

DYNE-401 demonstrates potential to deliver functional improvement in Pompe disease with low and infrequent dosing¹

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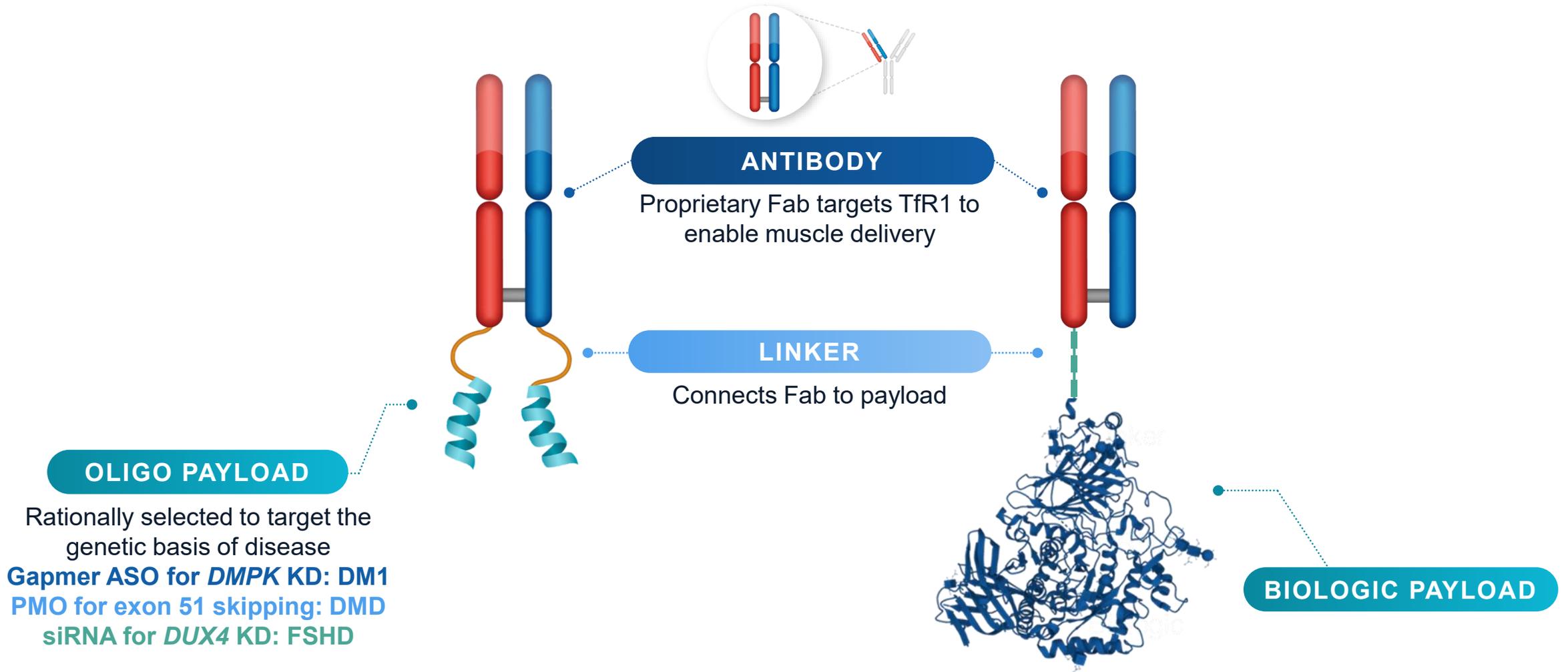
¹ Previously presented: Picariello, T. et al., (2026) *Molecular Genetics and Metabolism*, 147;(2).



Disclosures

I Tyler Picariello am an employee of Dyne Therapeutics, Inc.

Dyne FORCE platform modularity enables diversified pipeline to address DM1, DMD, FSHD, and Pompe disease



Notes: The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

Pompe disease is a rare and serious neuromuscular lysosomal storage disorder (LSD)

~4,500 patients in US

Low GAA activity leads to lysosomal glycogen accumulation

Infantile-onset (IOPD; 10% of population)

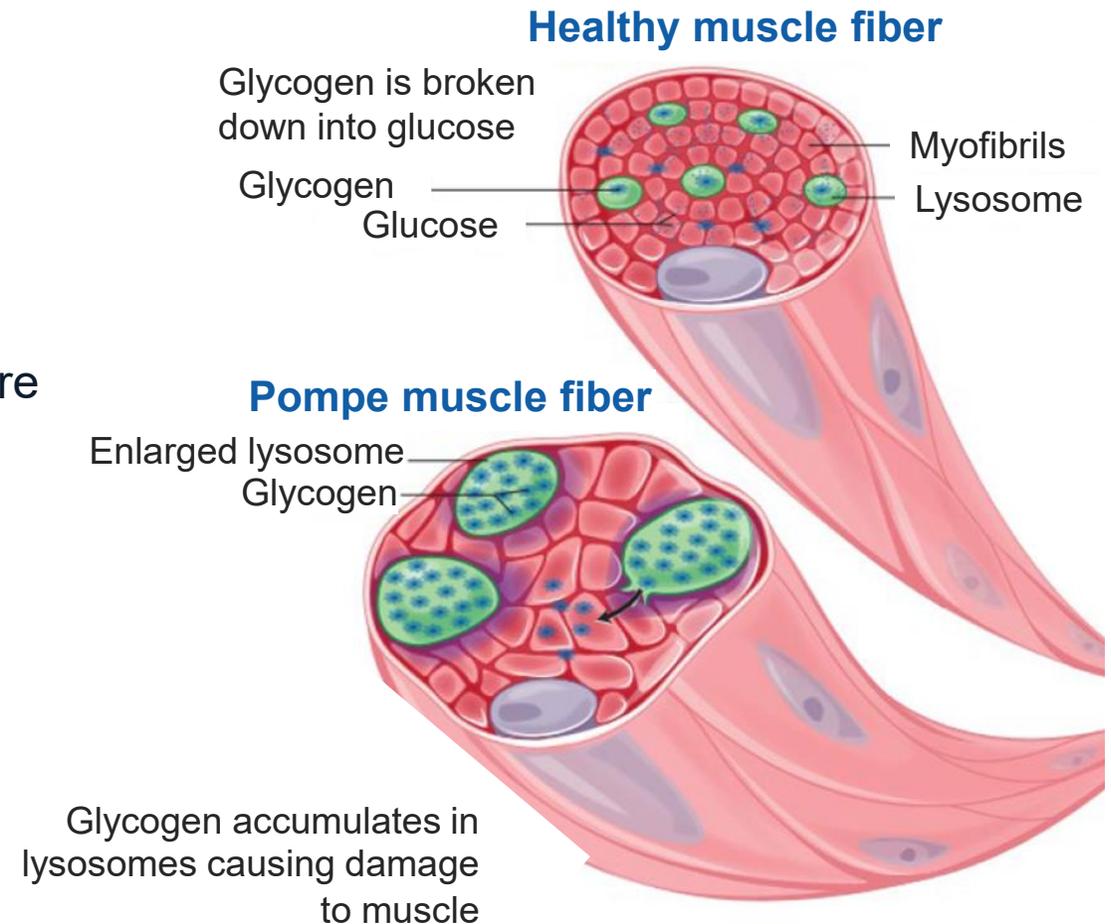
- Cardiomyopathy and cardiomegaly
- Progressive muscle weakness and respiratory failure
- CNS manifestations including decreased IQ

Late-onset (LOPD; 90% of population)

- Progressive muscle weakness with mobility issues
- Respiratory insufficiency

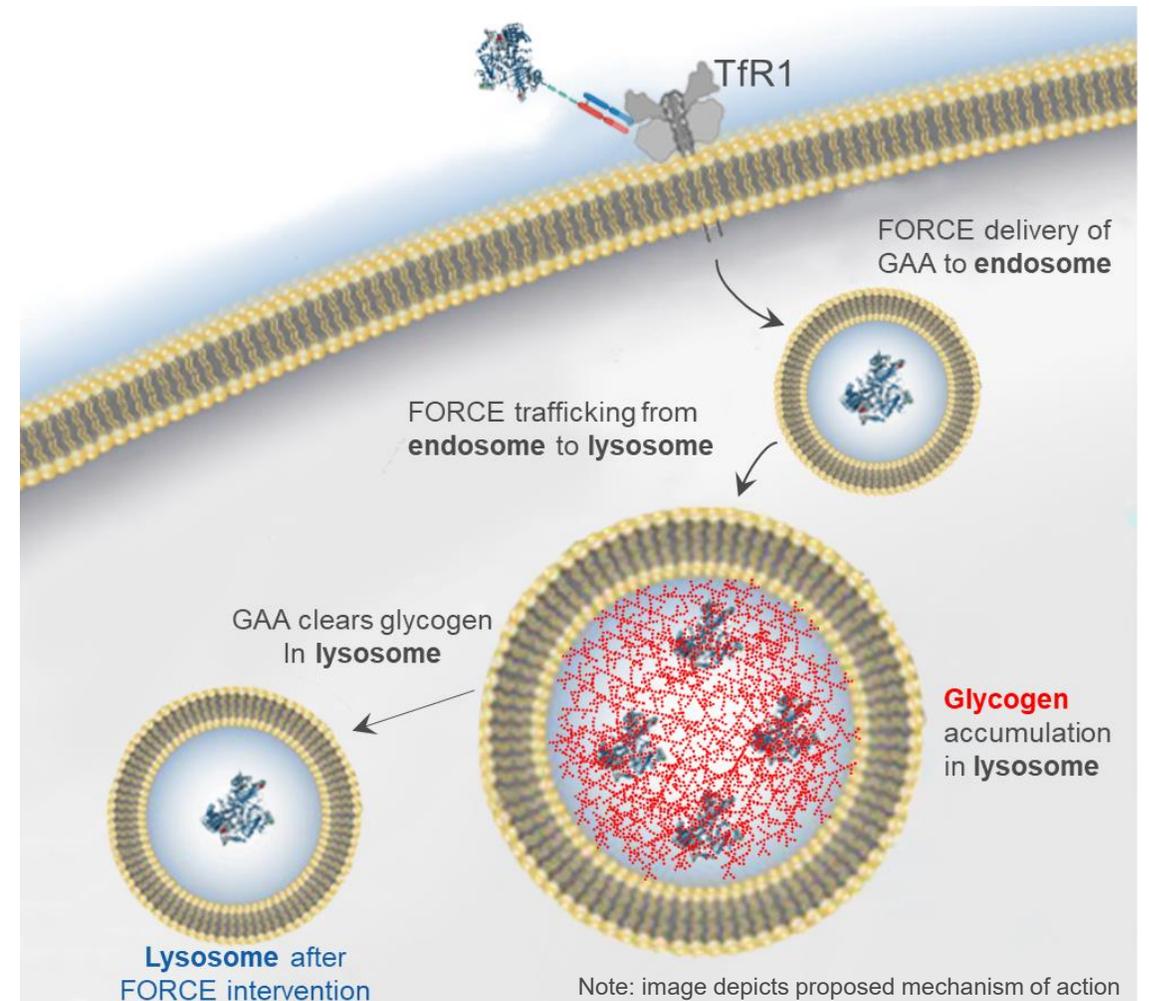
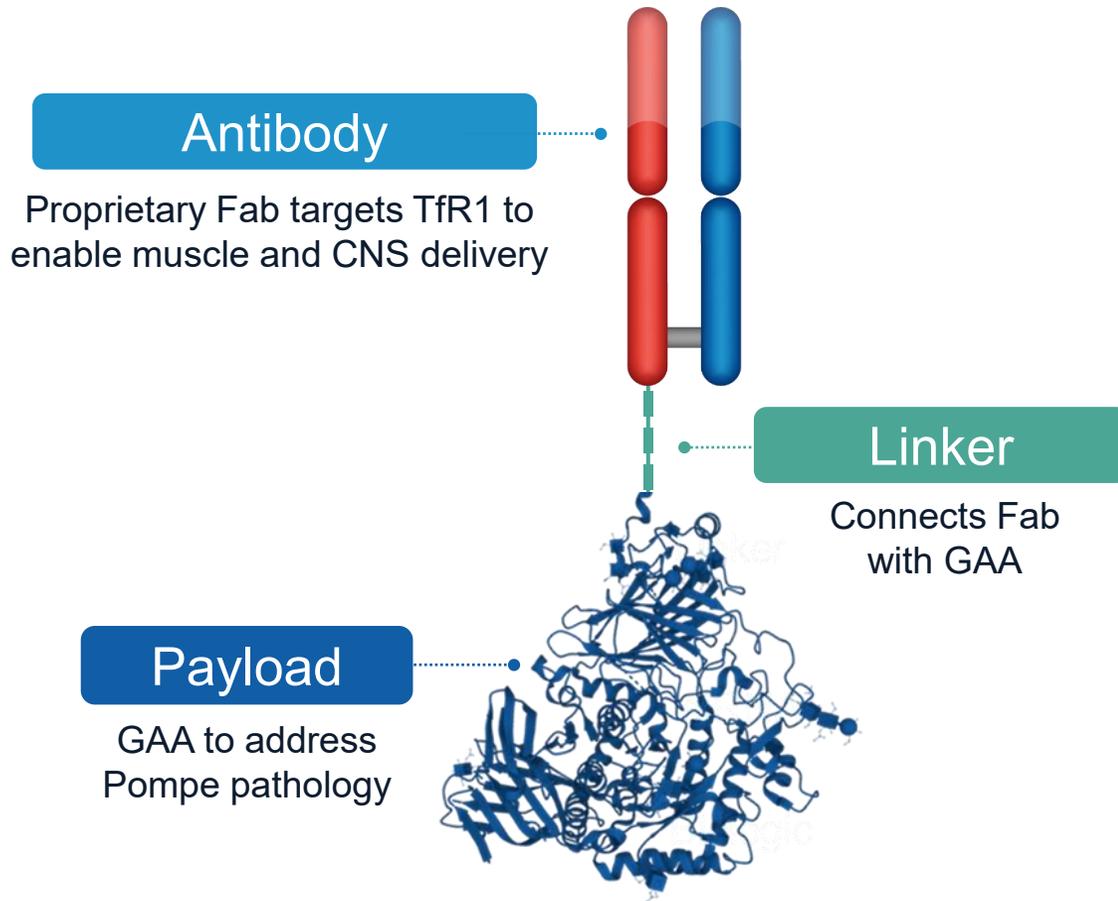
Therapeutic modalities:

- ERT with GAA
- SRT with *GYS1* siRNA
- Gene therapy

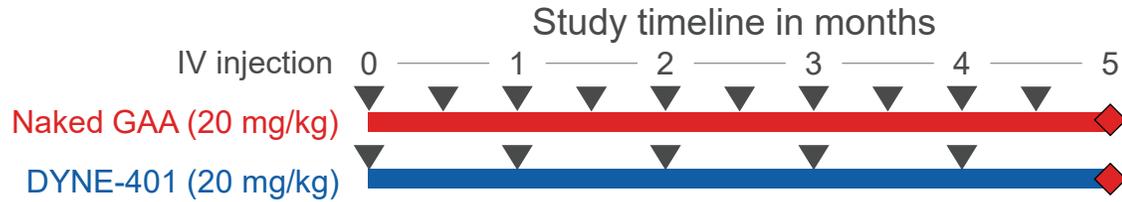


Leveraging FORCE to improve efficacy of ERT in Pompe disease

DYNE-401 enables TfR1-targeted ERT



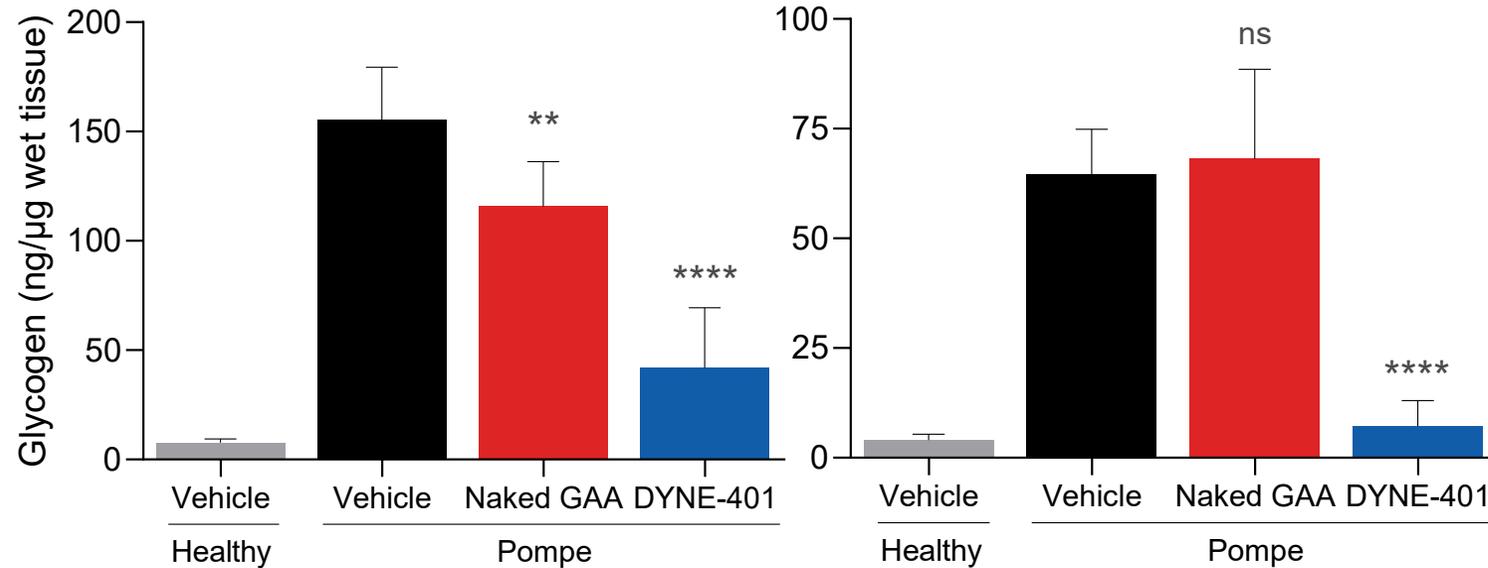
Monthly DYNE-401 is superior to naked GAA and sustains functional improvement in Pompe disease mice



Glycogen reduction

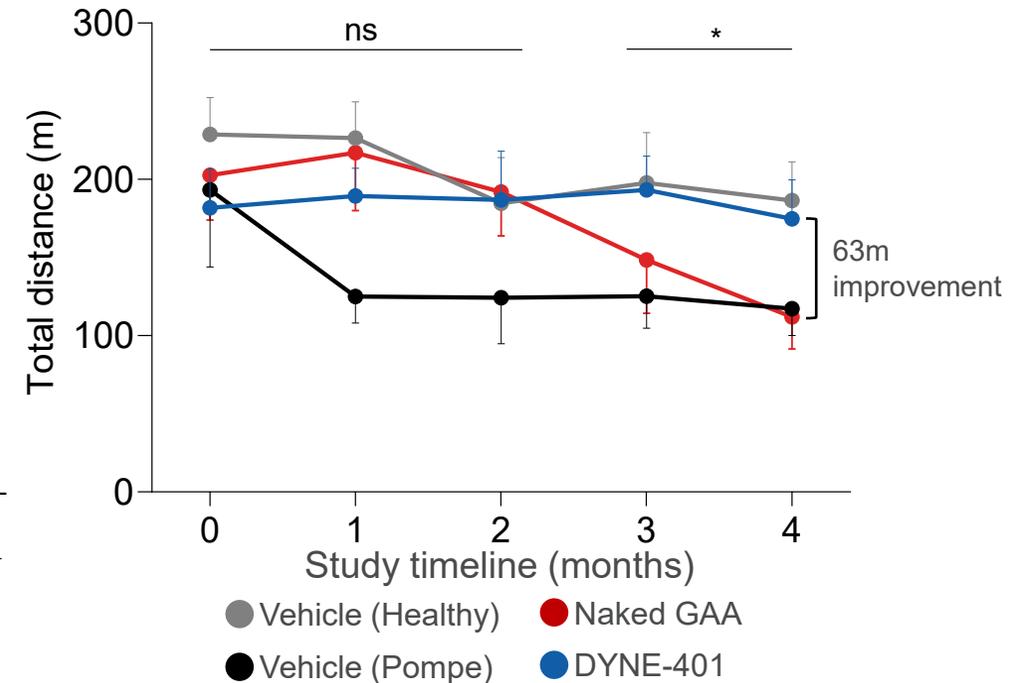
Tibialis anterior

Cerebral cortex



Functional improvement

Running distance

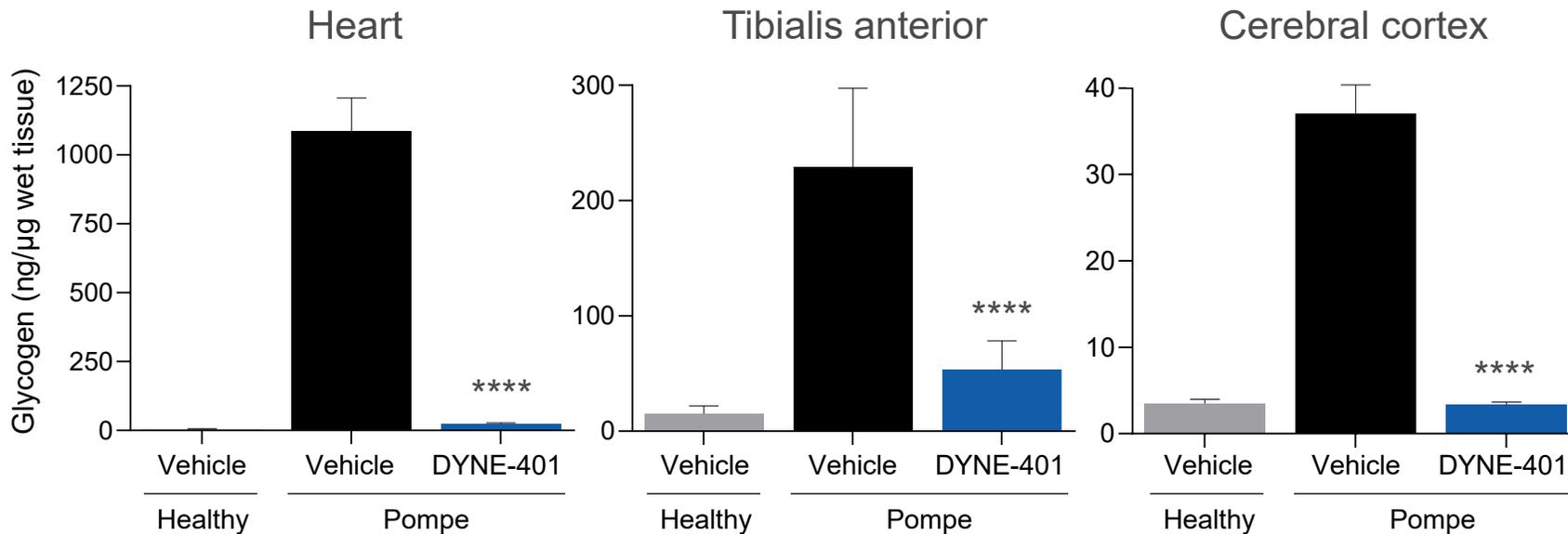


Notes: Mice were dosed with naked GAA every other week or DYNE-401 every month for the duration of the study. Mice were necropsied five months after study start. Doses are mg/kg GAA-equivalents. Healthy mice are $hTfR1^{hu/mu};Gaa^{WT/Neo}$; Pompe mice are $hTfR1^{hu/mu};Gaa^{Neo/Neo}$ mice. N=7-9 mice per group; data are mean \pm SD; Data analyzed by one-way ANOVA followed by Turkey's test; ** = $p \leq 0.01$; **** $p \leq 0.0001$. The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

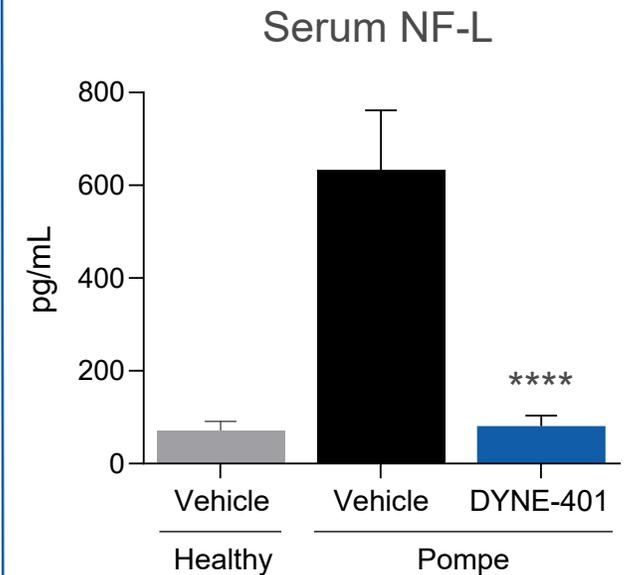
DYNE-401 demonstrates potential for every other month dosing



DYNE-401 clears glycogen in muscle and CNS

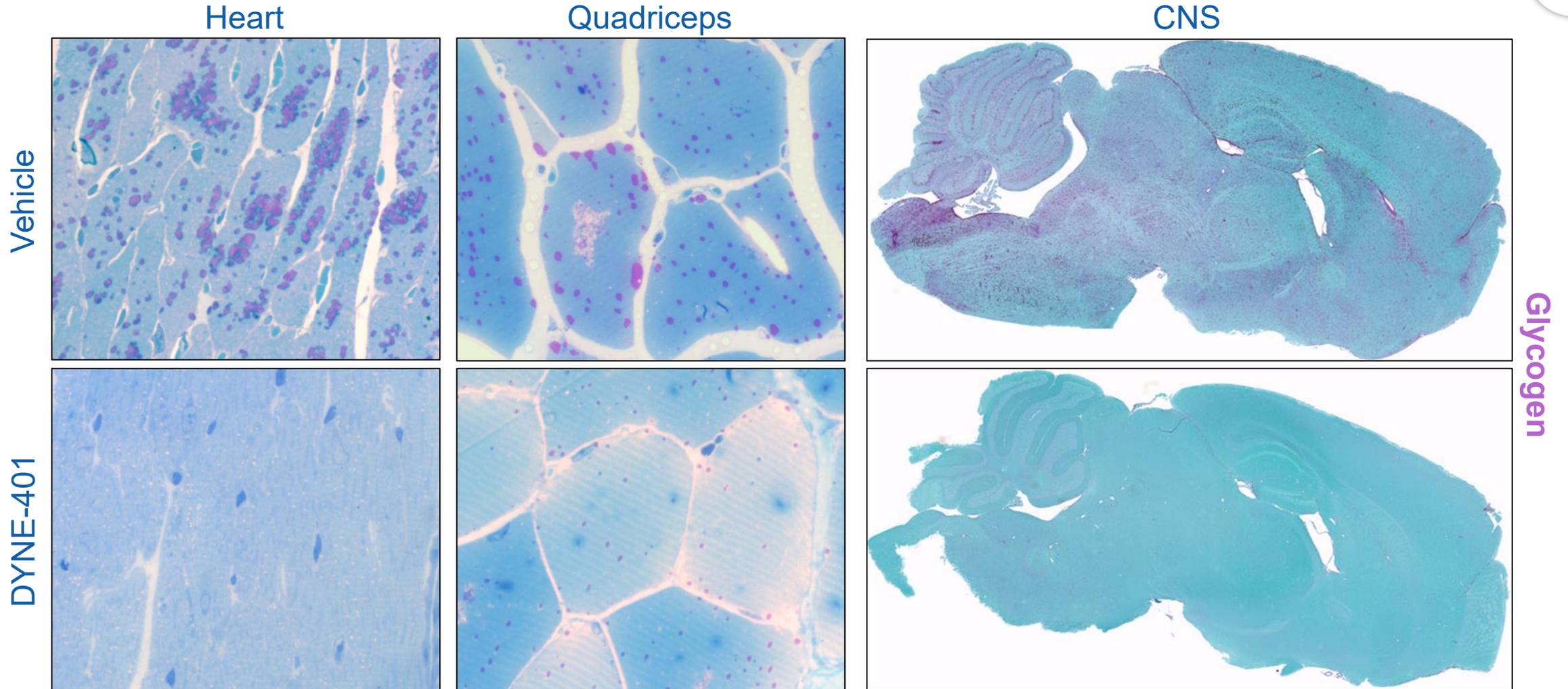


DYNE-401 reduces serum NF-L, a biomarker of axon damage



Notes: Mice we dosed with DYNE-401 at study start and at month two. Mice were necropsied four months after study start. Doses are mg/kg GAA-equivalents. Healthy mice are hTfR1^{hu/mu};Gaa^{WT/Neo}; Pompe mice are hTfR1^{hu/mu};Gaa^{Neo/Neo} mice. N=4-5 mice per group; data are mean ± SD; statistical significance determined by One-way ANOVA with Turkey's multiple comparisons test; *=*p*<0.05; **=*p*<0.01; ****=*p*<0.0001; The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

DYNE-401 achieves uniform glycogen clearance in muscle and CNS with every other month dosing



Notes: : Mice we dosed with DYNE-401 at study start and at month two. Necropsy occurred at month four. Muscle sections were processed in Epon-Araldite resin. Brains were formalin fixed and paraffin embedded. The FORCE platform and DYNE-401 are investigational or otherwise in development and have not been approved as safe or effective by the US FDA, EMA, or any regulatory authority.

Conclusions

- DYNE-401 demonstrates superior efficacy in muscle compared to naked GAA in a well-established mouse model of Pompe disease
- DYNE-401 addresses CNS pathology in Pompe mice
- DYNE-401 has the potential to deliver functional improvement in Pompe disease with infrequent dosing
- FORCE is a modular drug delivery platform that enables muscle and CNS distribution of biologics as well as oligonucleotide payloads

Acknowledgements

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