



# The FORCE™ Platform Achieves Robust Knock Down of Toxic Human Nuclear *DMPK* RNA and Foci Reduction in DM1 cells and in Newly Developed hTfR1/DMSXL Mouse Model

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Joachim, living with DM1

# Forward-Looking Statements

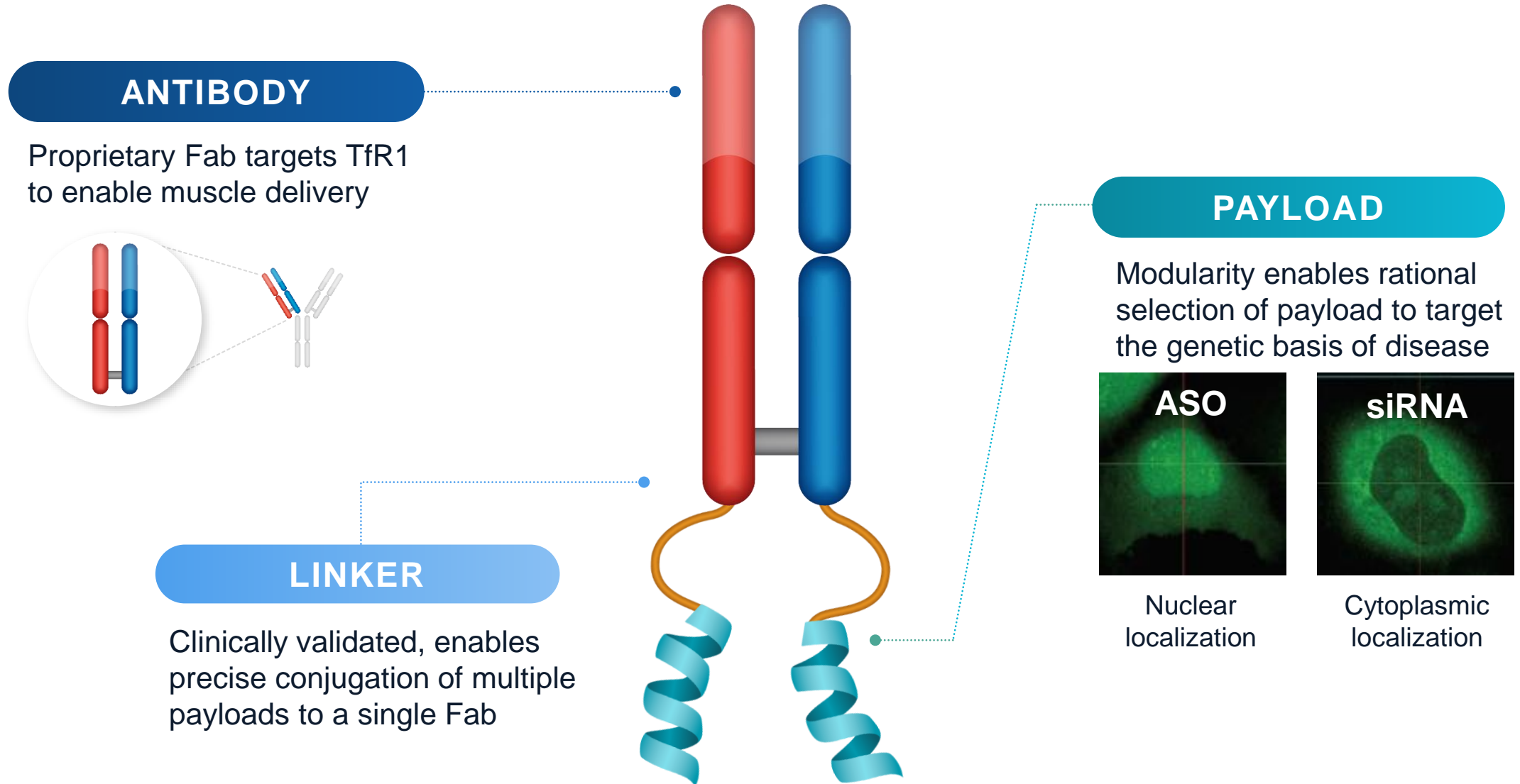
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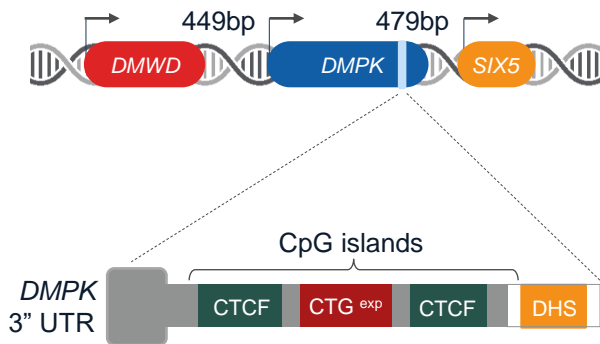


# Dyne FORCE Platform: Modern Oligo Therapeutics for Muscle Diseases

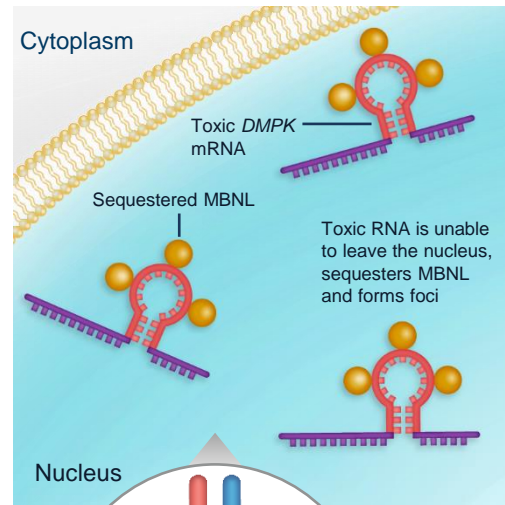


# FORCE Targets the Genetic Basis of DM1

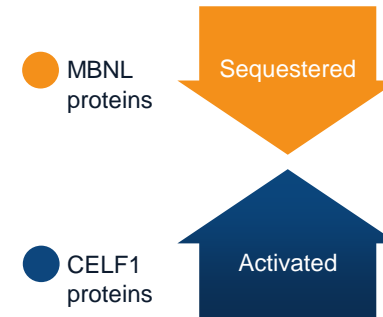
## DNA Triplet Repeats



## Toxic RNA Forms Foci



## RNA Binds Splicing Proteins

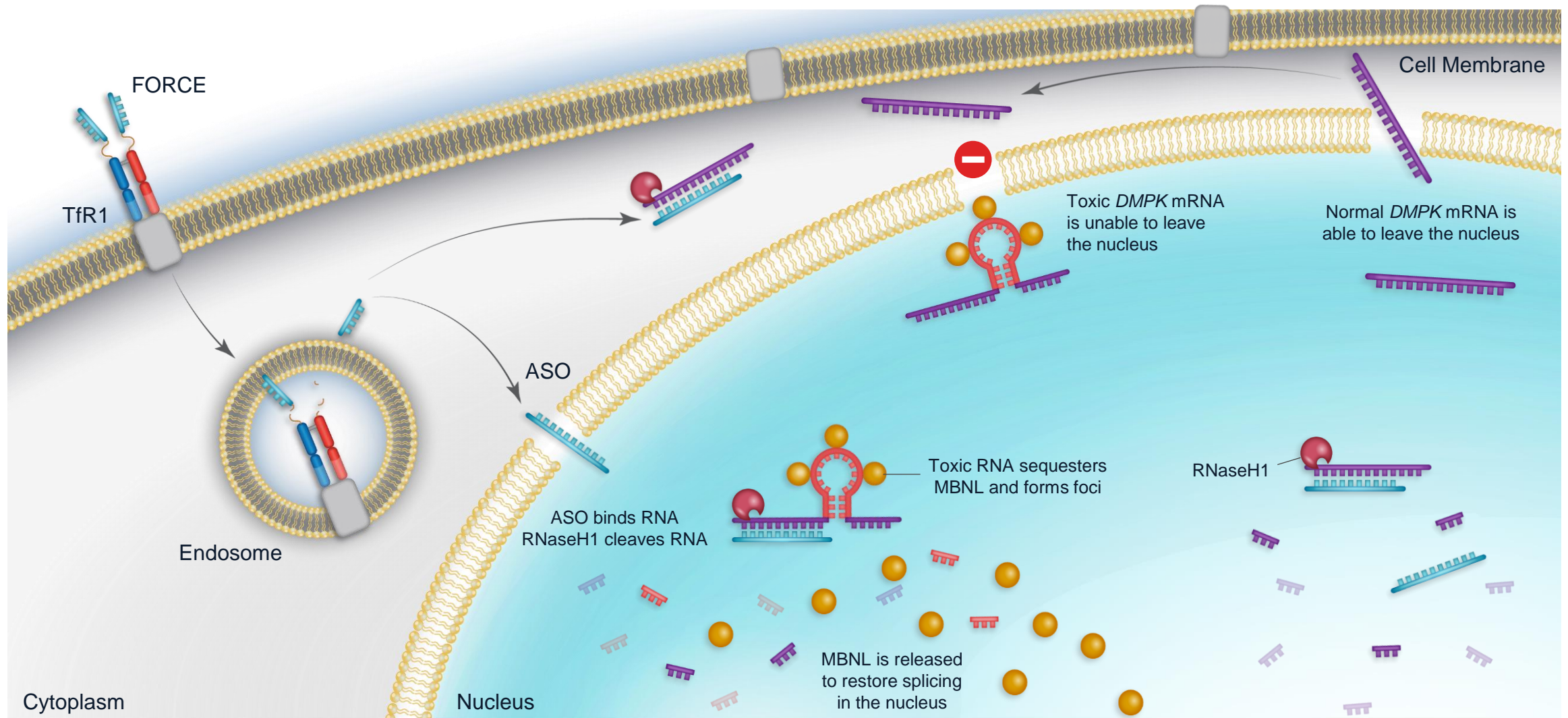


## Clinical Presentation

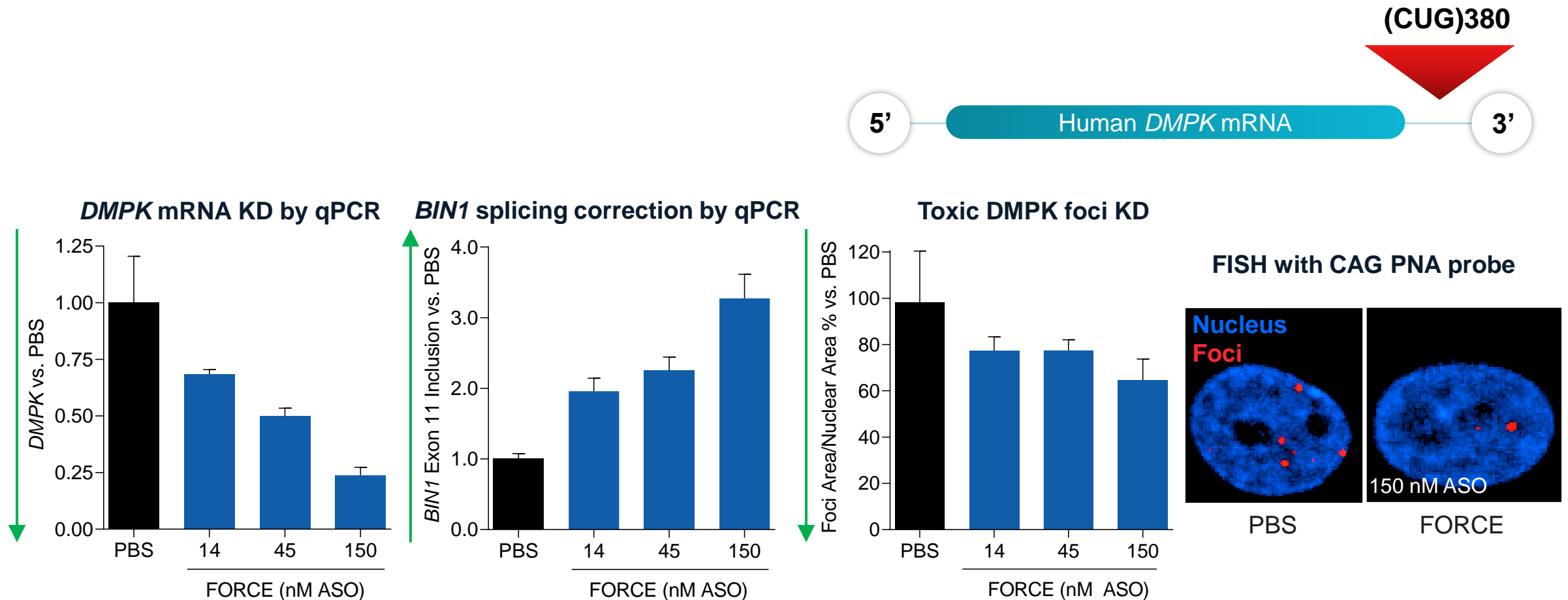
- Myotonia
- Muscle weakness
- Cardiac arrhythmia
- Pulmonary abnormalities

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

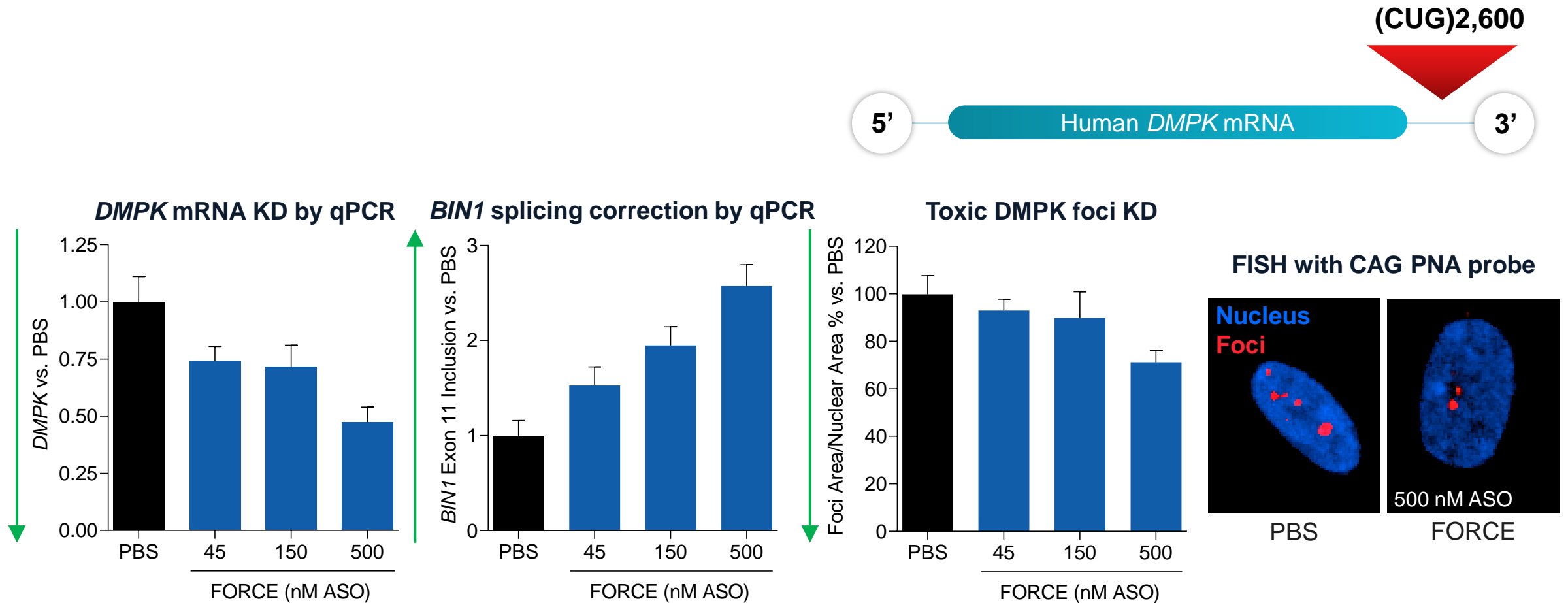
# FORCE Targets Toxic Nuclear *DMPK* RNA



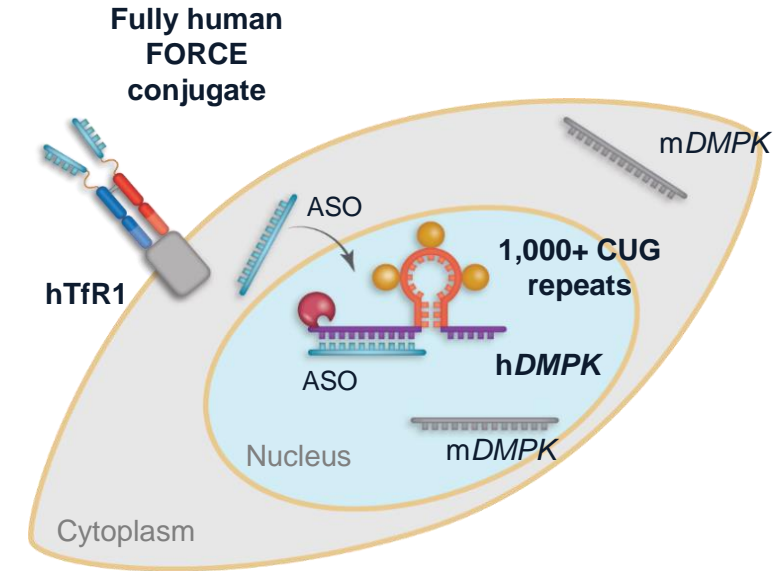
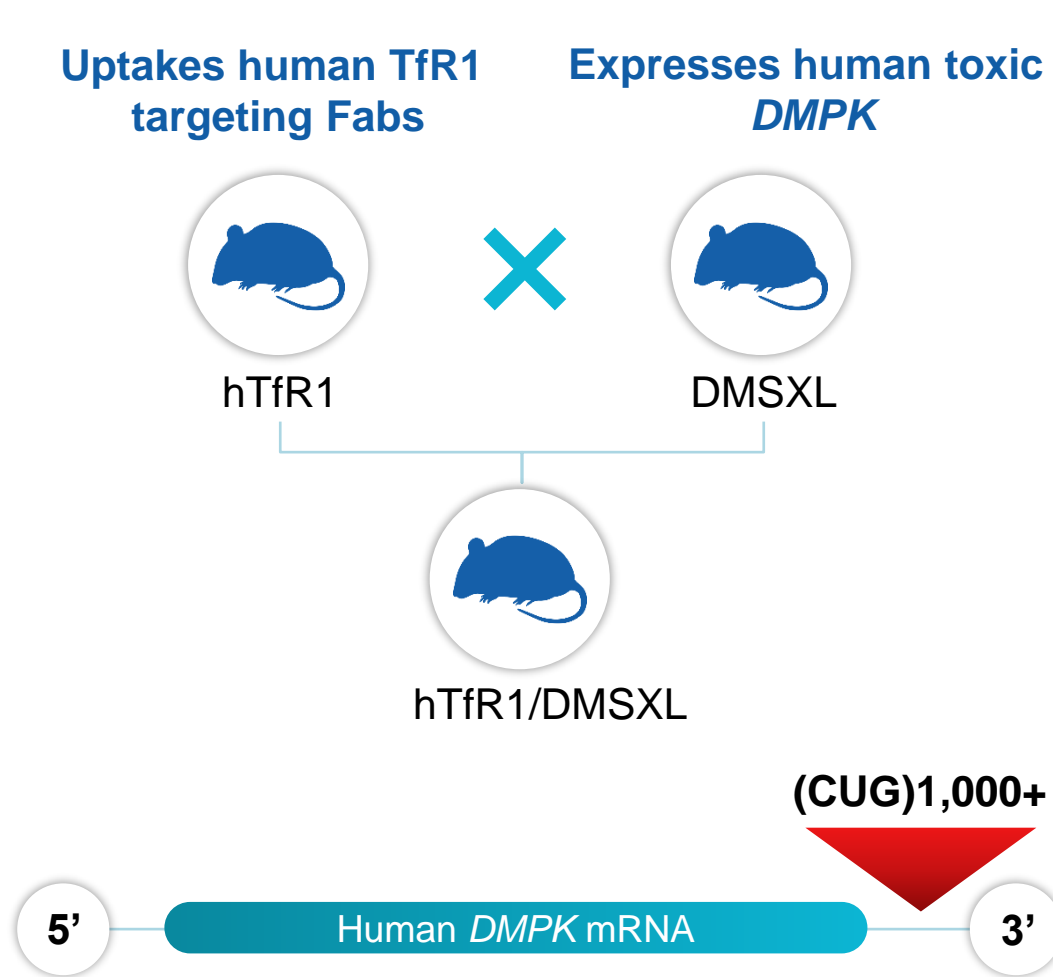
# FORCE Conjugate Demonstrated Dose-dependent *DMPK* KD, Splicing Correction, and Foci Reduction in DM1 Myotubes with 380 CTG Repeats



# FORCE Conjugate Demonstrated Dose-dependent *DMPK* KD, Splicing Correction, and Foci Reduction in DM1 Myotubes with 2,600 CTG Repeats



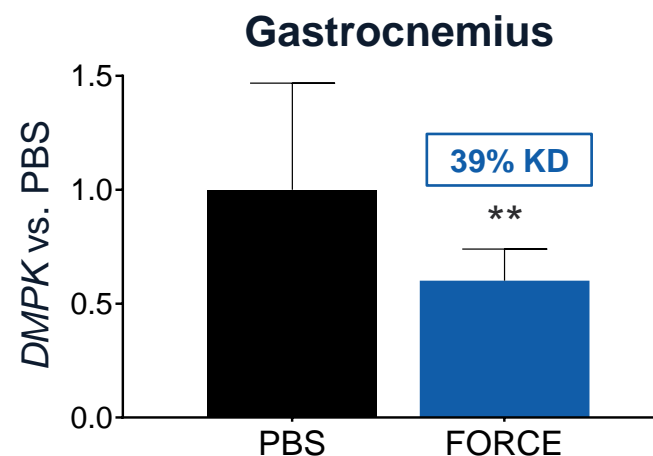
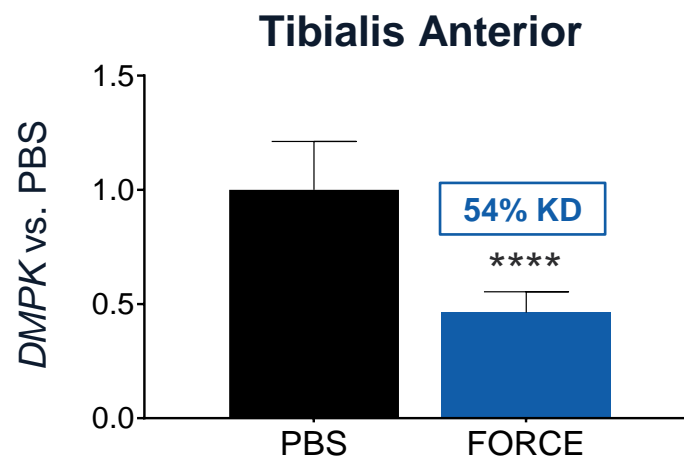
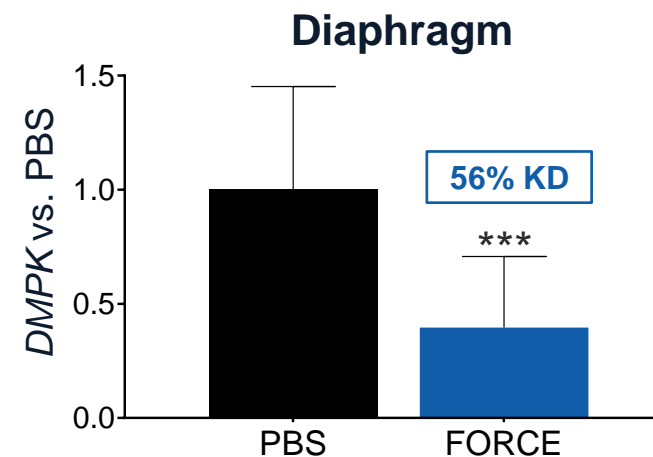
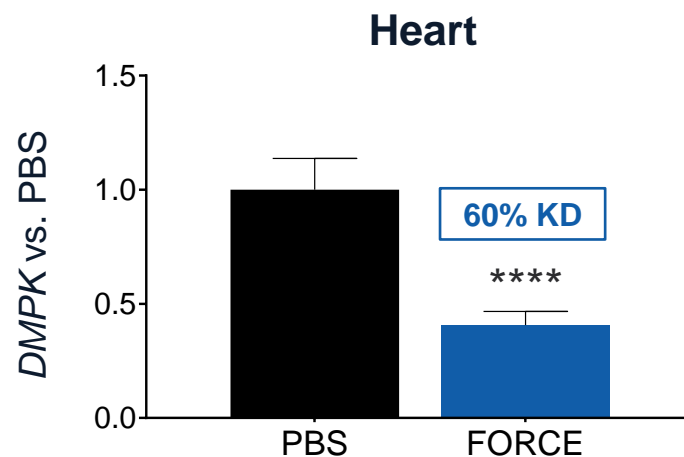
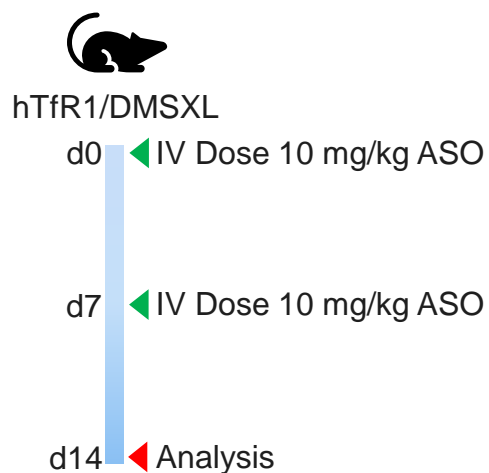
# hTfR1/DMSXL Mice: Innovative Model to Evaluate FORCE Conjugate Pharmacodynamics By Measuring Toxic Human Nuclear *DMPK* KD



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

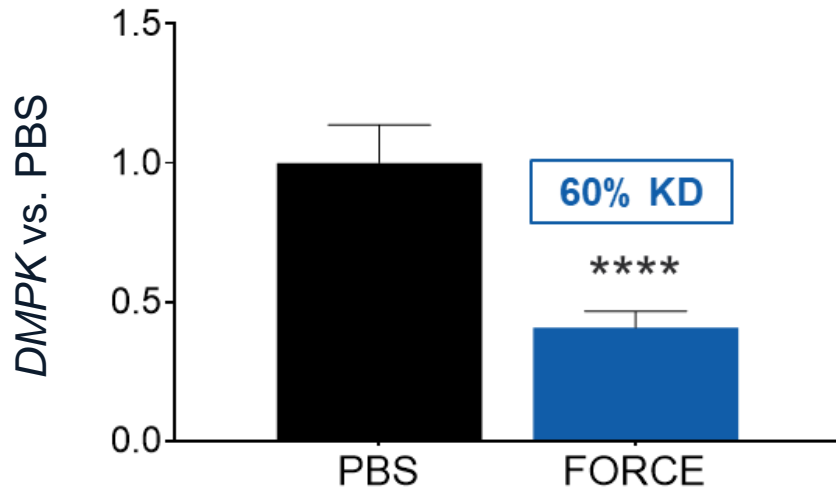


# FORCE Conjugate Demonstrated Robust Toxic Human *DMPK* KD in hTfR1/DMSXL Mice after 14 Days

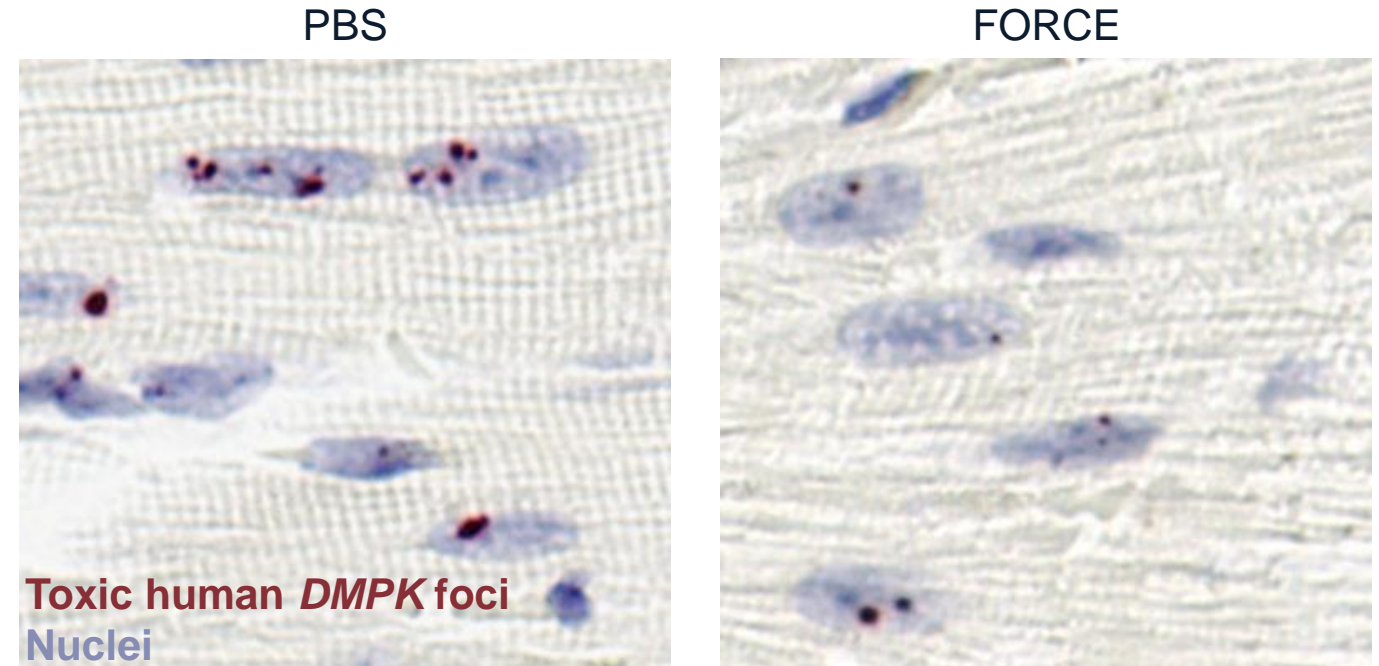


# FORCE Conjugate Demonstrated Robust Toxic Human *DMPK* mRNA and Foci KD in the Heart of hTfR1/DMSXL Mice

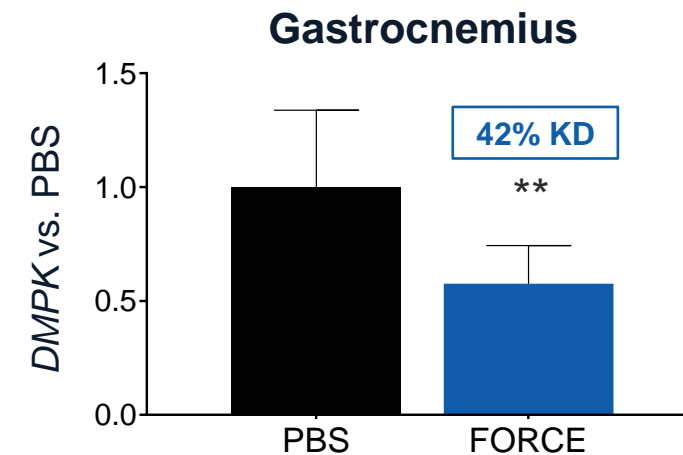
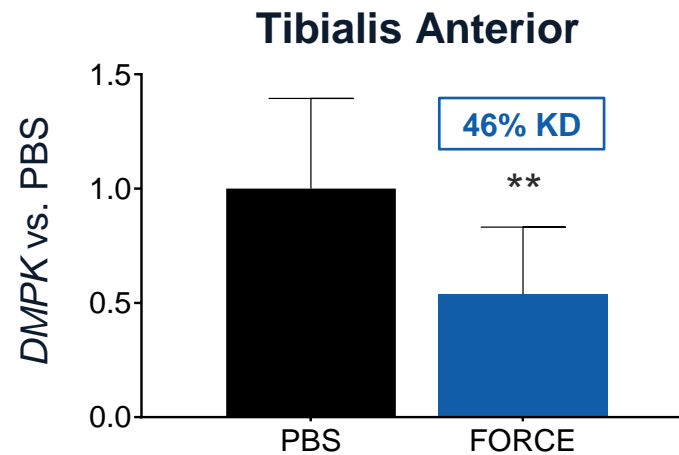
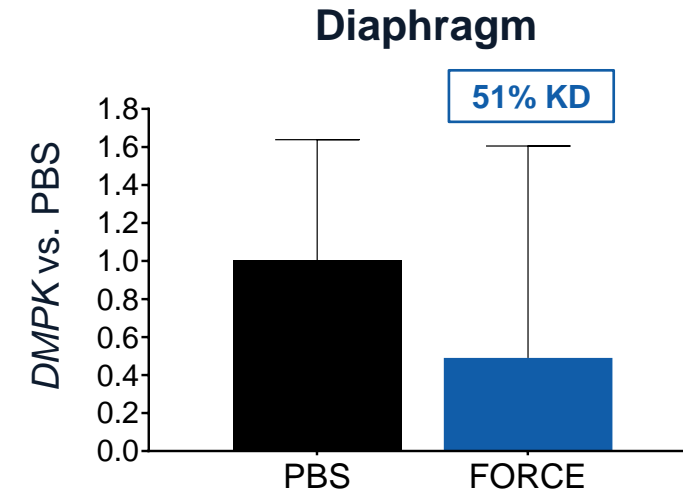
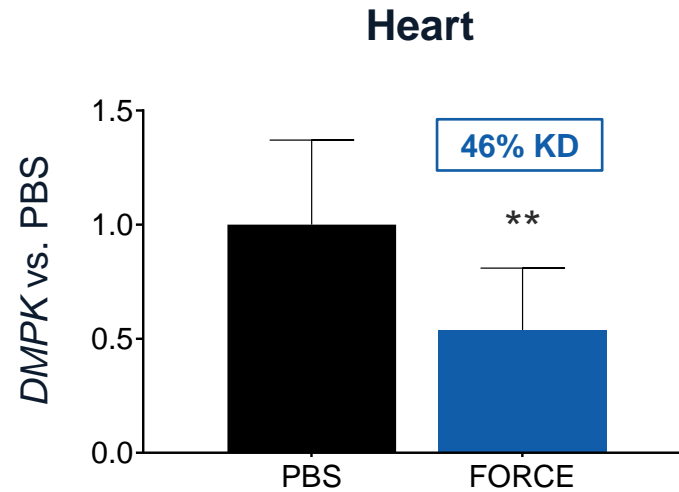
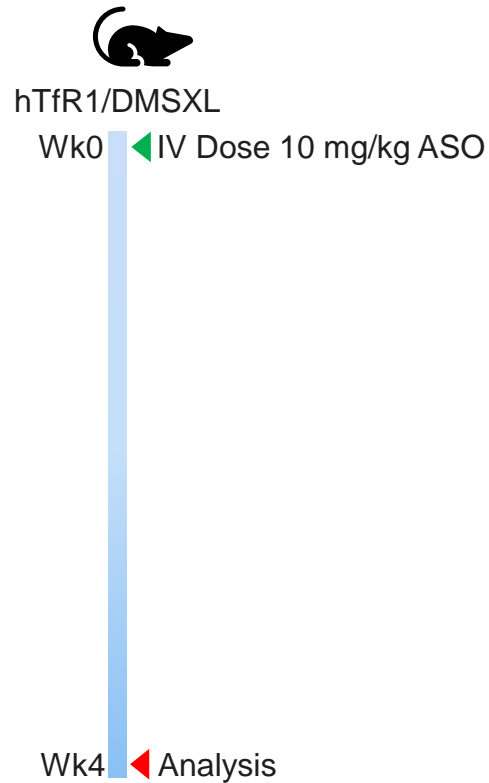
***DMPK* mRNA KD by qPCR**



***DMPK* foci reduction in the heart by *in situ* hybridization**



# Single Dose of FORCE Conjugate Achieved Sustained Toxic Human *DMPK* KD at Week 4 in hTfR1/DMSXL Mice



# Conclusions

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- FORCE is designed to address the genetic basis of DM1 by targeting toxic nuclear DMPK RNA
- These new data demonstrated that a fully human FORCE conjugate can:
  - Correct the DM1 phenotype of patient-derived myoblast cultures with a range of repeats, including those representative of severe DM1
  - Reduce toxic nuclear human *DMPK* foci in cardiac muscle of hTfR1/DMSXL mice
  - Lead to sustained KD of toxic nuclear human *DMPK* in hTfR1/DMSXL mice after a single dose
- These data strongly support further development of our DM1 therapeutic candidate, including a planned clinical study



# Acknowledgements

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- Oxana Beskrovnaya

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