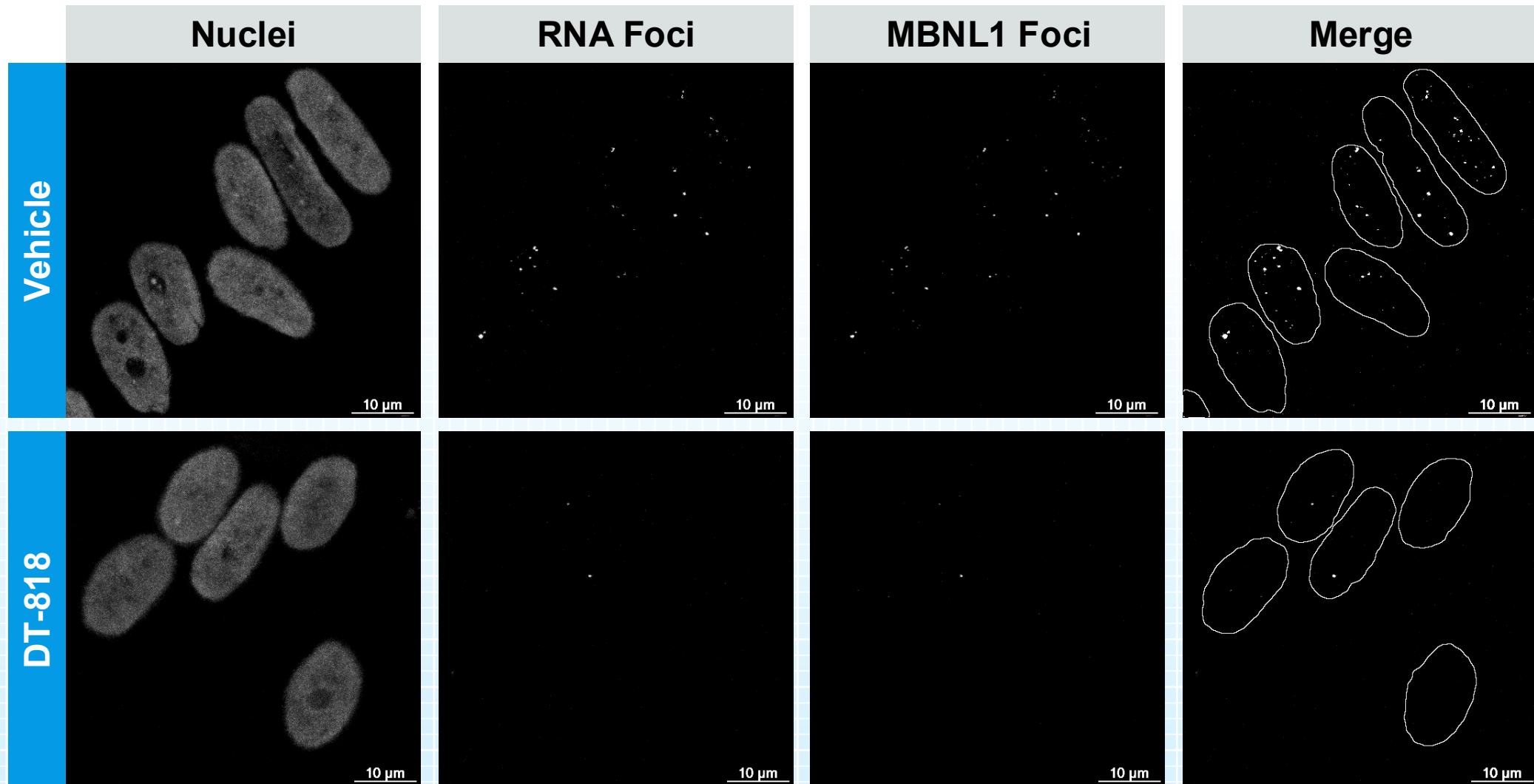
DT-818 corrects splicing in DM1 myotubes

Splice index

Index relative to healthy control myotubes

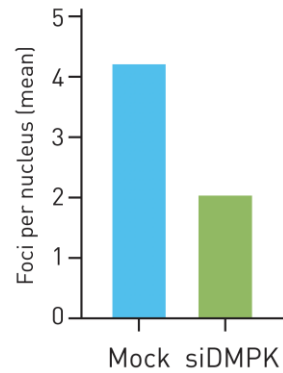


DT-818 treatment reduces toxic RNA foci and liberates MBNL1 protein in DM1 patient myotubes

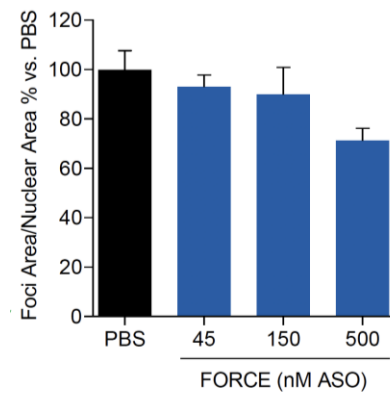


DT-818 treatment shows best-in-disease potential for foci reduction in patient cell line with 2,600 repeats

AVIDITY BIOSCIENCES Estimated*¹ ~55%

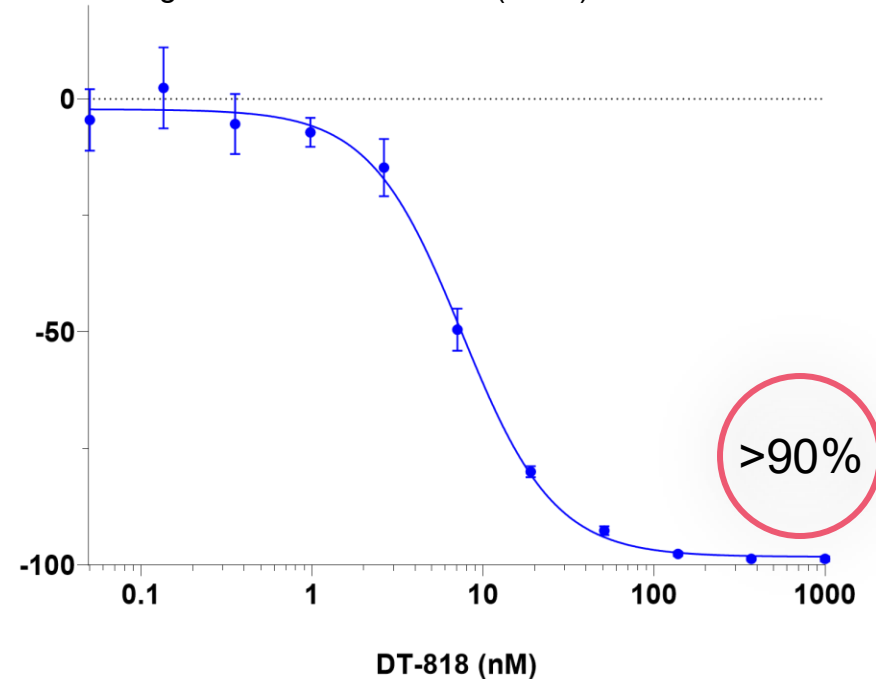


Dyne THERAPEUTICS Estimated*² ~30%

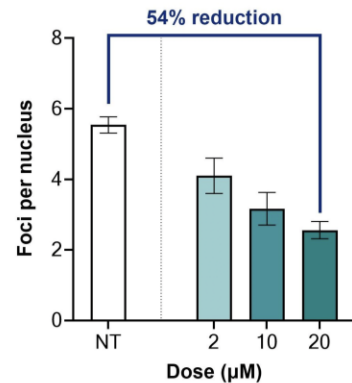


DESIGN THERAPEUTICS

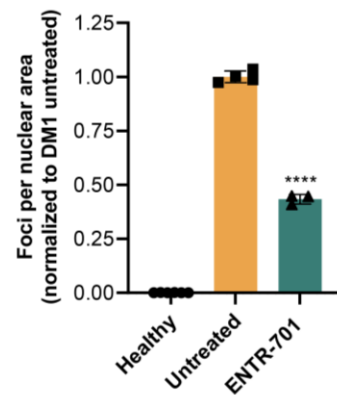
Foci per nucleus
Percent change relative to untreated (FISH)



PepGen™ 54% foci reduction³



entrada THERAPEUTICS Estimated*⁴ ~55%

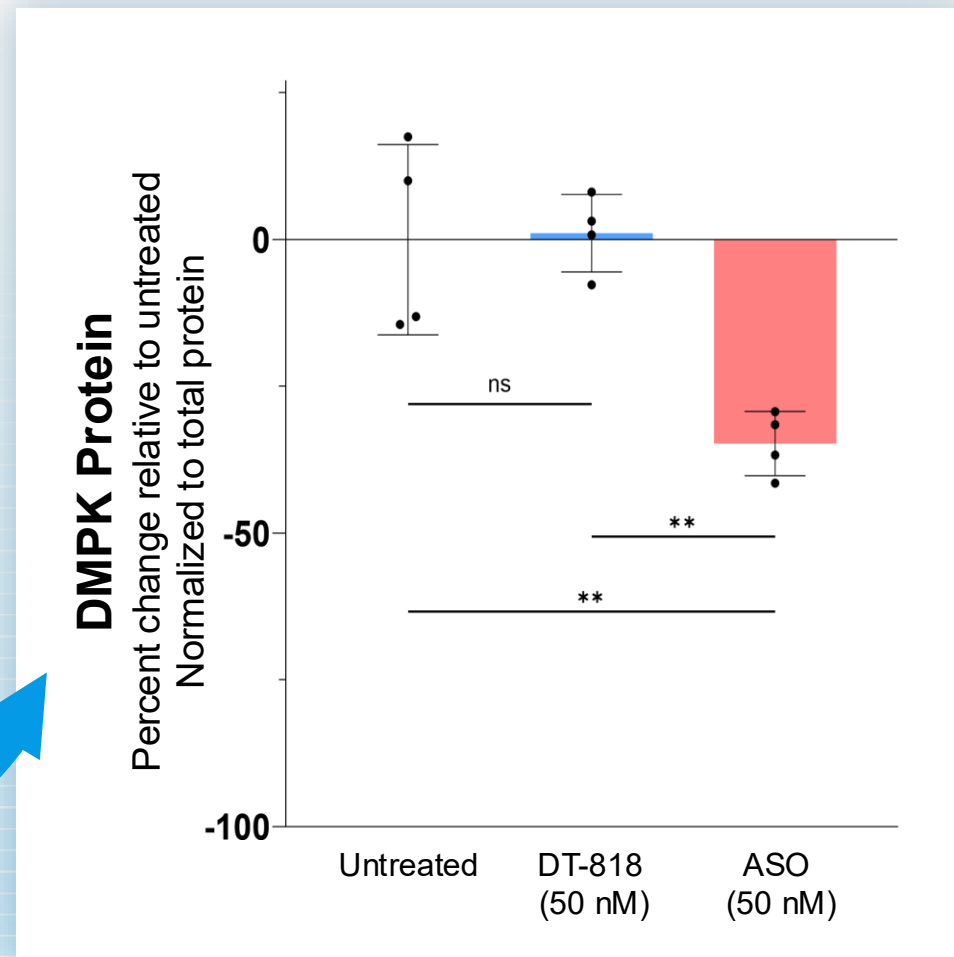
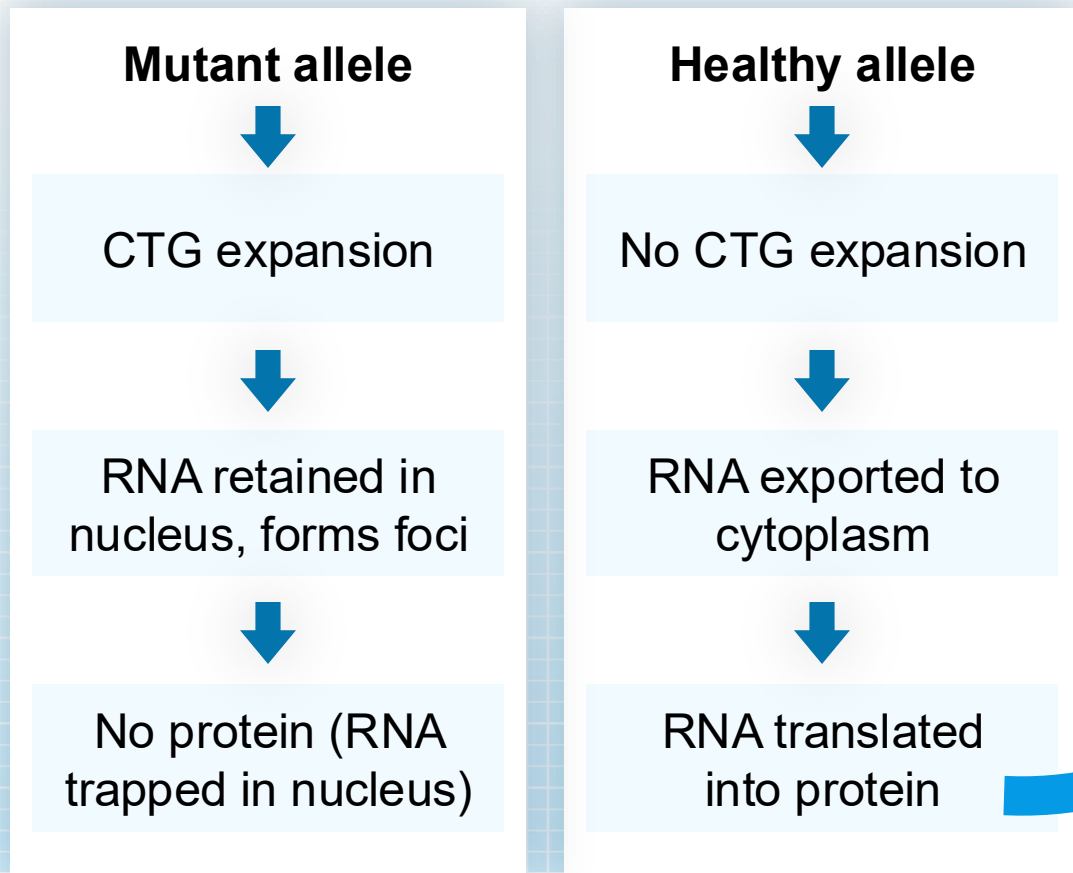


Note: Foci reduction evaluated in DM1 patient myotubes containing ~2600 repeats in all cases except Avidity where repeat length not noted. *.Estimates are based on the graphs provided since the company has not provided quantitative values from graphs; References: 1. Avidity Biosciences, WMS 2023 Poster; 2. Dyne Therapeutics, ASGCT 2021 Presentations; 3. PepGen, Corporate Presentation, Jan 2024; 4. Entrada Therapeutics, WMS 2022 Presentation

DT-818 selectively targets mutant DMPK

Allele-specific mechanism spares DMPK protein

DM1 patients have two DMPK alleles

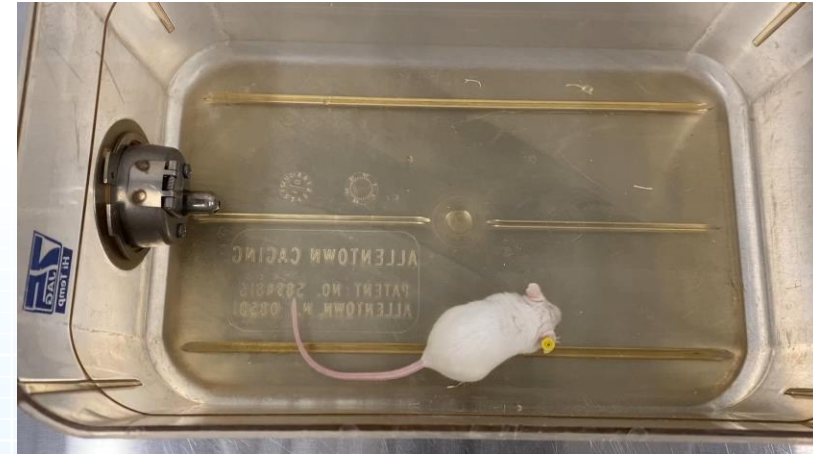


Splicing and myotonia improved in actin repeat (HSA^{LR}) mice treated with DT-818

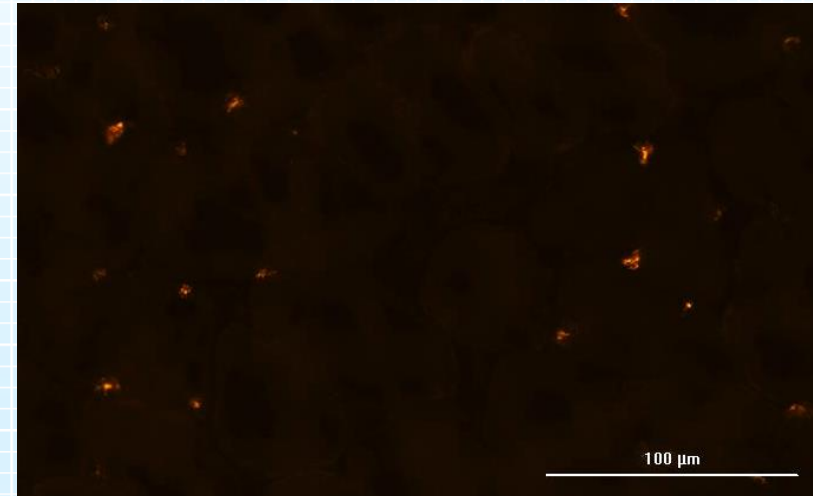
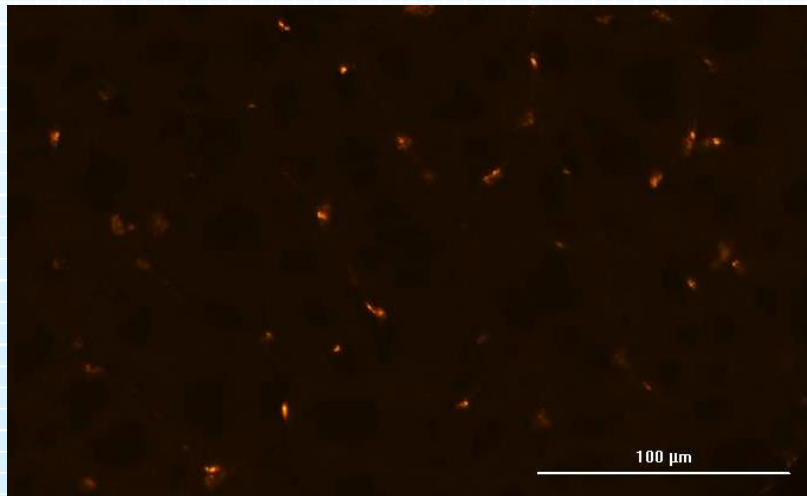
Vehicle

DT-818

Myotonia



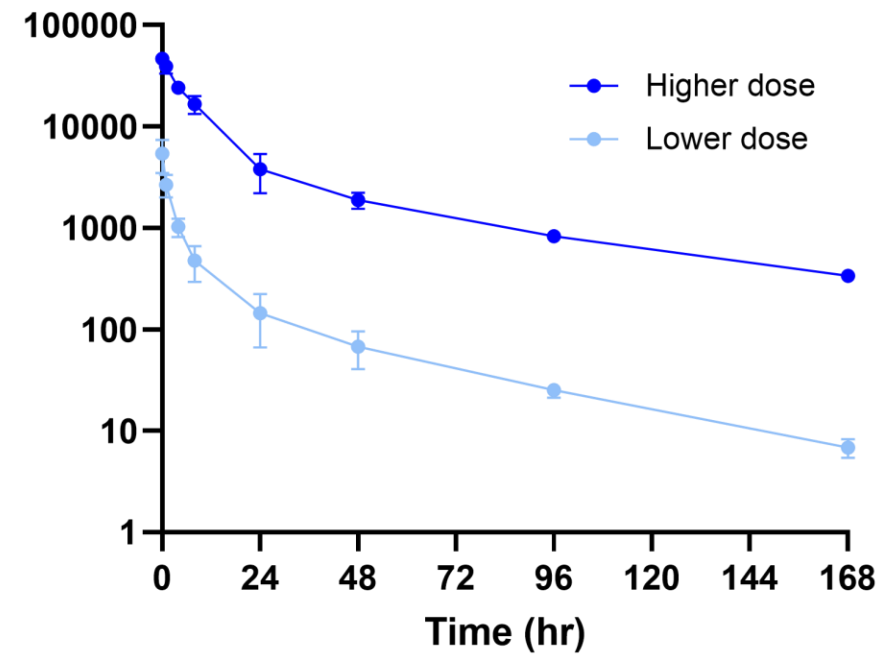
Foci



DT-818 shows good exposure and long half-life

NHP PK

Single IV dose
nM DT-818 in plasma



DT-818 summary and next steps

Summary

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- In preclinical studies, DT-818 has demonstrated a greater than 90% reduction in toxic RNA foci in DM1 patient cells, corresponding splicing correction and selective targeting of mutant DMPK
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Phase 1

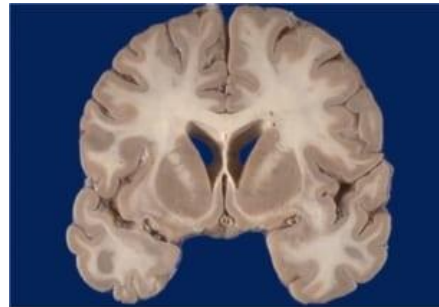
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Huntington's Disease (HD)

Huntington's Disease (HD)

GeneTAC[®] molecules selectively reduce mutant Huntingtin and spare the normal Huntingtin allele

- Causes brain atrophy due to death of neurons
- Symptoms range from motor function to neurological
- Universally fatal
- HD Prevalence: >40,000 in the U.S.



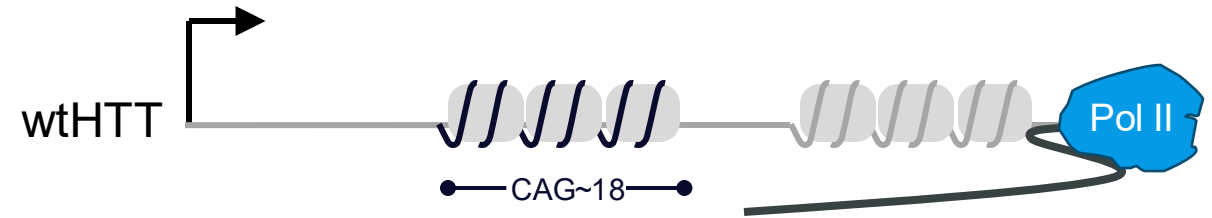
Control – no atrophy



HD

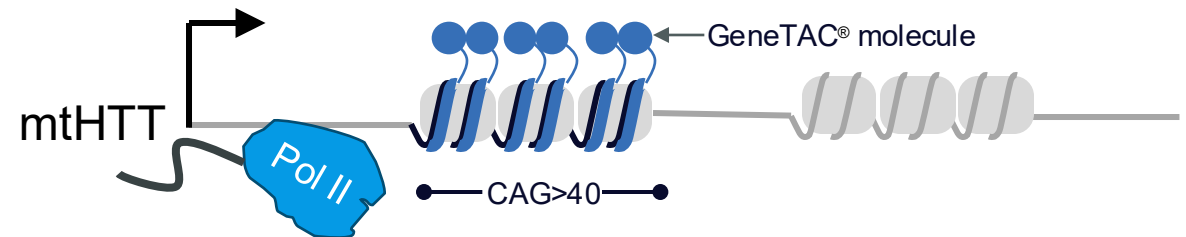
Normal HTT gene — *thought to be important to normal state*

GeneTAC[®] molecules *preserve transcription* at the *wild type locus*

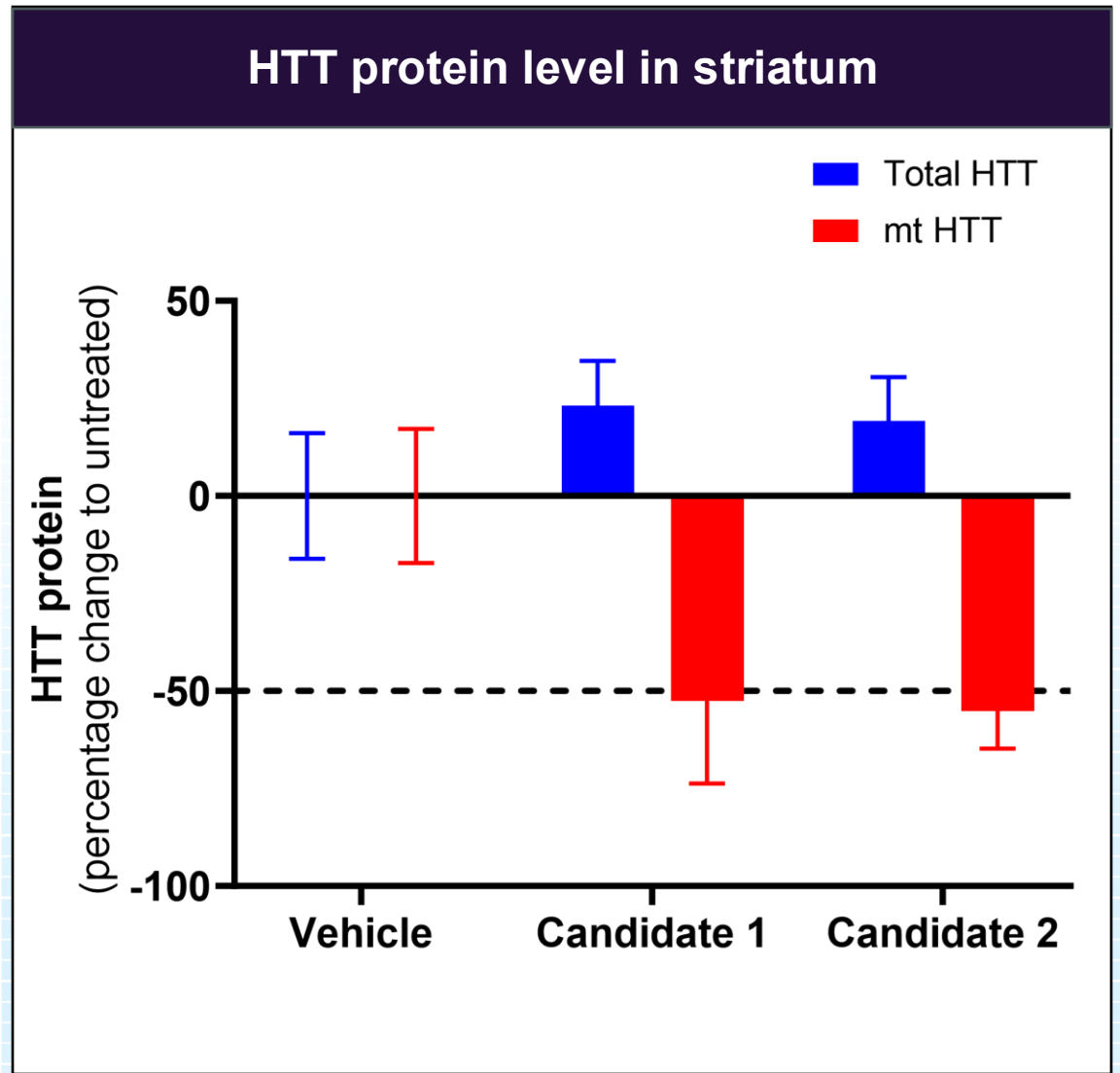
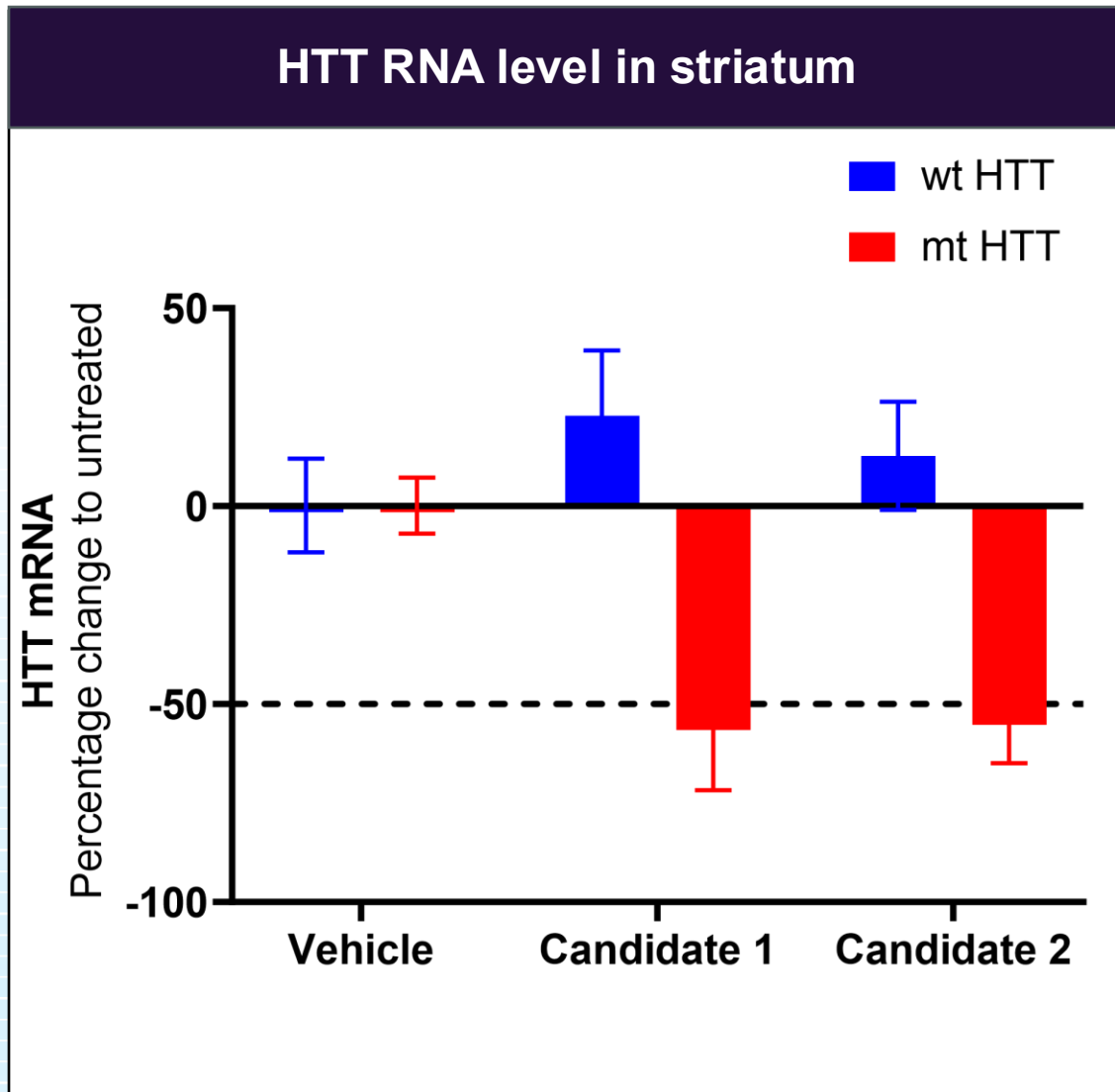


HTT gene with expansion

GeneTAC[®] molecules *block transcription* specifically at the *mutant locus*



Allele-specific reductions of RNA and protein observed in the brain in zQ175DN HD mouse model after 8 weeks of systemic administration



Note: mice were treated with Candidate 1 or Candidate 2 for 8 weeks, vehicle group treated for 4 weeks. Percent change calculated based on treated compared to untreated. RNA level determined with RT-PCR. Protein level determined with TR-FRET. Data presented as Mean \pm SD.

GeneTAC[®] HD candidates have significant advantages over other HTT lowering therapeutic approaches

Allele-selective

Reduce mutant Huntingtin and spare the normal Huntingtin

Non-selective
Reduce both normal and mutant Huntingtin

	GeneTAC [®] HD candidates	WAVE [™] LIFE SCIENCES WVE-003
Modality	Small molecule Facilitate drug biodistribution to the whole brain	ASO
Delivery	Parenteral administration	Intrathecal administration
Target somatic expansion	Yes Target repeats, increased efficacy as repeats expand during disease progression	No Target SNP3
Patient population	All HD patients	~40% of patients with SNP3
Status	<ul style="list-style-type: none"> • Selective reduction of mtHTT in patient cells (IC50≈~1nM) • Characterizing several candidates prior to DC selection 	Phase 1/2 <ul style="list-style-type: none"> • Reduced mtHTT • Increased NfL observed

uniQure
AMT-130

 **IONIS**[™]
Tominersen


PTC-518

Strong financial position to enable programs and platform

PLATFORM

- **Proprietary GeneTAC[®] platform** designed to generate blockbuster products with first/best-in-class profiles for severe monogenic disorders

PROGRAMS

- **Three clinical-stage programs** (FA, FECD, and DM1) in 2026
 - DT-216 restores endogenous frataxin with broad tissue distribution
 - DT-168 eye drop targeting the genetic mutation in FECD
 - DT-818 potential for best-in-disease profile in DM1
- Active research pipeline with HD GeneTAC[®] program

CASH POSITION

- Balance sheet of **\$222.8 million** as of *March 31, 2026*, expected to fund planned operations into 2029