



Repeat dosing with DYNE-101 is well tolerated and leads to a sustained reduction of DMPK RNA expression in key muscles for DM1 pathology in hTfR1/DMSXL mice and NHPs

Stefano Zanotti, Ph.D.

Forward-looking statements

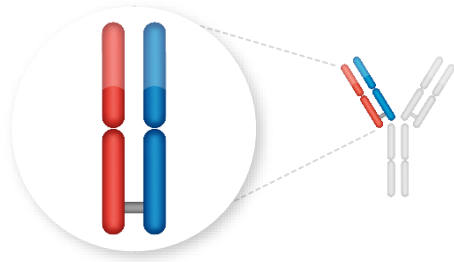
This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding Dyne's strategy, future operations, prospects and plans, objectives of management, the potential of the FORCE platform, the expected timeline for dosing patients in trials, the anticipated design of the trials, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," or "would," or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Dyne may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the identification and development of product candidates, including the conduct of research activities and the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies; uncertainties as to the timing of and Dyne's ability to submit and obtain regulatory clearance for investigational new drug applications and other regulatory filings and initiate clinical trials, including with respect to its response to the DYNE-251 clinical hold letter and its ability to obtain regulatory clearance of the DYNE-251 IND; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; whether investigators and regulatory agencies will agree with the design of Dyne's planned clinical trials; whether Dyne's cash resources will be sufficient to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; uncertainties associated with the impact of the COVID-19 pandemic on Dyne's business and operations; as well as the risks and uncertainties identified in Dyne's filings with the Securities and Exchange Commission (SEC), including the Company's most recent Form 10-Q and in subsequent filings Dyne may make with the SEC. In addition, the forward-looking statements included in this presentation represent Dyne's views as of the date of this presentation. Dyne anticipates that subsequent events and developments will cause its views to change. However, while Dyne may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Dyne's views as of any date subsequent to the date of this presentation.

This presentation also contains estimates, projections and other statistical data made by independent parties and by the Company relating to market size and growth and other data about the Company's industry and business. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. The Company has not independently verified the accuracy and completeness of the information obtained by third parties included in this presentation. In addition, projections, assumptions and estimates of the Company's future performance and the future performance of the markets in which the Company operates are necessarily subject to a high degree of uncertainty and risk.

Dyne FORCE™ platform: Modern oligo therapeutics for muscle diseases

ANTIBODY

Proprietary Fab targets TfR1 to enable muscle delivery

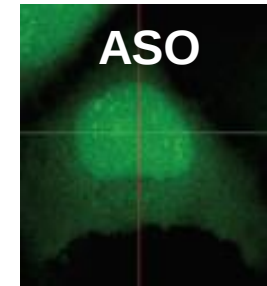


LINKER

Clinically validated, enables precise conjugation of multiple payloads to a single Fab

PAYLOAD

Modularity enables rational selection of payload to target the genetic basis of disease



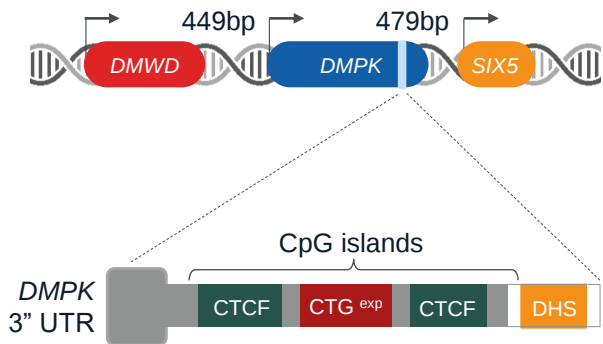
Nuclear
localization



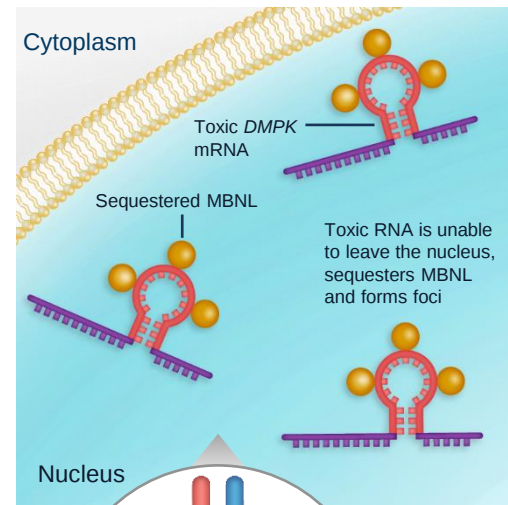
Cytoplasmic
localization

FORCE targets the genetic basis of DM1 to correct splicing

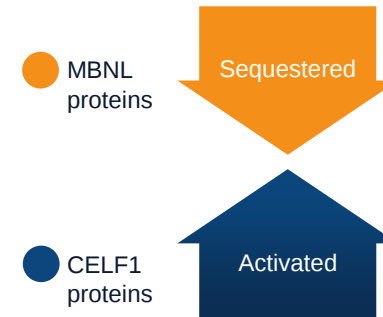
DNA Triplet Repeats



Toxic RNA Forms Foci



RNA Binds Splicing Proteins

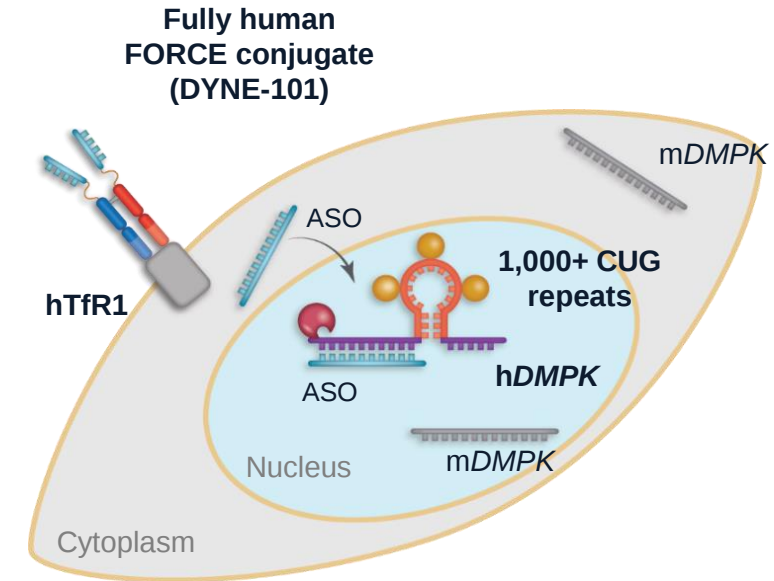
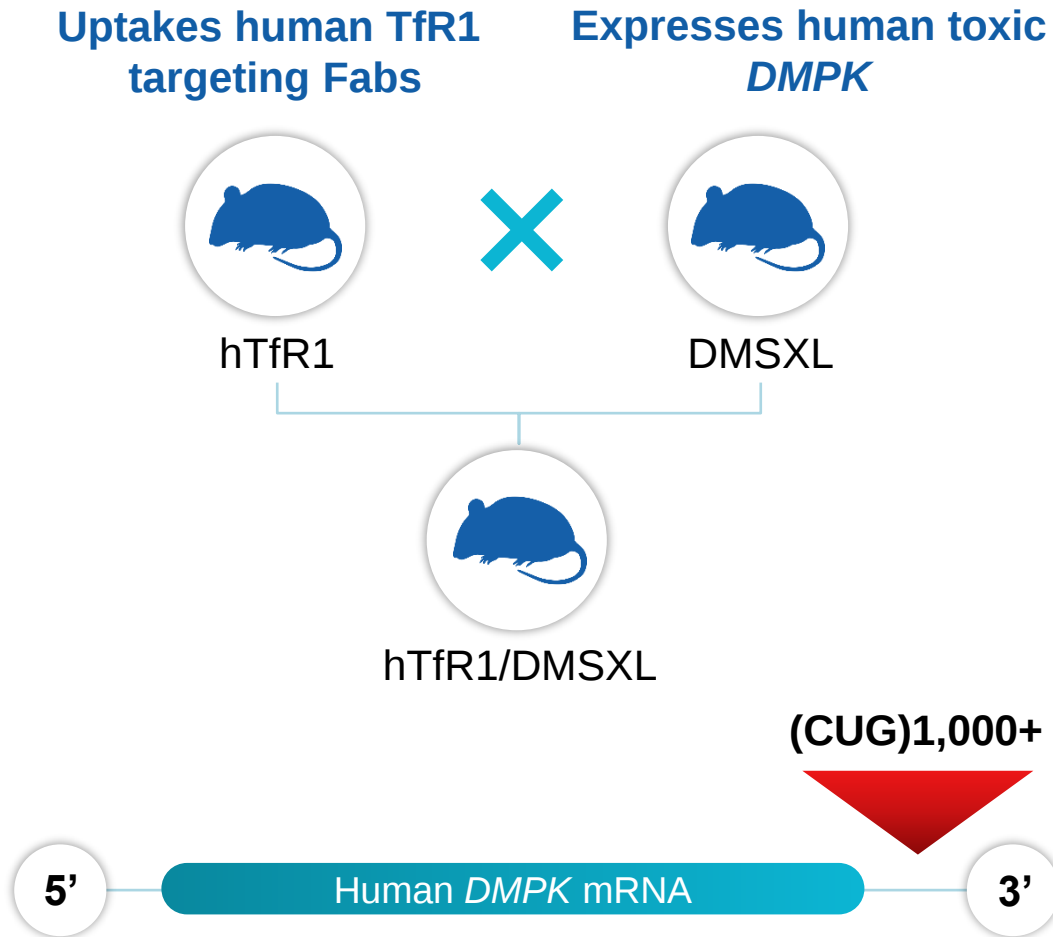


Clinical Presentation

- Myotonia
- Muscle weakness
- Cardiac arrhythmia
- Pulmonary abnormalities

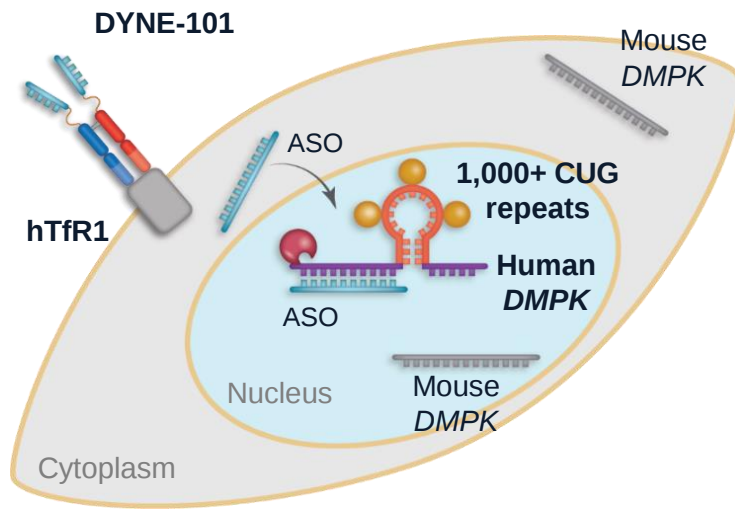
FORCE designed to address the genetic basis of disease by **targeting toxic nuclear DMPK RNA to correct spliceopathy**

hTfR1/DMSXL: Innovative model developed by Dyne to evaluate PD by measuring toxic human nuclear *DMPK* KD

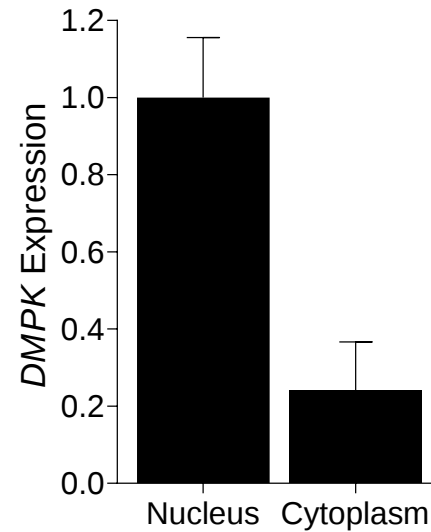


- Expresses human TfR1 receptor, enabling use of a human TfR1-targeting Fab
- Underestimates potency, expressing >10 times less human toxic *DMPK* vs. mouse *DMPK*

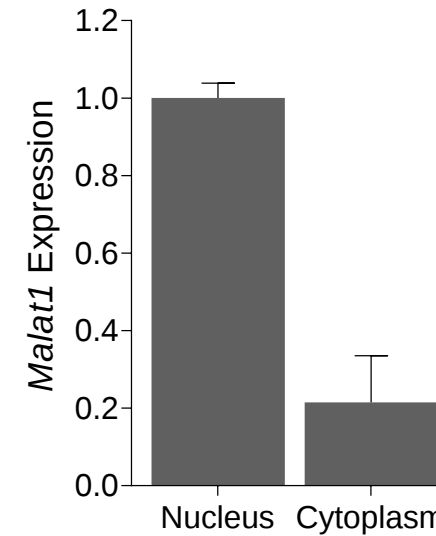
Toxic human *DMPK* is trapped in nuclei in hTfR1/DMSXL mice



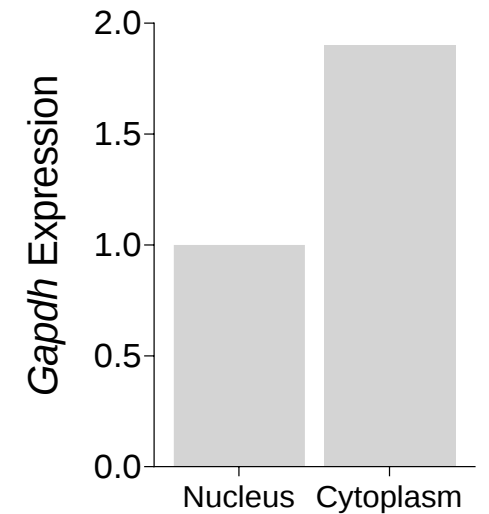
Human mutant *DMPK* enrichment in the nucleus



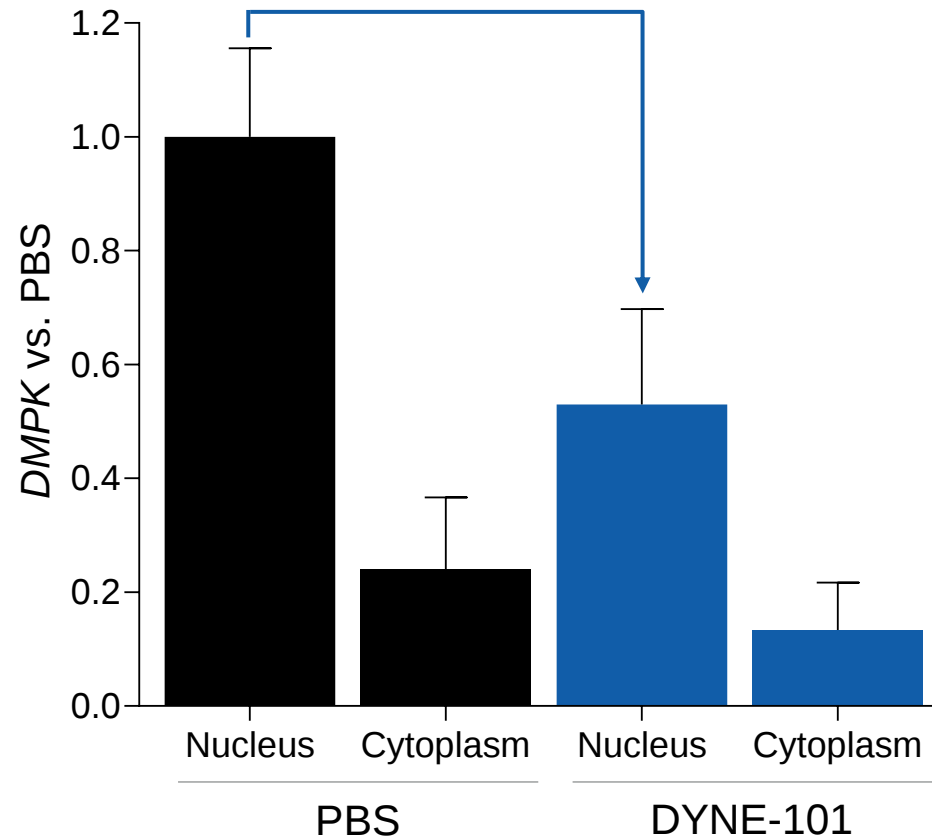
***Malat1* nuclear control**



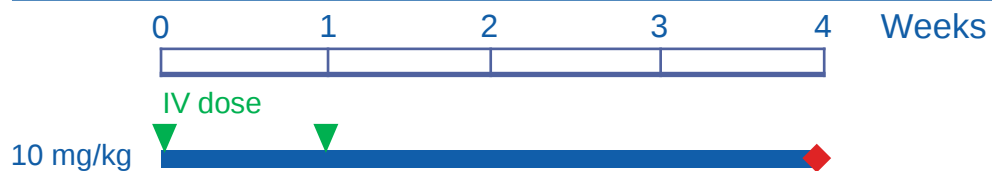
***Gapdh* cytoplasmic control**



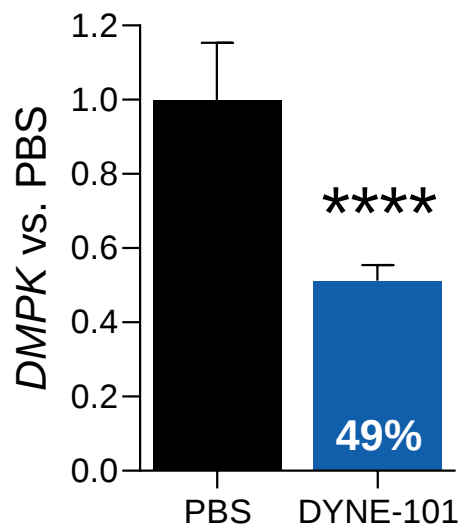
DYNE-101 achieved robust toxic human *DMPK* KD in nuclei of hTfR1/DMSXL mice



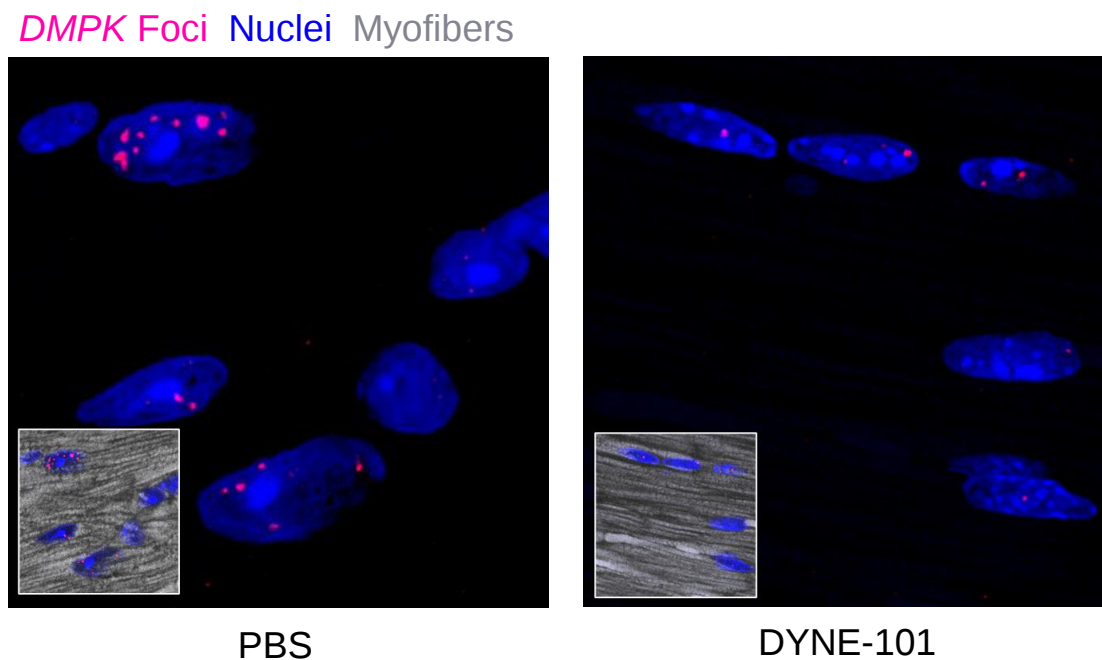
DYNE-101 demonstrated significant toxic human *DMPK* KD, foci reduction, and splicing correction in heart of hTfR1/DMSXL mice



Toxic human *DMPK* expression (%KD)

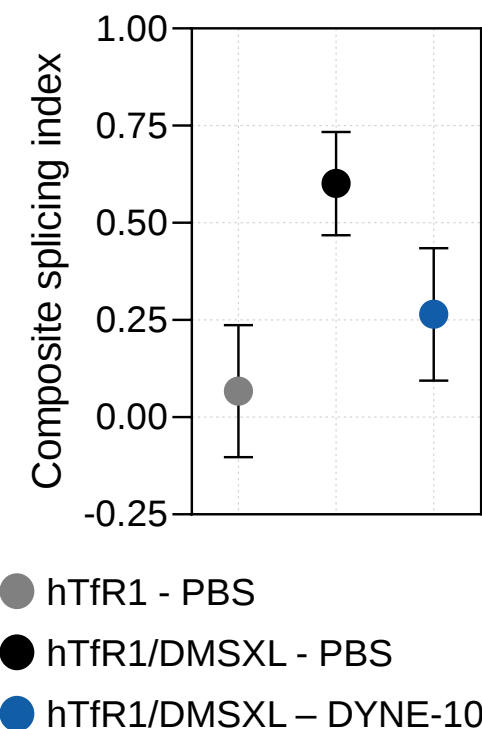


Toxic human *DMPK* foci reduction



DYNE-101 reduces foci area by 49%*

Splicing correction

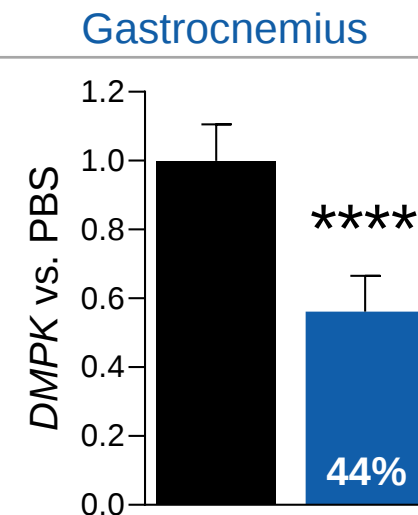
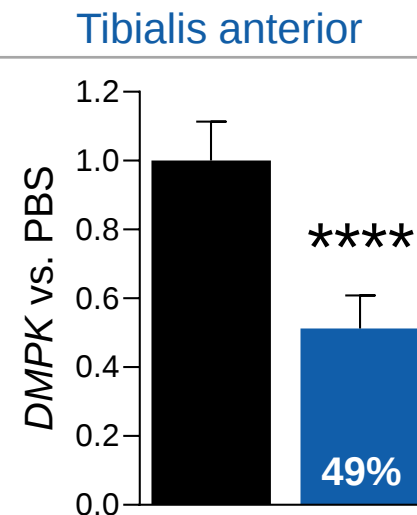
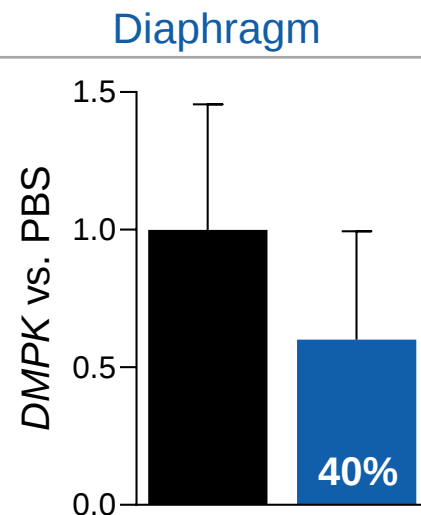


DYNE-101 demonstrated toxic human *DMPK* KD and splicing correction in skeletal muscle of hTfR1/DMSXL mice



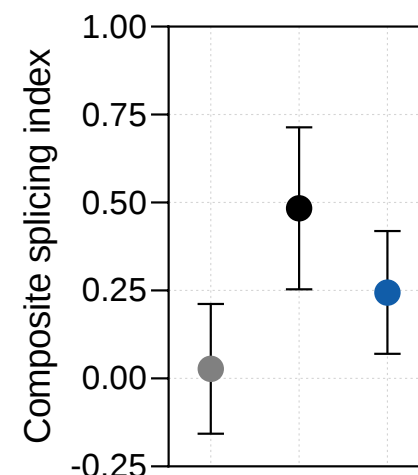
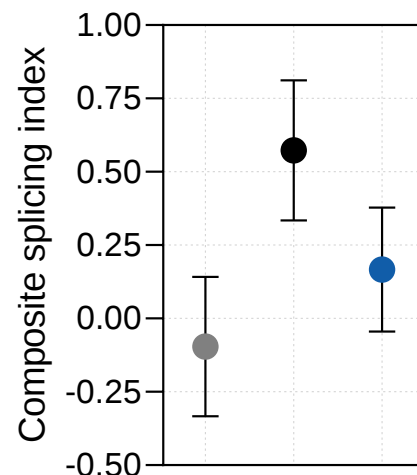
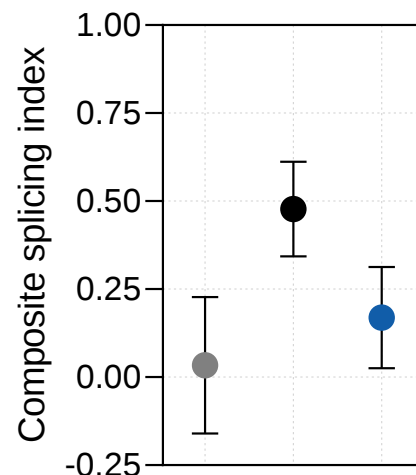
Toxic human *DMPK* expression (% KD)

- hTfR1/DMSXL - PBS
- hTfR1/DMSXL – DYNE-101

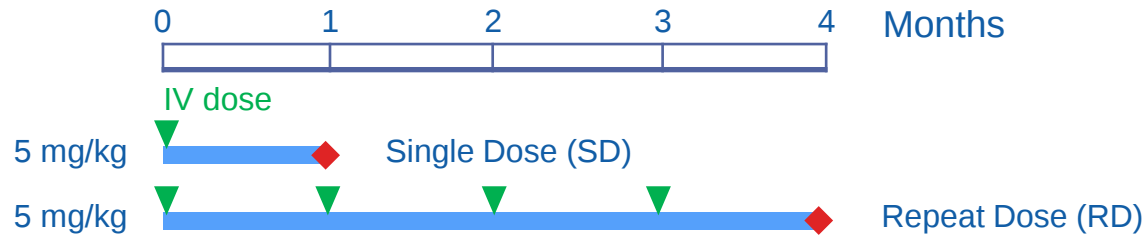


Splicing correction

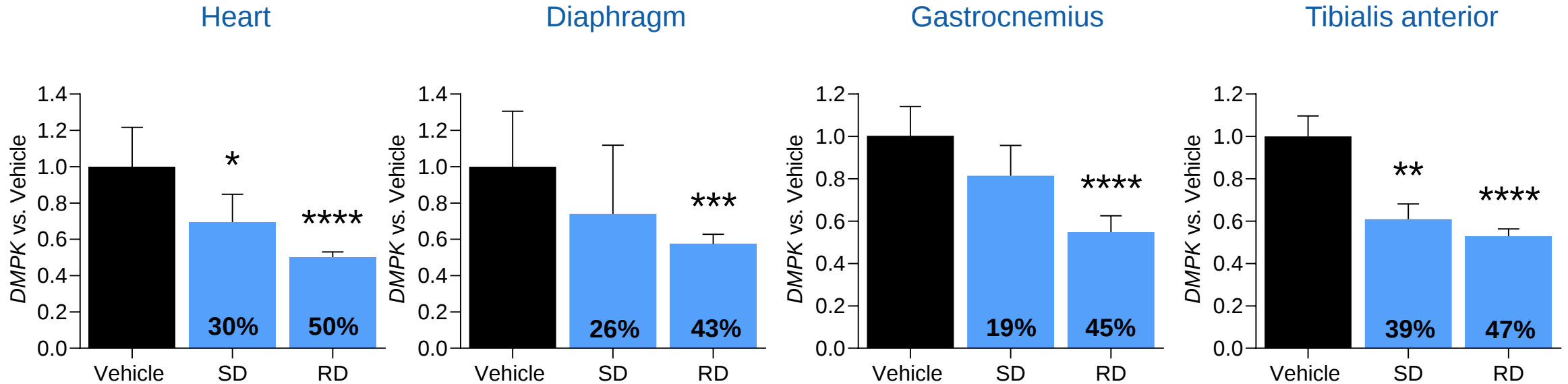
- hTfR1 - PBS
- hTfR1/DMSXL - PBS
- hTfR1/DMSXL – DYNE-101



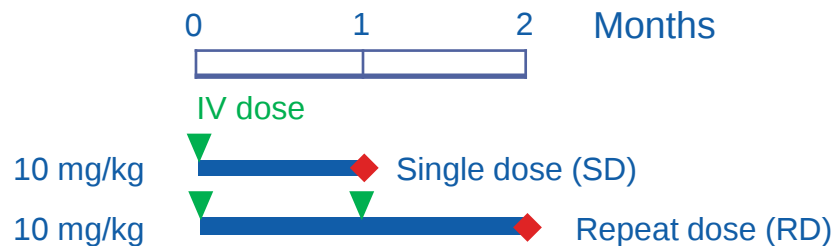
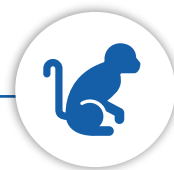
Low monthly dosing of DYNE-101 in hTfR1/DMSXL mice enhanced toxic human *DMPK* KD in cardiac and skeletal muscle



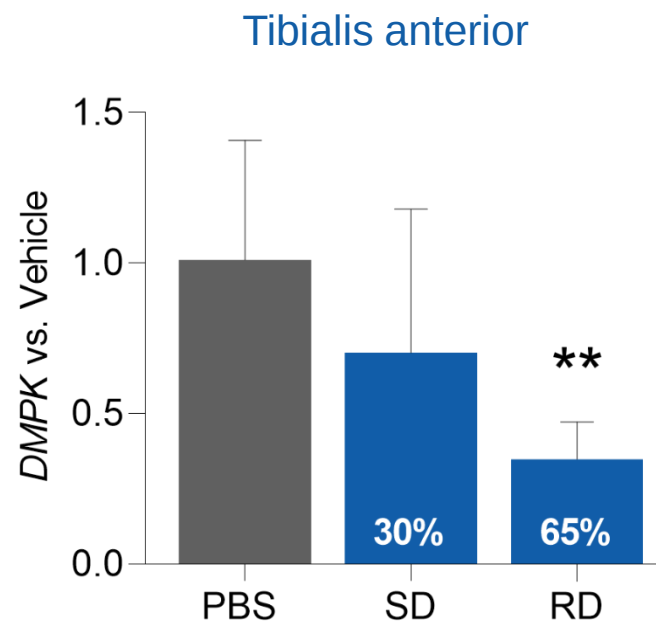
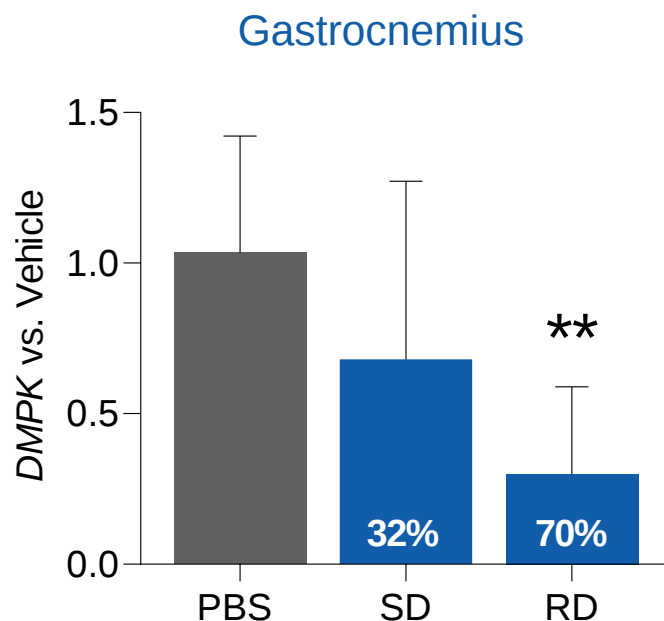
Toxic human *DMPK* expression (% KD)



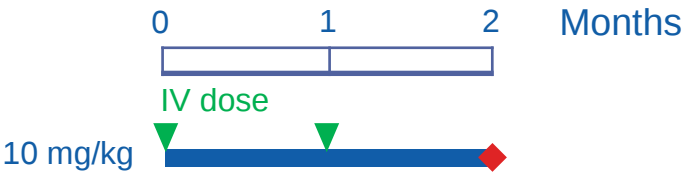
DYNE-101 repeat monthly dosing in NHPs enhanced *DMPK* KD in skeletal muscle



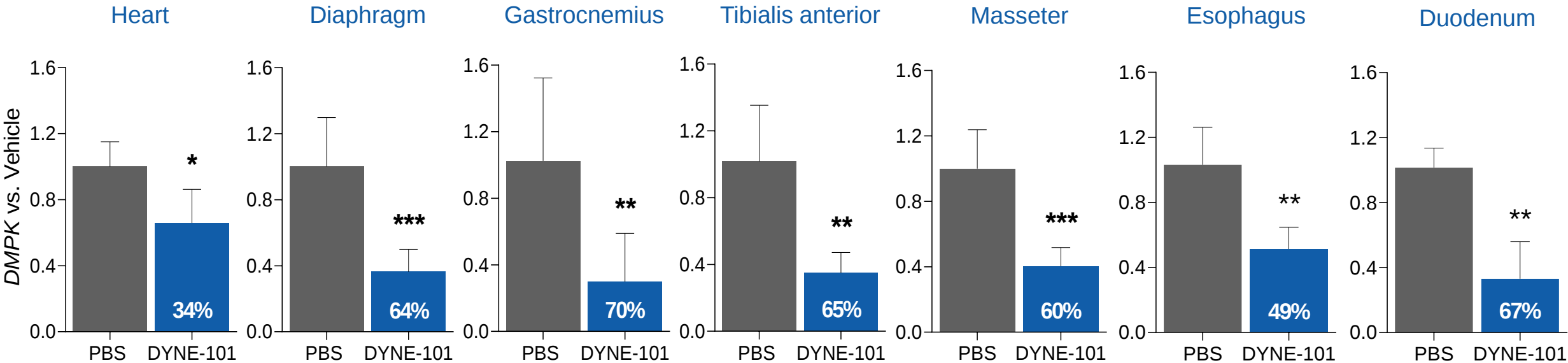
WT *DMPK* expression (% KD)



Repeat monthly dosing of DYNE-101 in NHPs achieved significant WT *DMPK* KD demonstrating translatability to higher species



WT *DMPK* expression (% KD)



DYNE-101 was well-tolerated in an NHP 13-week GLP toxicology study¹



- No dose limiting toxicity observed up to a maximally feasible dose²
- No changes in cardiac, respiratory, neurologic, or ophthalmic endpoints
- No effect on kidney function
- No effect on liver function
- No effect on coagulation
- NOAEL was identified at the highest dose tested

Conclusions

- DYNE-101 demonstrated ability to target toxic human *DMPK* RNA in the nucleus, reduce *DMPK* foci, and correct splicing in the hTfR1/DMSXL mouse model of DM1
- DYNE-101 monthly dosing in hTfR1/DMSXL mice and NHP achieved significant *DMPK* RNA KD in different muscle types affected by DM1 pathology
- Low monthly dosing achieves comparable *DMPK* KD to a higher dose administered weekly

Data support advancement of DYNE-101 into the clinic for the treatment of DM1

Acknowledgements

Dyne Research

- Tyler Picariello
- Jin Cui
- Ryan Russo
- Lydia Schlaefke
- Ann Chang
- John Harrell
- Qifeng Qiu
- Pei-Yi Shen
- Sean Spring
- Timothy Weeden
- John Davis
- Oxana Beskrovnaya

Dyne CMC

- Scott Hildebrand
- John Najim

Collaborators

- Genevieve Gourdon
*Institute de Myologie
Paris, France*