



DYNE-302 leads to functional improvement and resolves muscle transcriptomic changes in mouse models of FSHD

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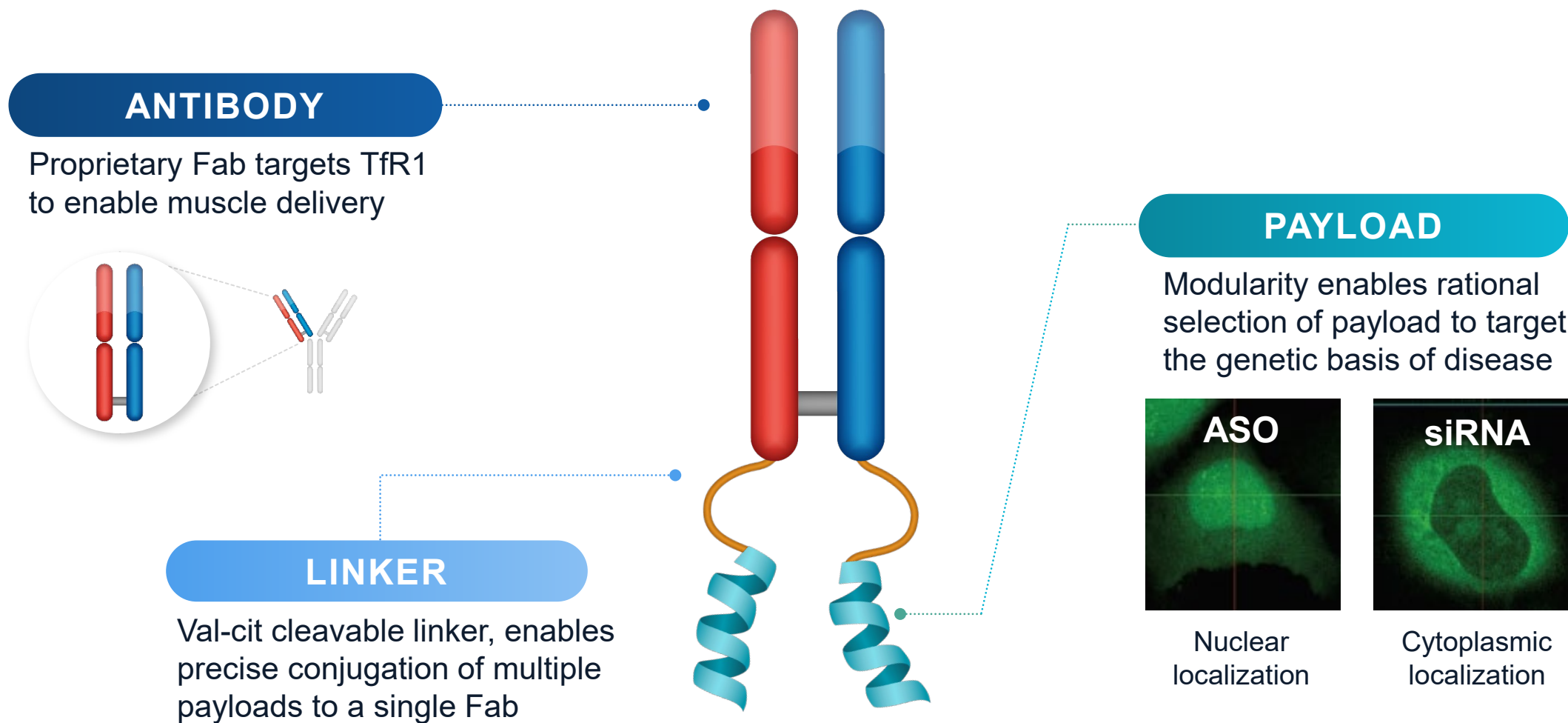
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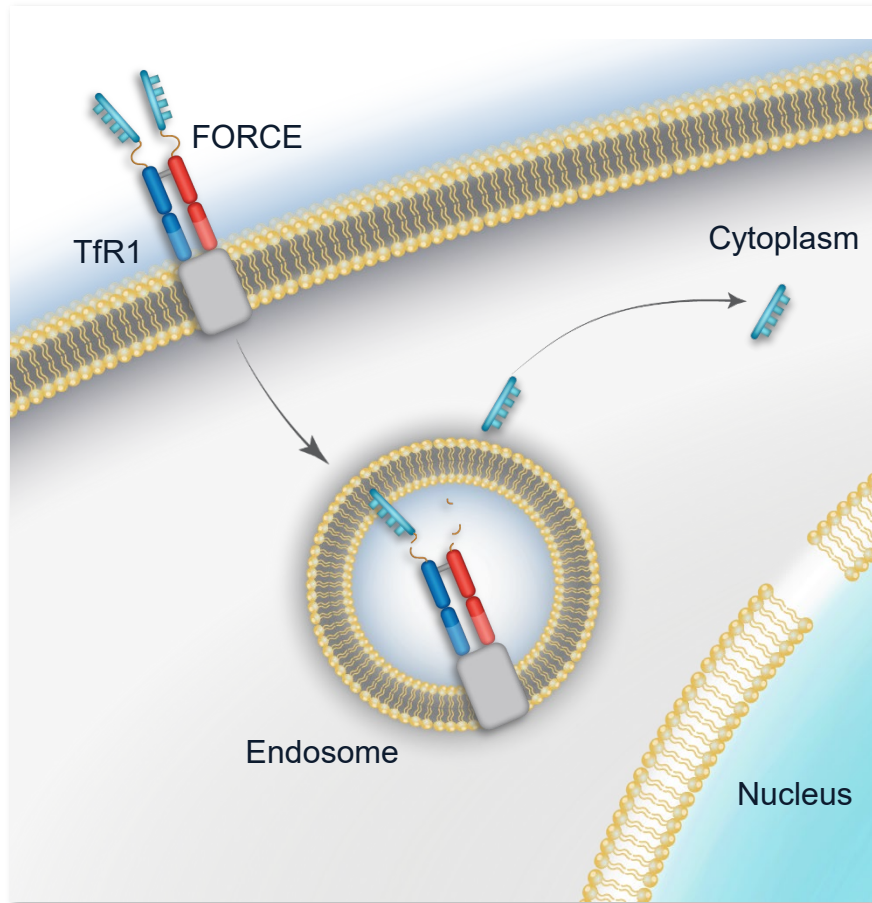
The FORCE™ platform and DYNE-302 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any other regulatory authority.

Dyne FORCE™ Platform: Modern Oligo Therapeutics for Muscle Diseases



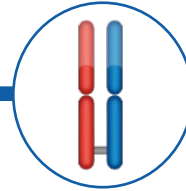
Fab and linker are components of FORCE molecules in clinical development for DM1 and DMD

FORCE Platform Harnesses Cell Biology to Modify Disease



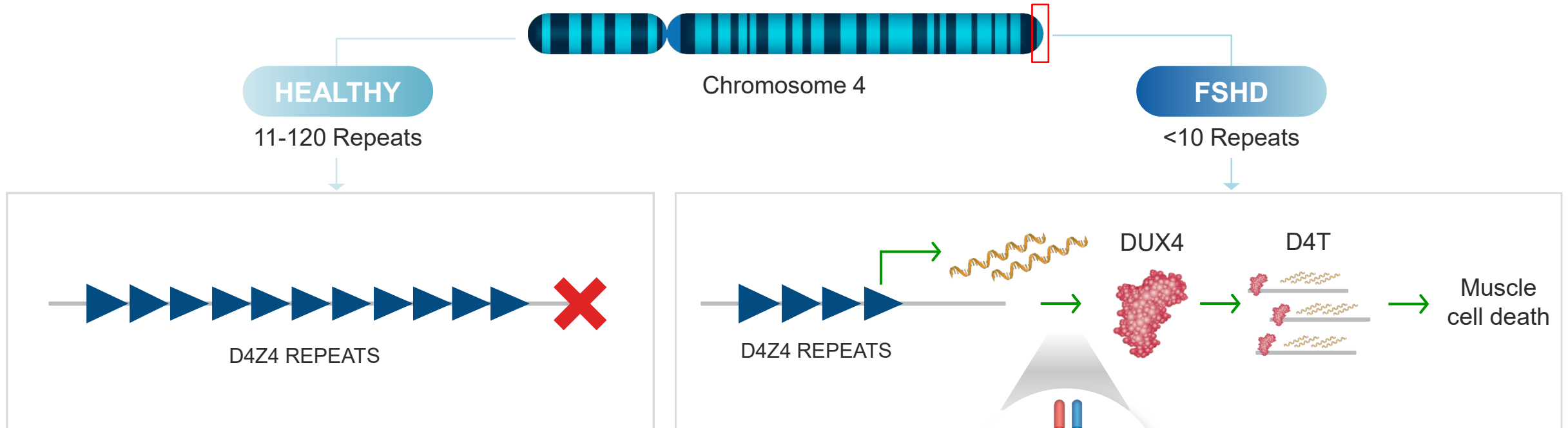
- Harnesses natural mechanism of TfR1 receptor-mediated delivery to transport therapeutics across the cell membrane
- Achieves endosomal escape without any membrane-destabilizing agents
- Distinctive pharmacokinetic profile creates opportunity for durable target engagement and wide therapeutic index

Fabs Offer Multiple Advantages for Targeted Delivery



Feature	Fab
Delivery to Muscle	Enhanced delivery of payloads ✓
Enhanced Tissue Penetration	1/3 size of mAb leads to increased tissue penetration ✓
Tolerability	Lower protein load leads to potentially increased tolerability ✓
Effector Cell Activation	Lower risk due to lack of Fc domain ✓
Complement Activation	Lower risk due to lack of Fc domain ✓
Large Scale Manufacturing	Yields enable large scale manufacturing ✓

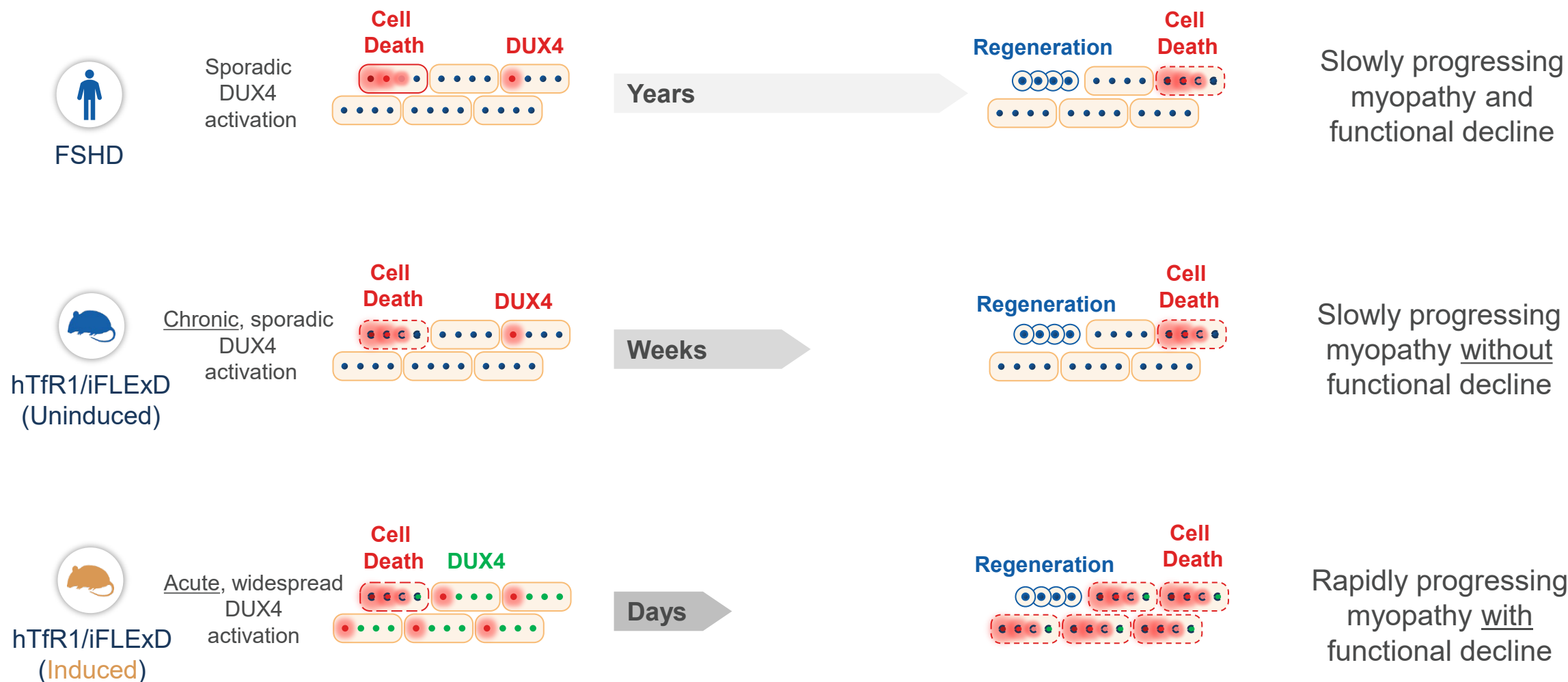
DYNE-302 Targets the Genetic Basis of FSHD



DYNE-302: a FORCE-siRNA conjugate designed to address the genetic basis of disease by **targeting toxic *DUX4* expression**

- Highly selective *DUX4* siRNA payload with favorable *in vitro* off-target and *in vitro* tolerability profile
- Extended duration of action intended to overcome sporadic *DUX4* activation

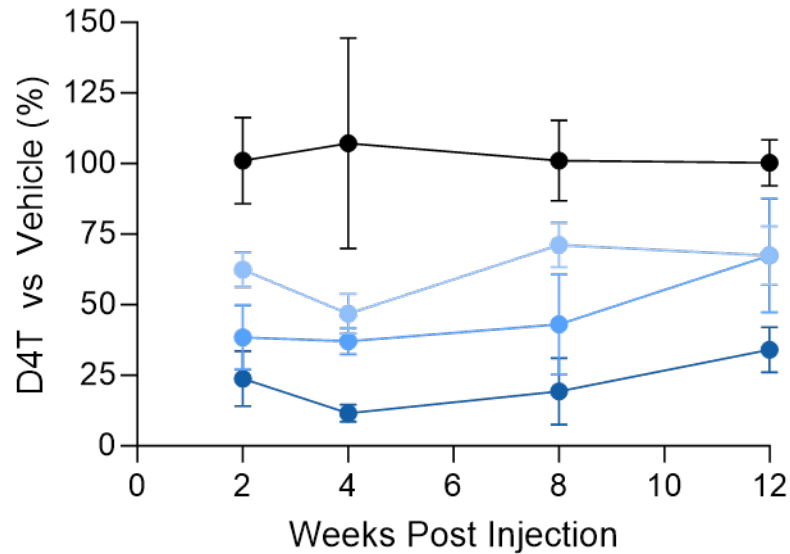
The hTfR1/iFLExD Mouse Model Recapitulates Multiple Aspects of Human FSHD



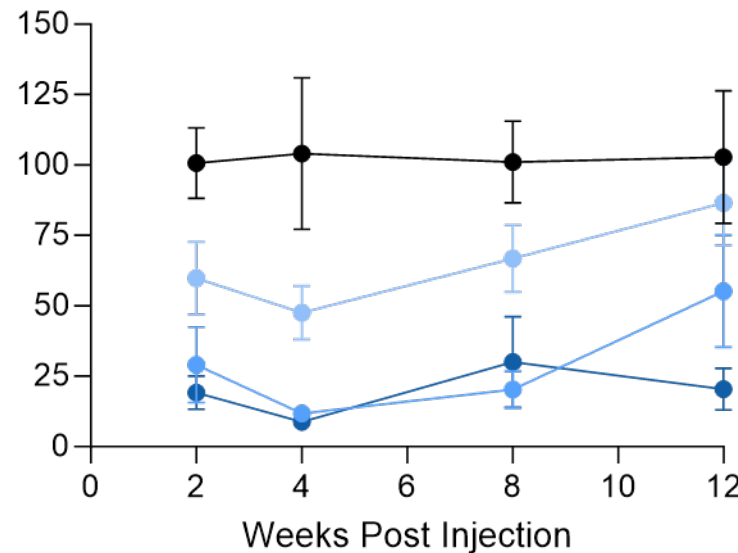
Single Dose of DYNE-302 Achieves Robust, Durable, and Dose-Dependent D4T KD in Skeletal Muscle of hTfR1/iFLExD FSHD Mice



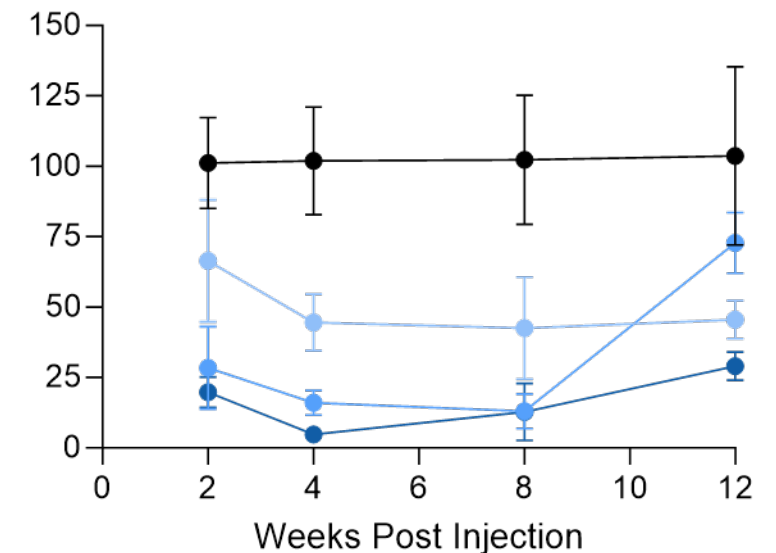
Quadriceps



Gastrocnemius



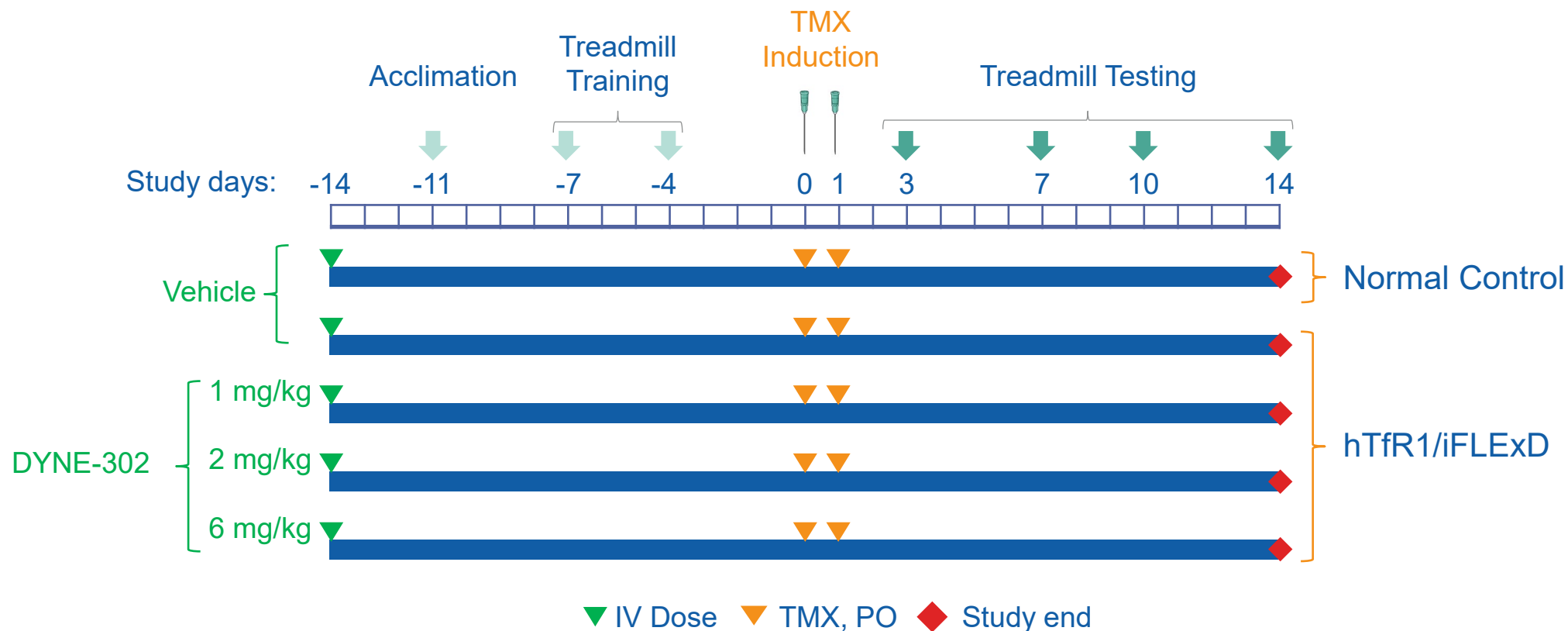
Tibialis anterior



● Vehicle ● DYNE-302 1 mg/kg ● DYNE-302 2 mg/kg ● DYNE-302 6 mg/kg

DYNE-302 demonstrates potential for infrequent dosing, out to Q12W

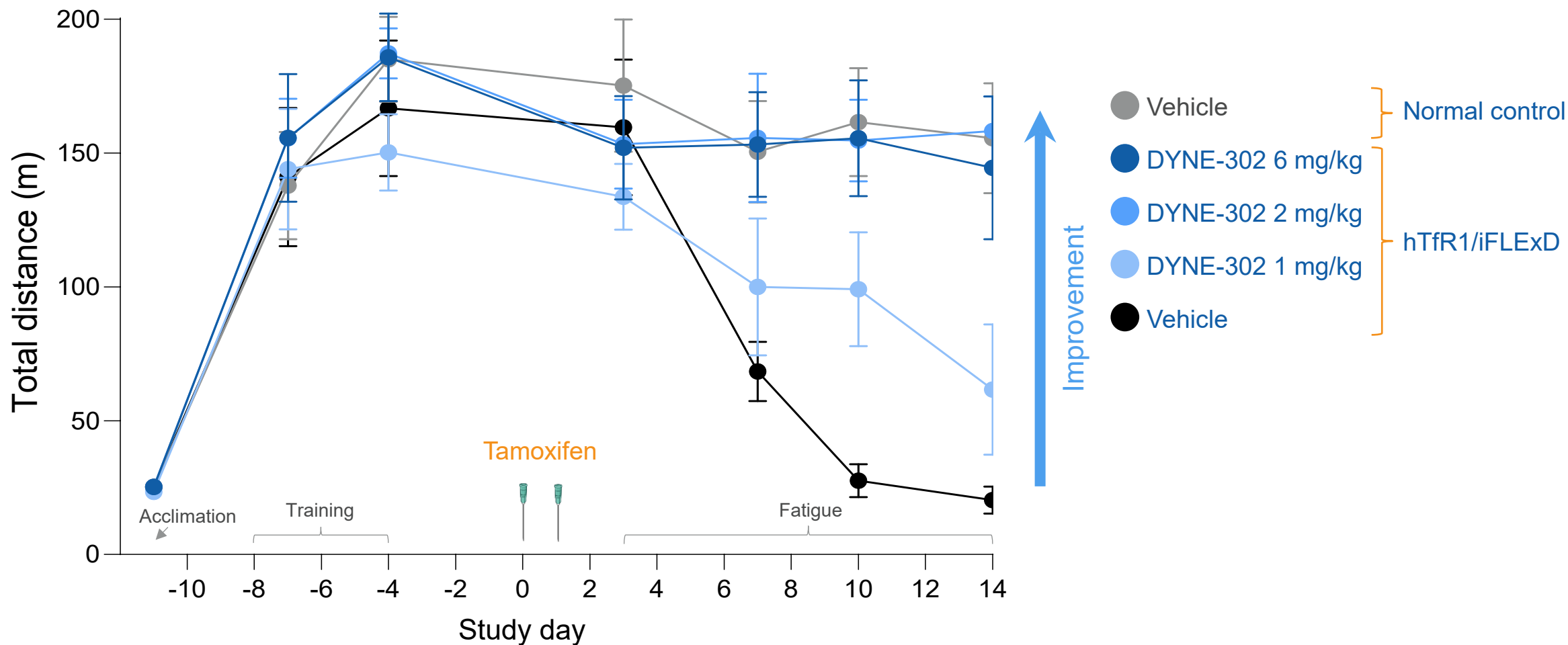
Study to Establish Impact of DYNE-302 Preventative Treatment in the Induced hTfR1/iFLExD Mice



Preventative Treatment with DYNE-302 Leads to Functional Improvement in hTfR1/iFLExD Mice



Functional improvement in forced treadmill run test



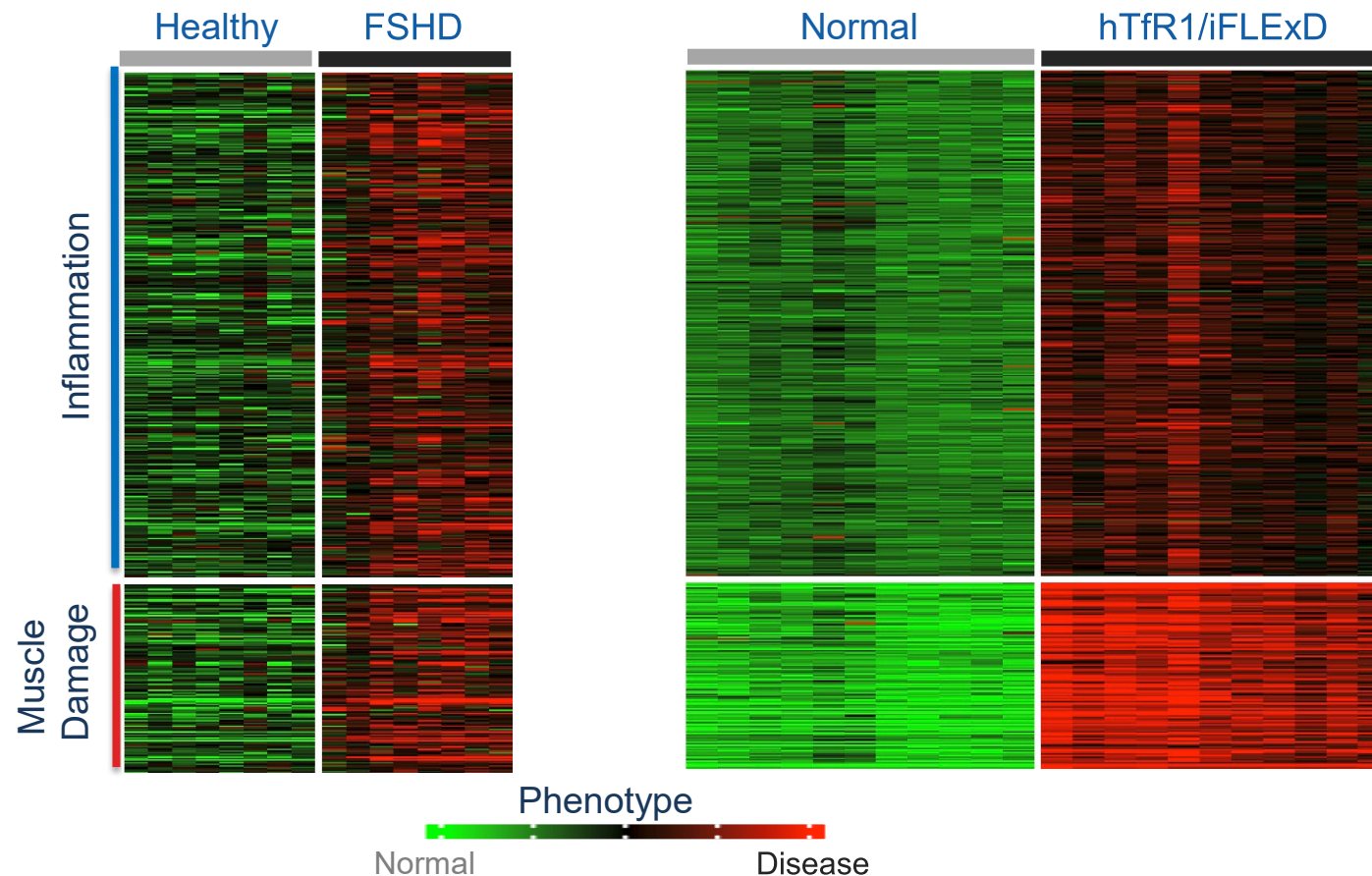
hTfR1/iFLExD Mice Recapitulate Transcriptional Profiles of Immune Response and Muscle Damage Seen in Human FSHD Muscle



Human transcriptome
in skeletal muscle biopsies



Mouse ortholog transcriptome
in quadriceps



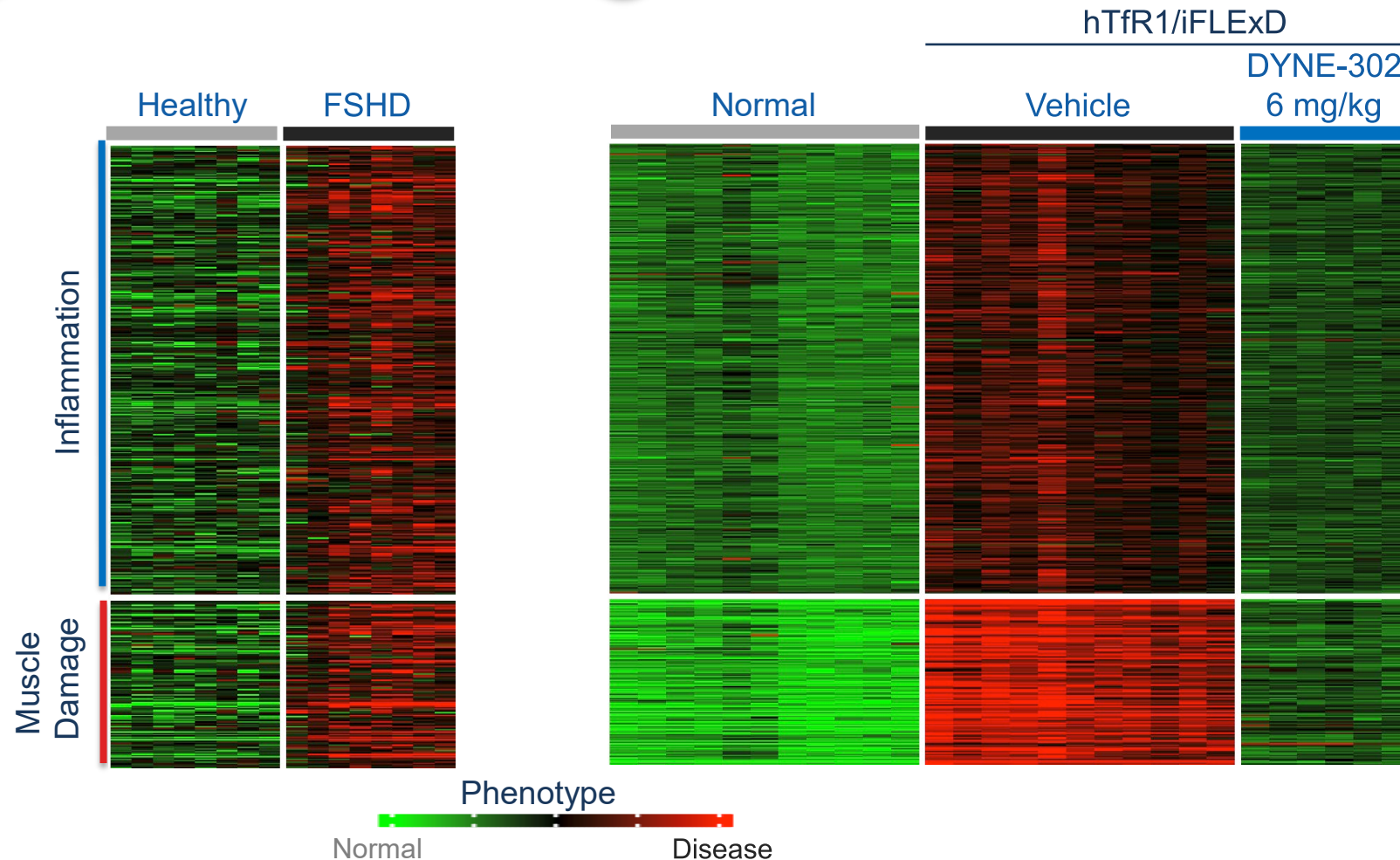
DYNE-302 Normalizes Transcriptional Profiles of Inflammation and Muscle Damage in hTfR1/iFLExD Mice



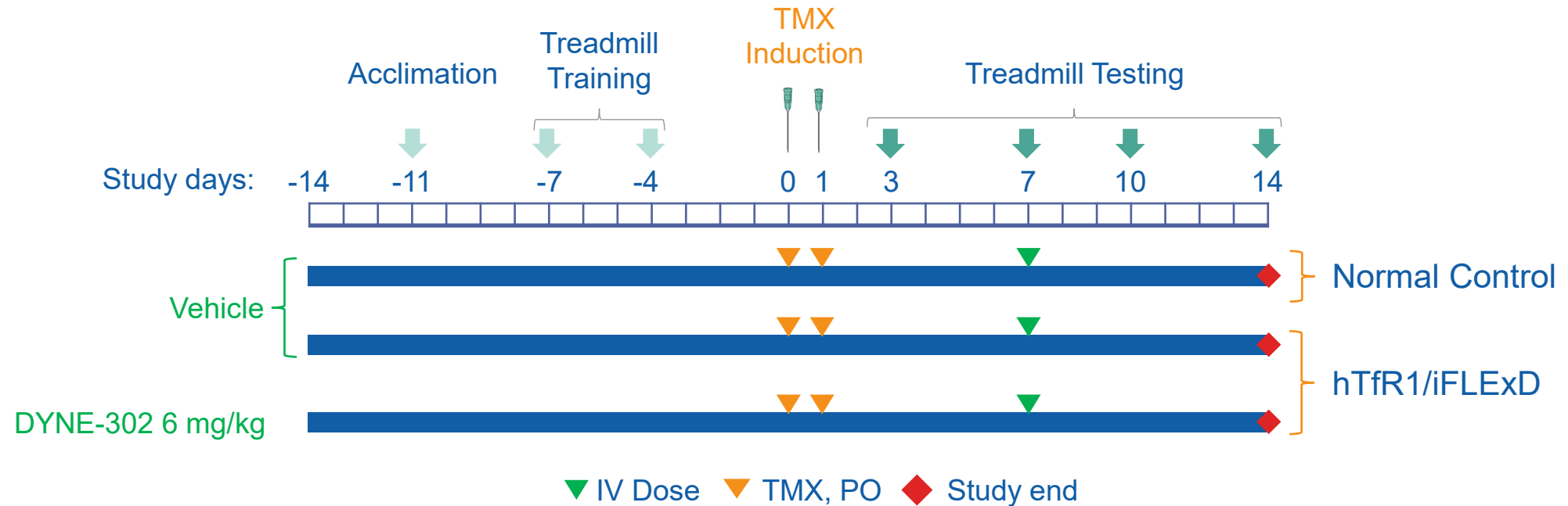
Human transcriptome
in skeletal muscle biopsies



Mouse ortholog transcriptome
in quadriceps



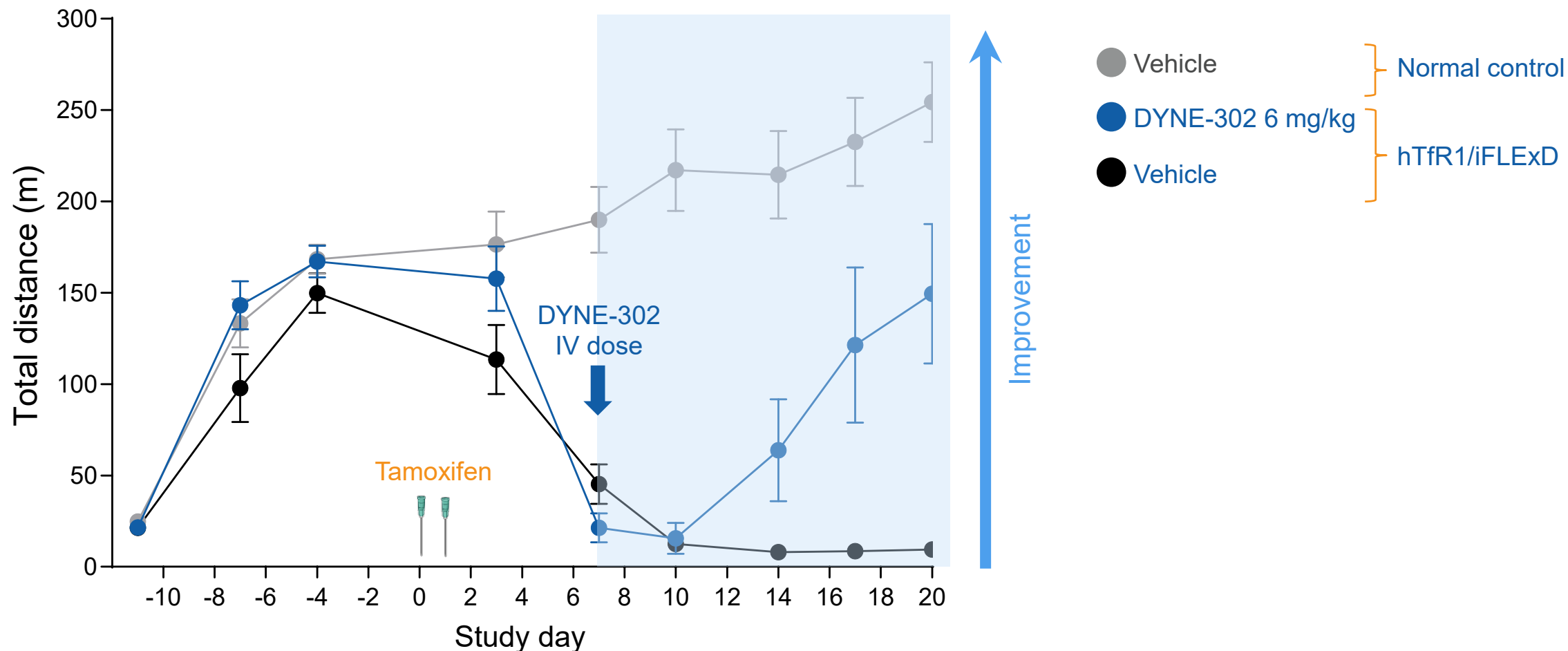
Study to Establish Impact of DYNE-302 Interventional Treatment in the Induced hTfR1/iFLExD Mice



DYNE-302 Interventional Treatment Leads to Functional Improvement in hTfR1/iFLExD Mice



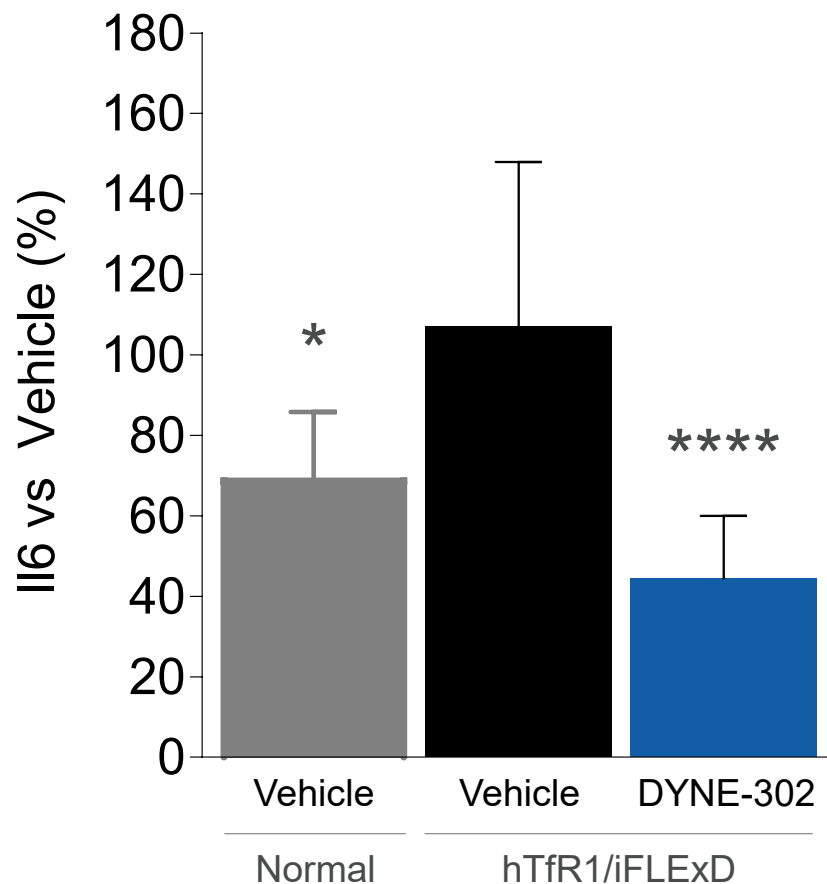
Functional improvement in forced treadmill run test



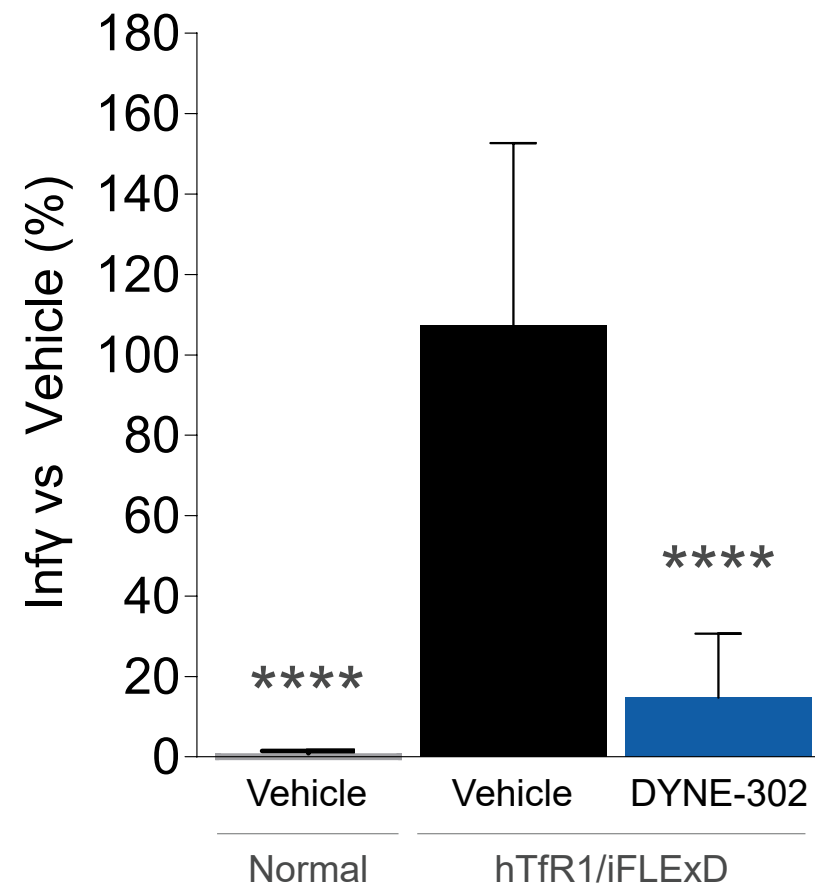
DYNE-302 Interventional Treatment Suppresses *Il6* and *Ifn γ* Expression in hTfR1/iFLExD Mice



Il6 suppression



Ifn γ suppression



Conclusions

- DYNE-302 achieves dose-dependent and durable D4T KD in a chronic mouse model of FSHD
- DYNE-302 normalizes inflammatory and muscle damage transcriptome in an FSHD mouse model
- DYNE-302 leads to functional improvement in an FSHD mouse model with pre-existing and severe disease

Data support the potential of DYNE-302 for the treatment of FSHD

Acknowledgements

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Dyne R&D

