EPI-321: A Potential Cure for FSHD

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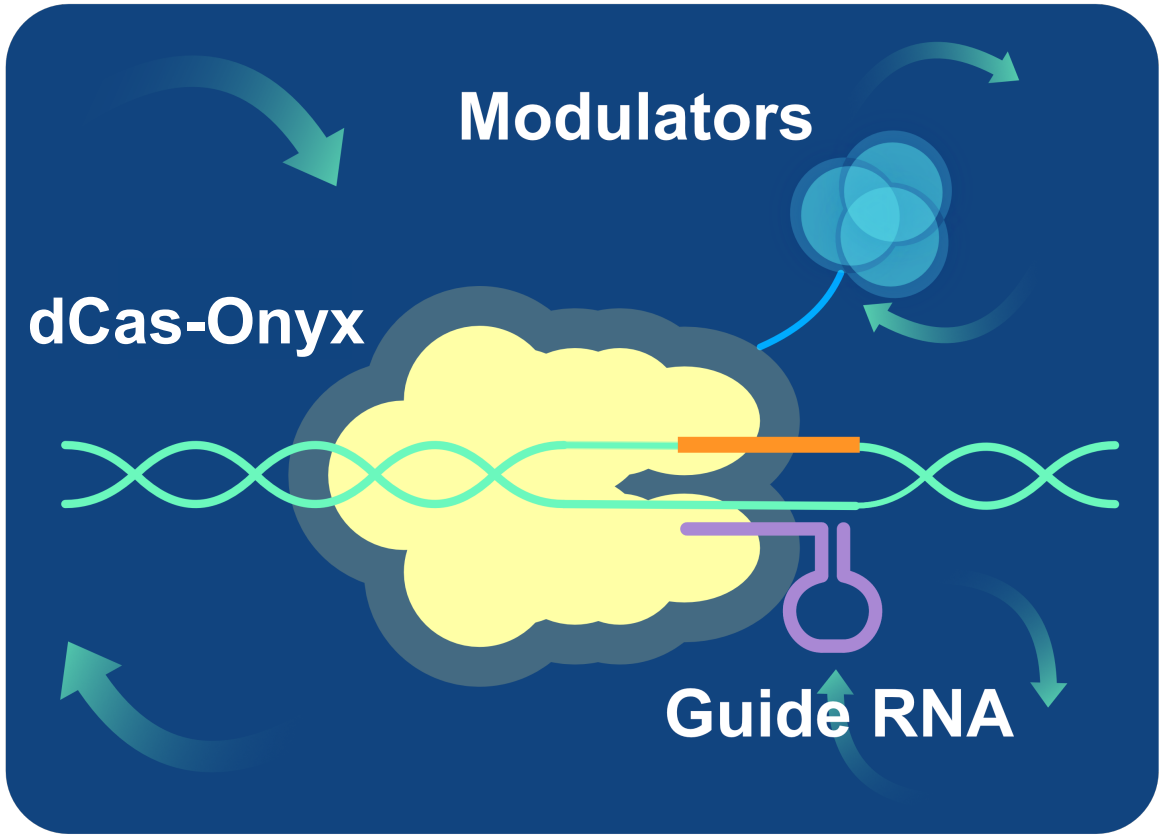
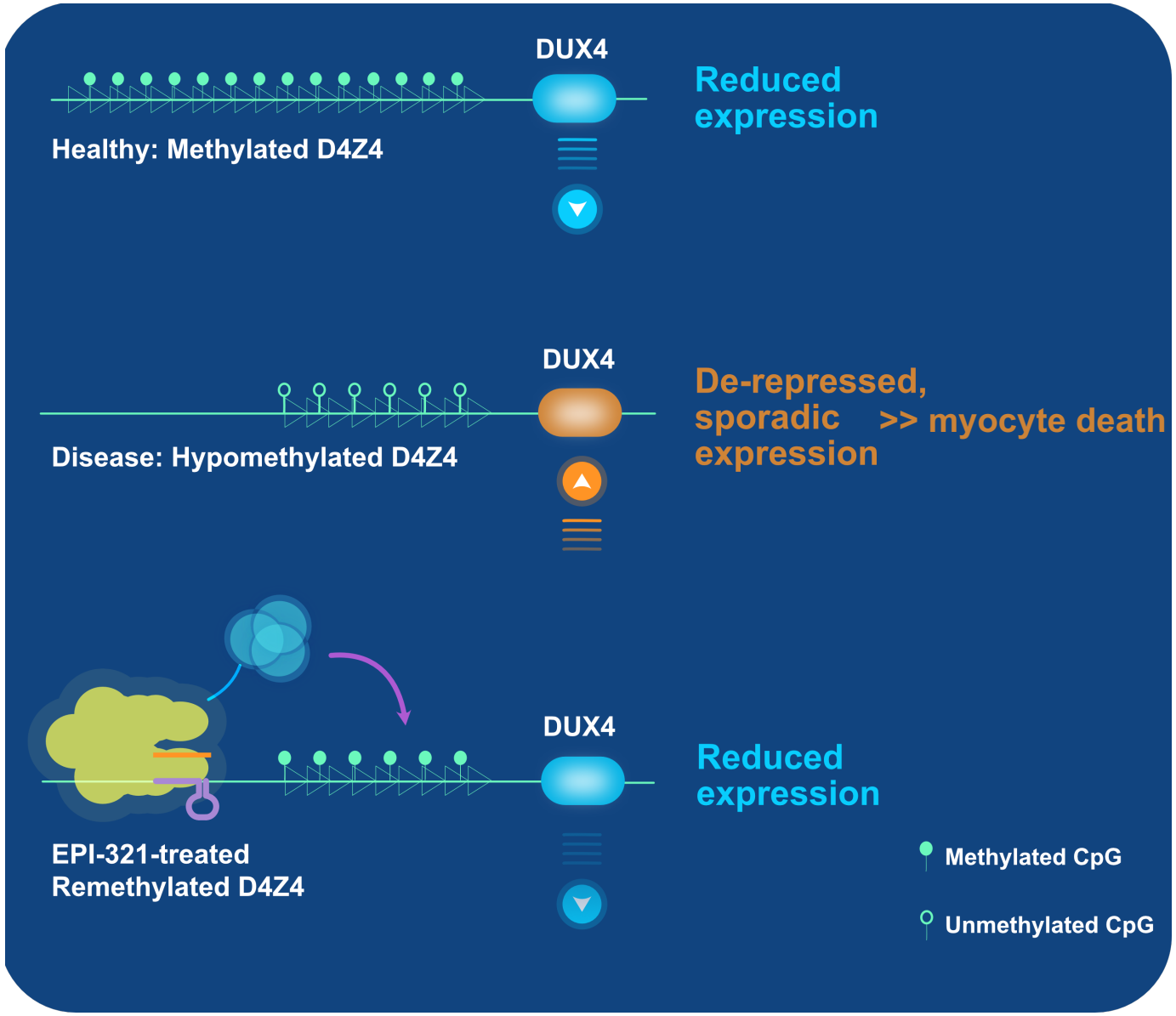
Proprietary Platform: *GEMS: Gene Expression Modulation System*

GEMS can persistently or transiently activate or suppress gene expression, facilitating a broad pipeline



Hypercompact and interchangeable components *support regulating multiple genes in vivo (using AAV and LNP) and ex vivo (lentivirus or retrovirus).*

Lead Program: EPI-321, Addresses Abnormal Epigenetics of FSHD



FSHD has 15y of Validated Disease Biology

*Chronic, degenerative disease of the muscle tissue with **no treatment available***

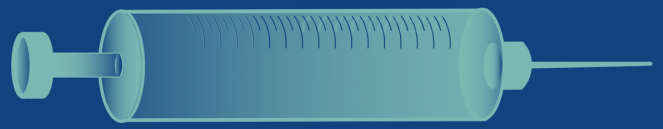
*GEMS can address underlying factors that cause FSHD by **remethylating the D4Z4** region to prevent toxic DUX4 expression*

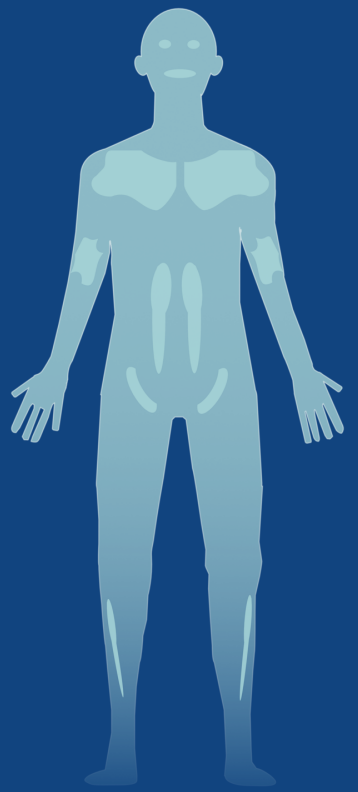
EPI-321: Proposed One and Done Treatment for FSHD

EPI-321

AAVrh74

One time
Intravenous Infusion

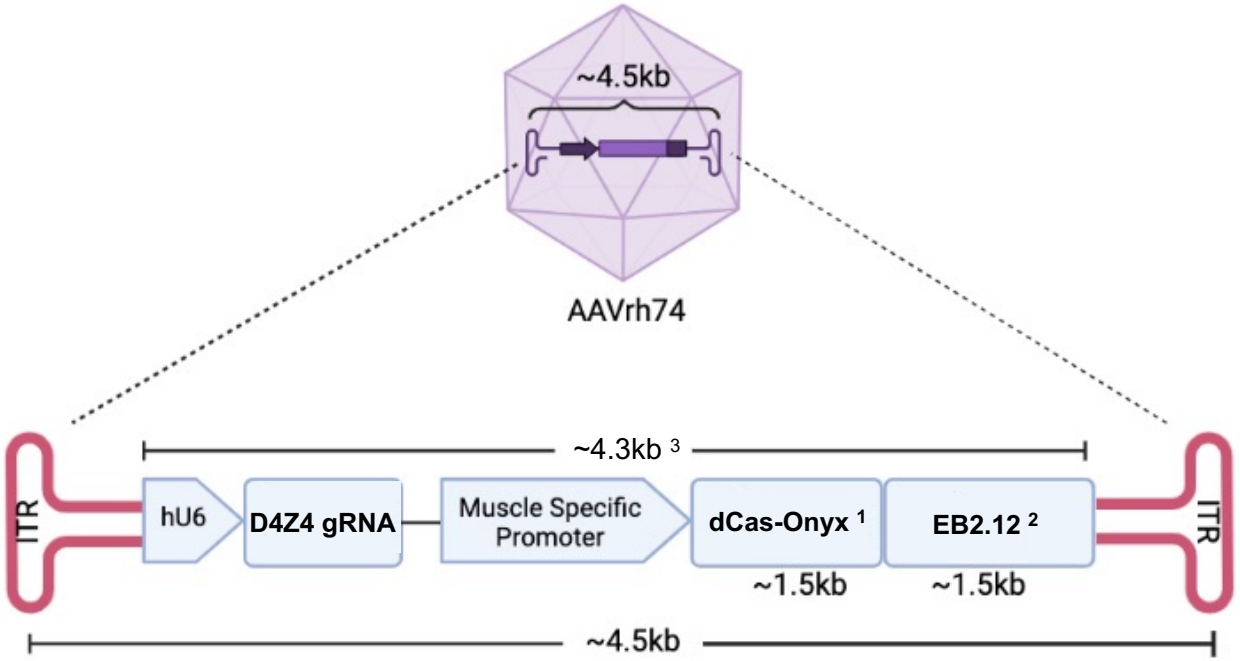




FSHD Patient

**AAVrh74 has demonstrated clinical safety and successful biodistribution in human skeletal muscle*

EPI-321 Overcomes the Limitations of Genetic Medicine

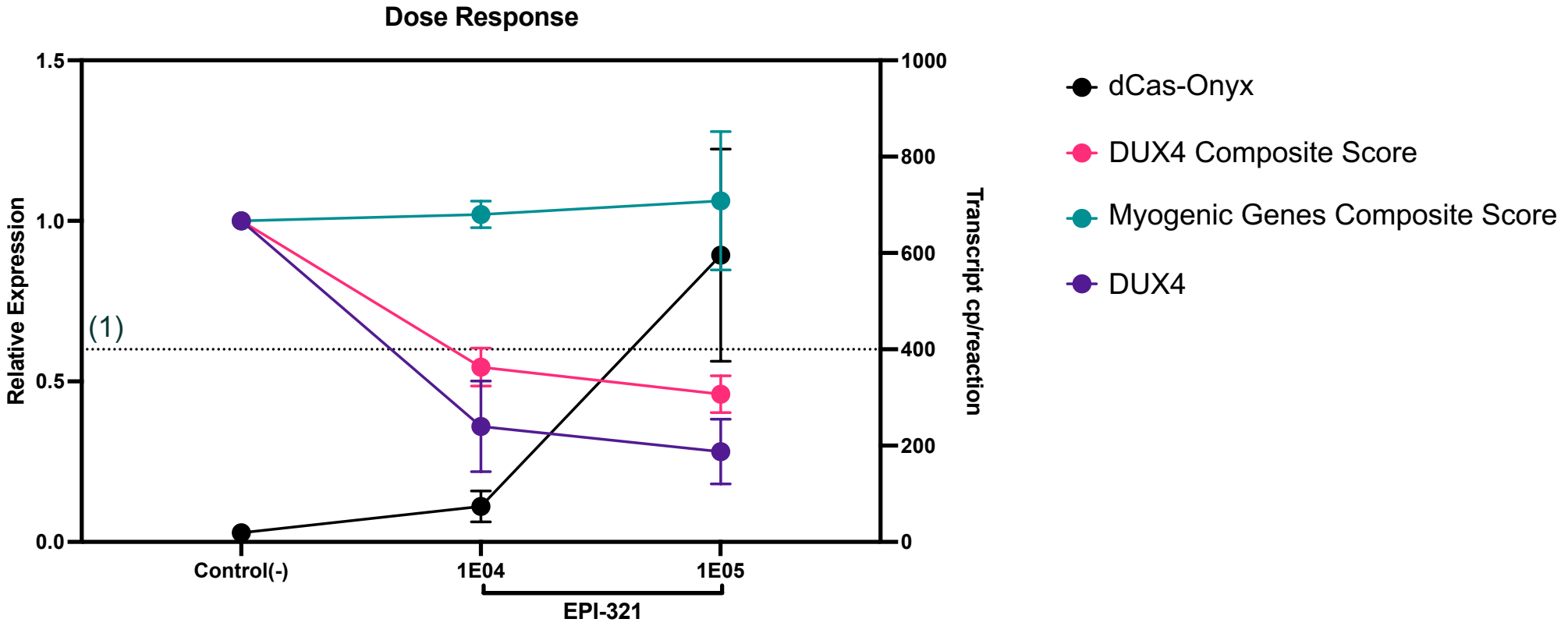


1. **Safety:** EPI-321 utilizes a proprietary library of compact nuclease-dead versions of CRISPR (dCas), resulting in NO DNA cuts

2. **Precision:** EPI-321 controls expression of the endogenous gene through methylation of the target sequence

3. **Delivery:** EPI-321 is ultracompact, allowing for to package it into AAVrh74

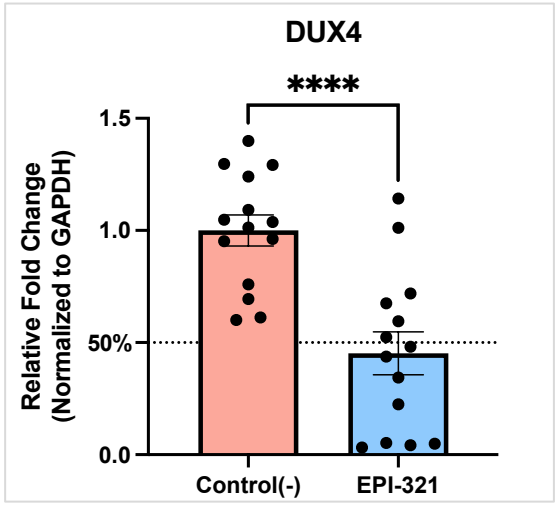
EPI-321 Suppresses DUX4 pathway in Patient-Derived FSHD Myoblasts in a Dose Dependent Manner without Altering Myogenic Gene Expression

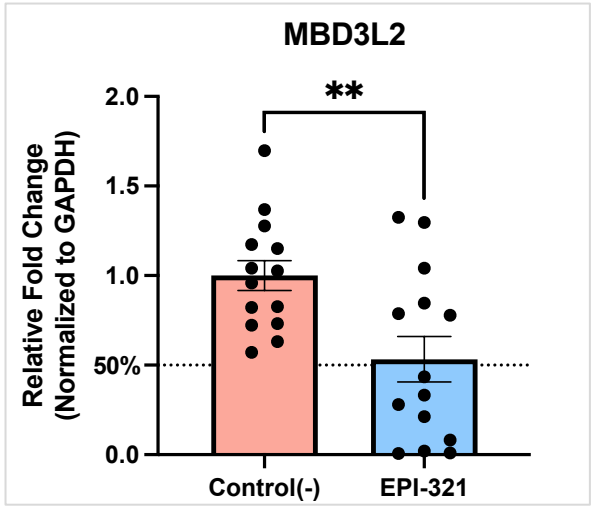


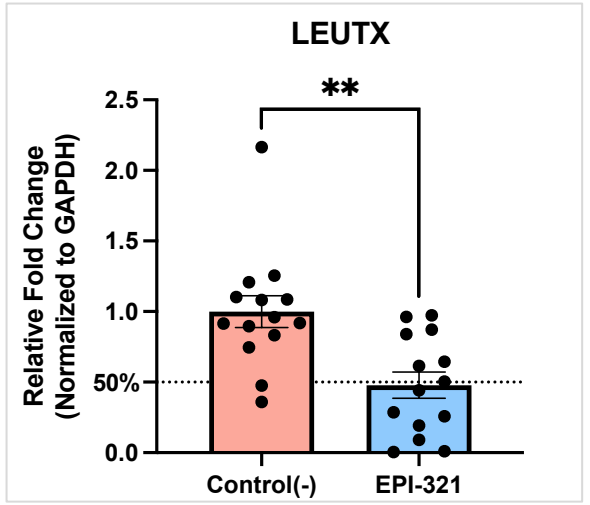
(1) Linde F Bouwman et al. Mol Ther Nucleic Acids (2021) Sep 27;26:813-827
Ngoc Lu-Nguyen et al. Biomedicines (2022) Jul 7;10(7):1623
Ngoc Lu-Nguyen et al. Hum Mol Genet (2021) Jul 9;30(15):1398-1412

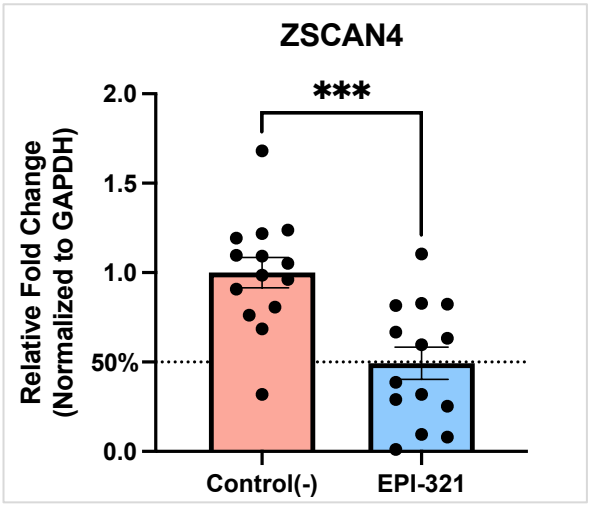
EPI-321 Suppresses DUX4 Pathway in Multiple Patient-Derived FSHD Myoblasts

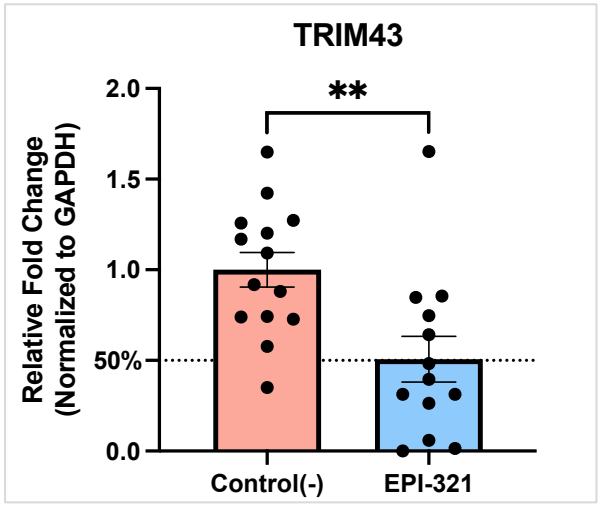
4 FSHD cell lines tested

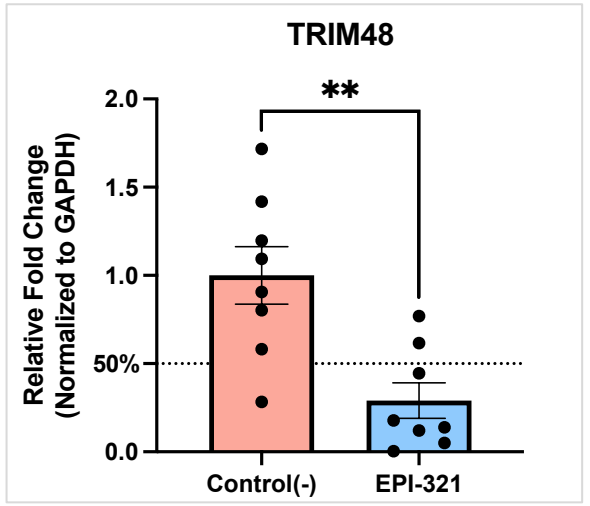


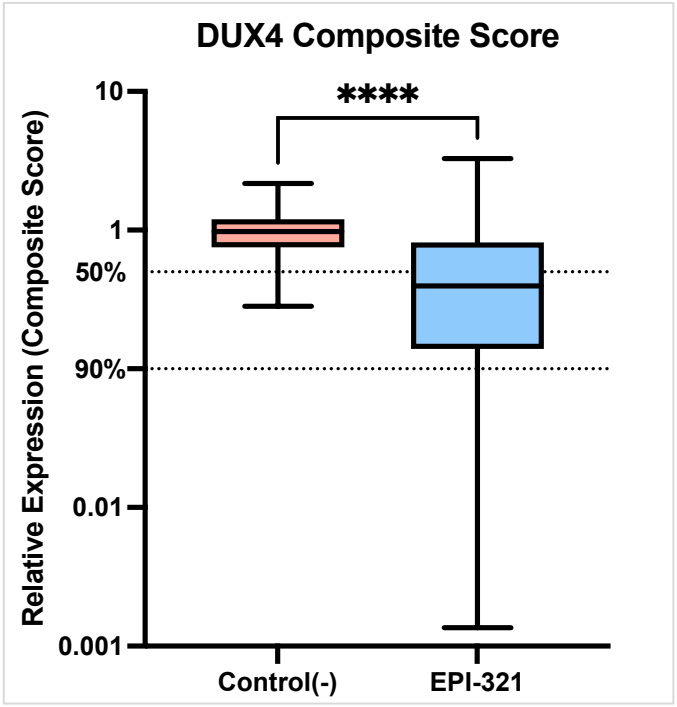






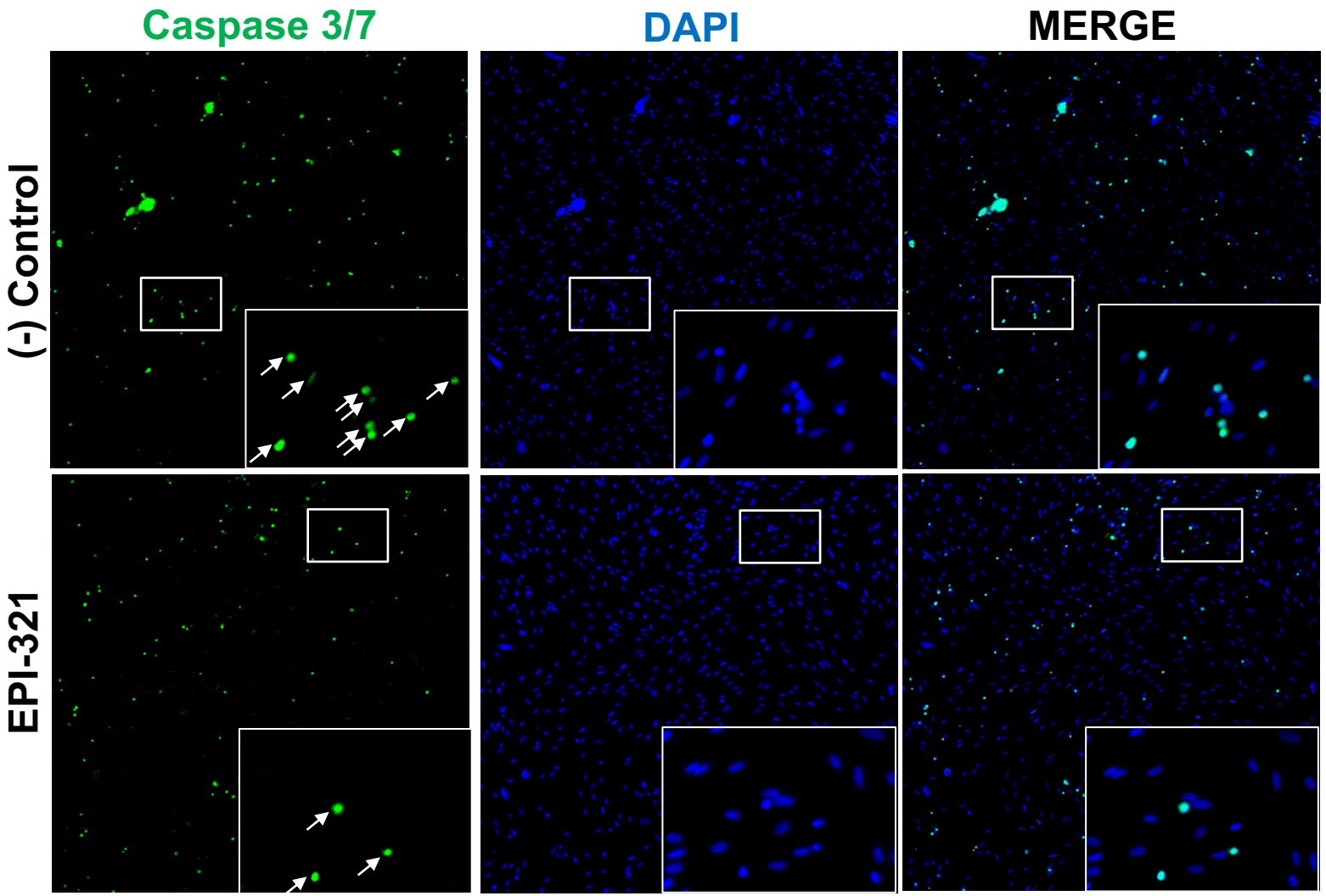


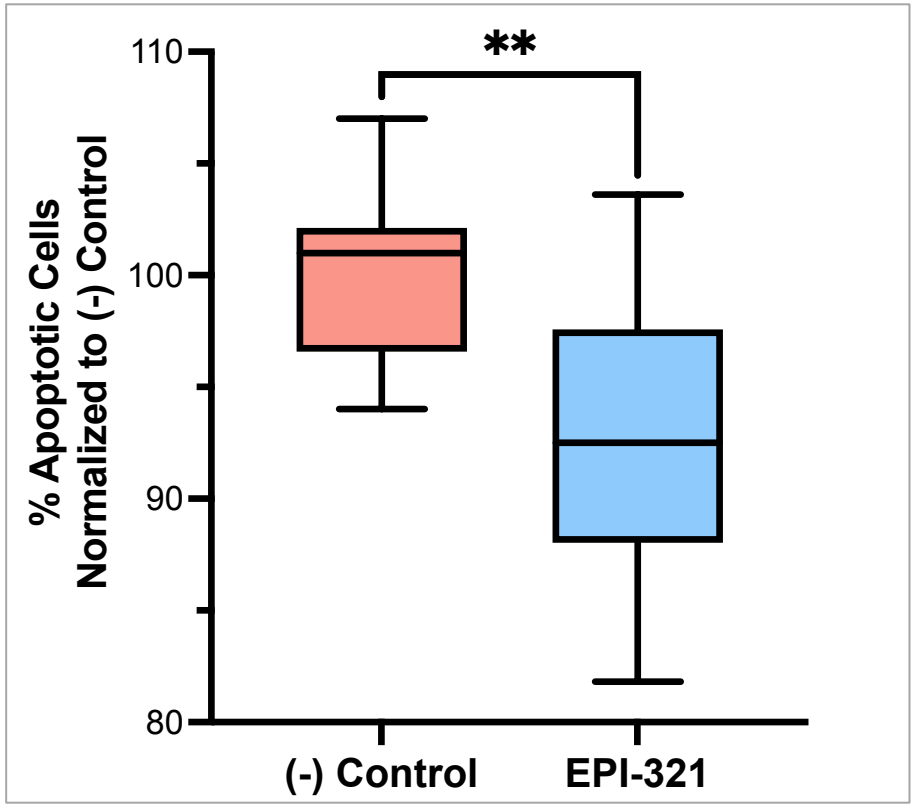




EPI-321 Rescues Muscle Cells Survival in Multiple Patient-Derived FSHD Myoblasts

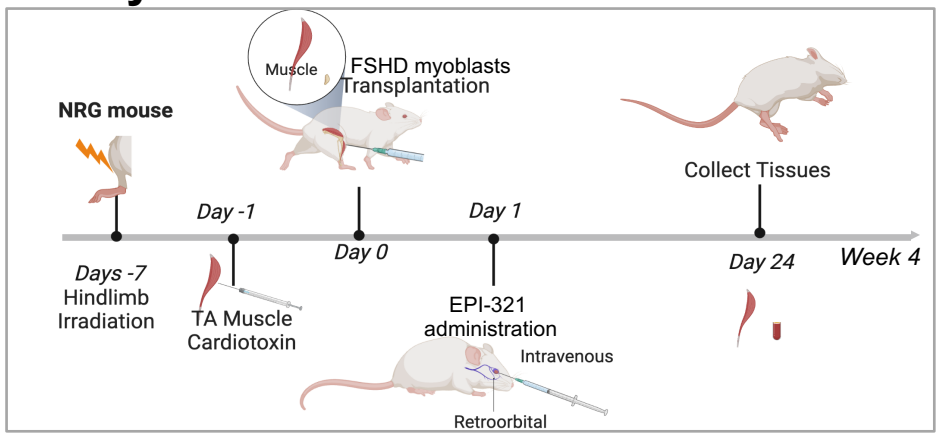
4 FSHD cell lines tested



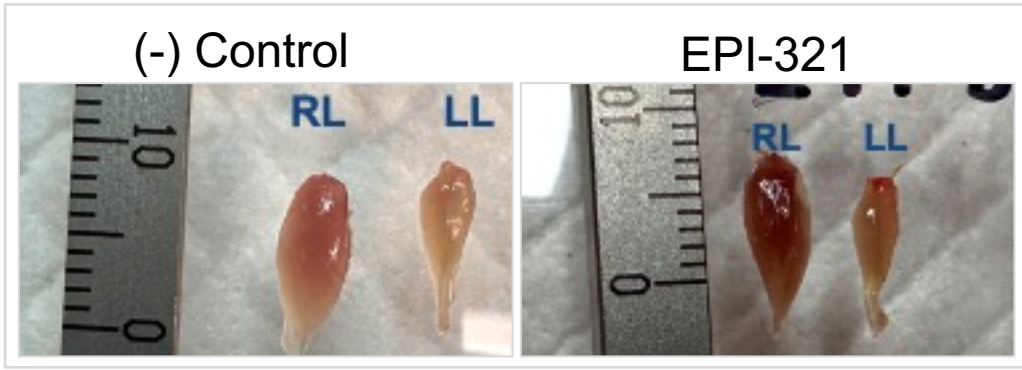


EPI-321 is delivered and expressed in skeletal muscle 4 weeks post administration

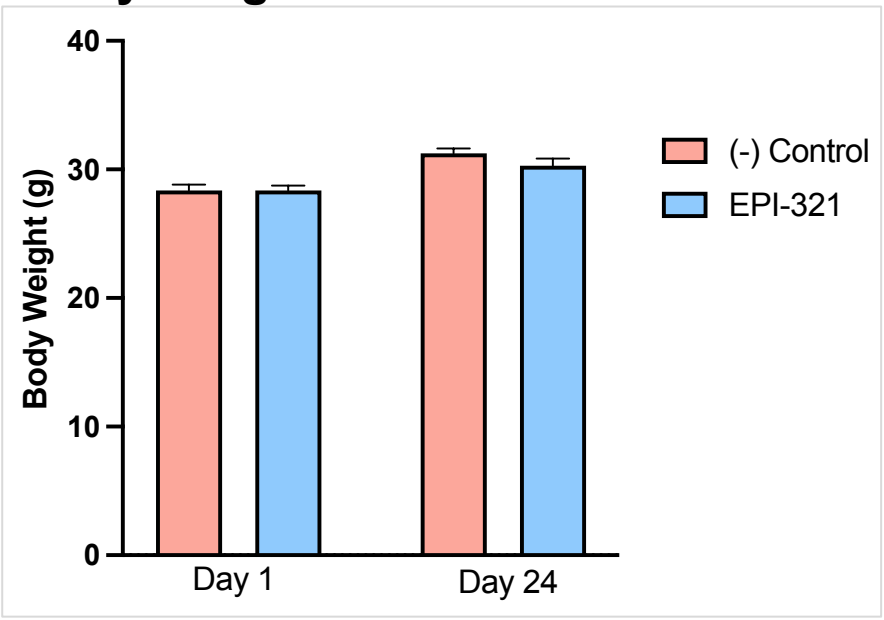
Study Schematic



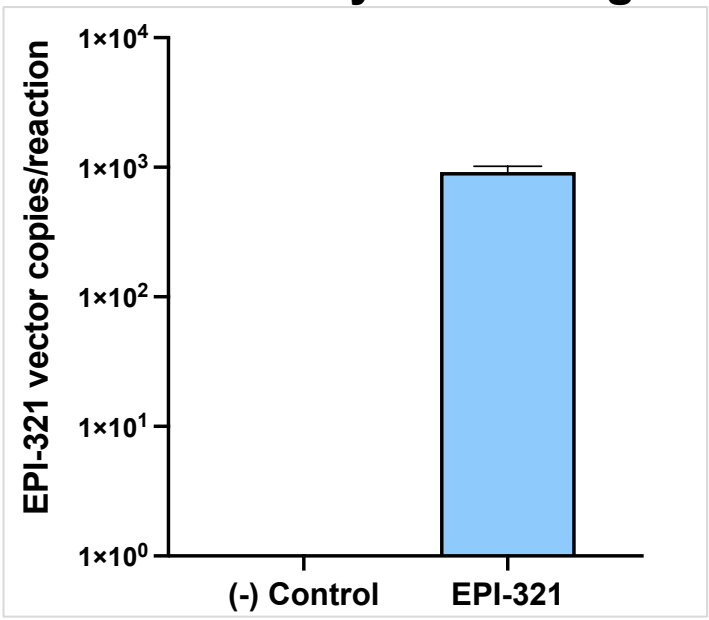
TA muscle at 4 weeks

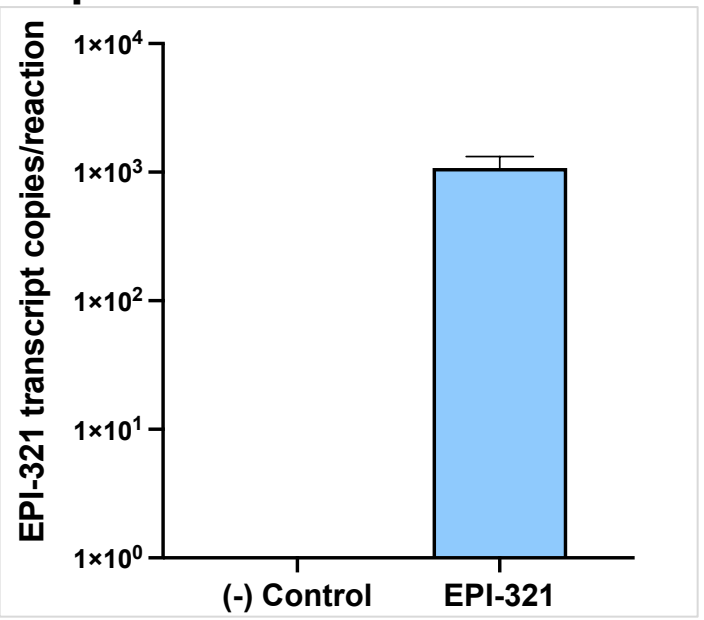


Body Weight

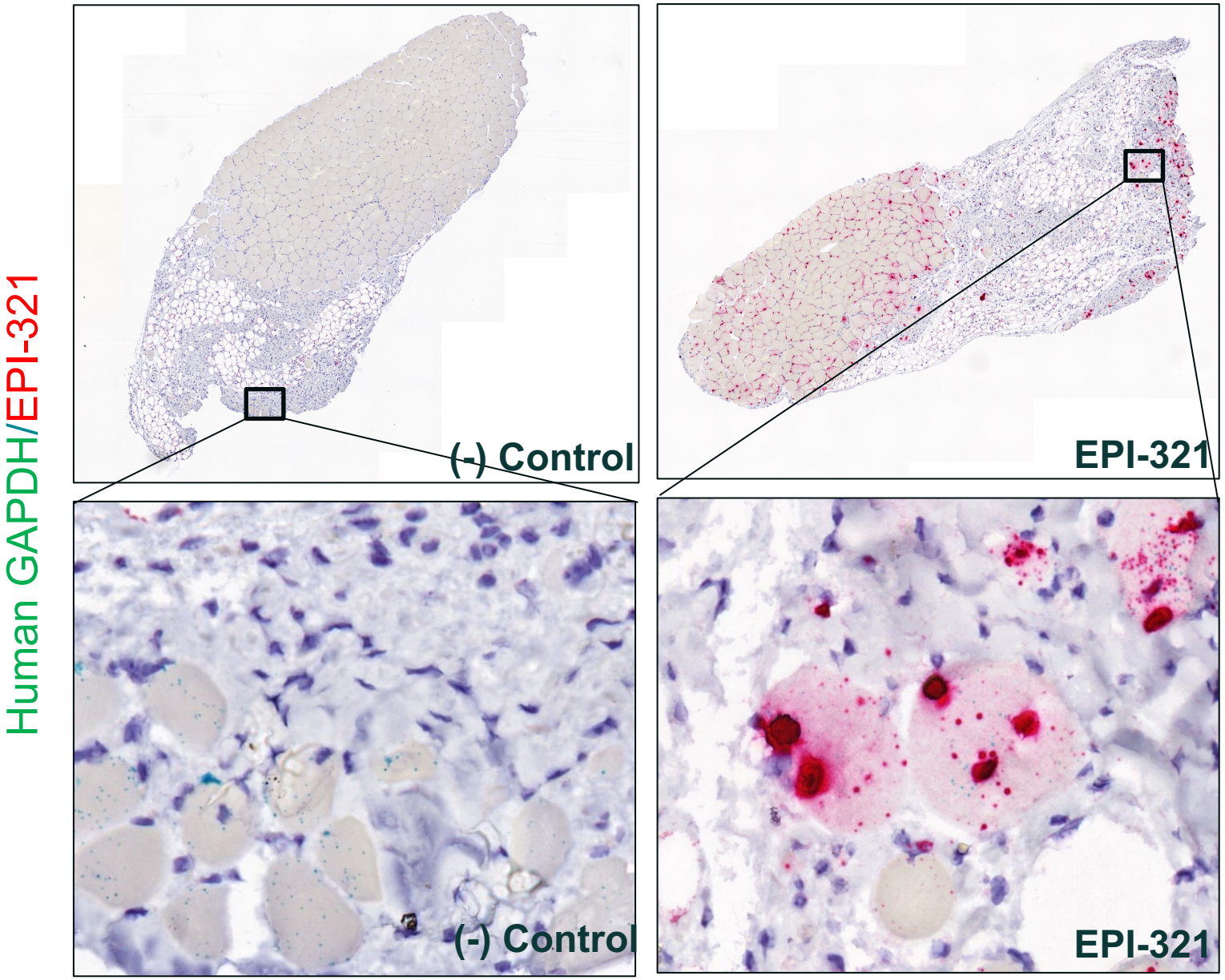


EPI-321 delivery and transgene expression





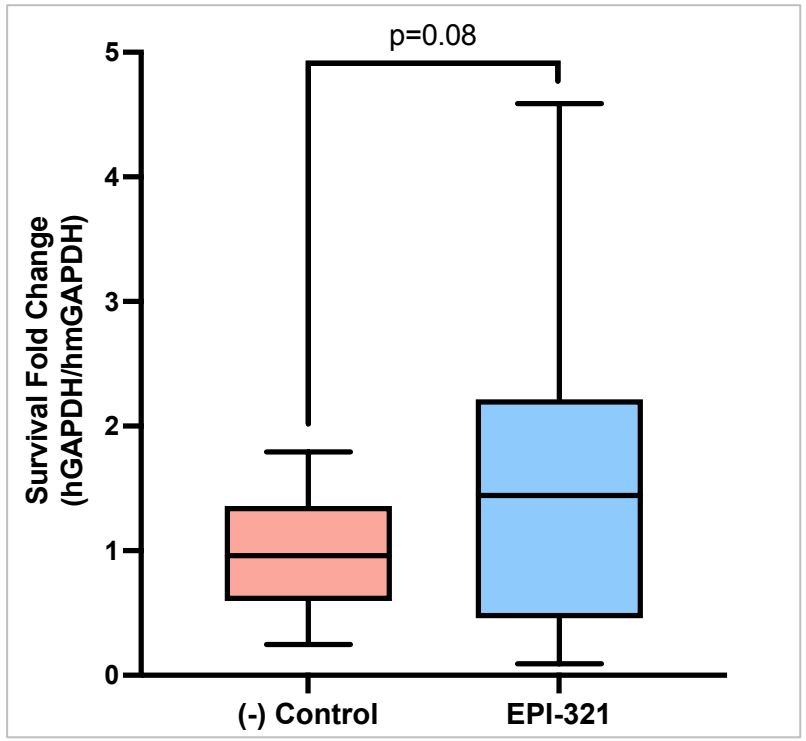
Excellent biodistribution of EPI-321 in vivo in FSHD humanized animals



Biodistribution Efficiency (Dual positive cells (GAPDH + EPI-321 / GAPDH)	
(-) Control	**EPI-321**
0%	76%-99%

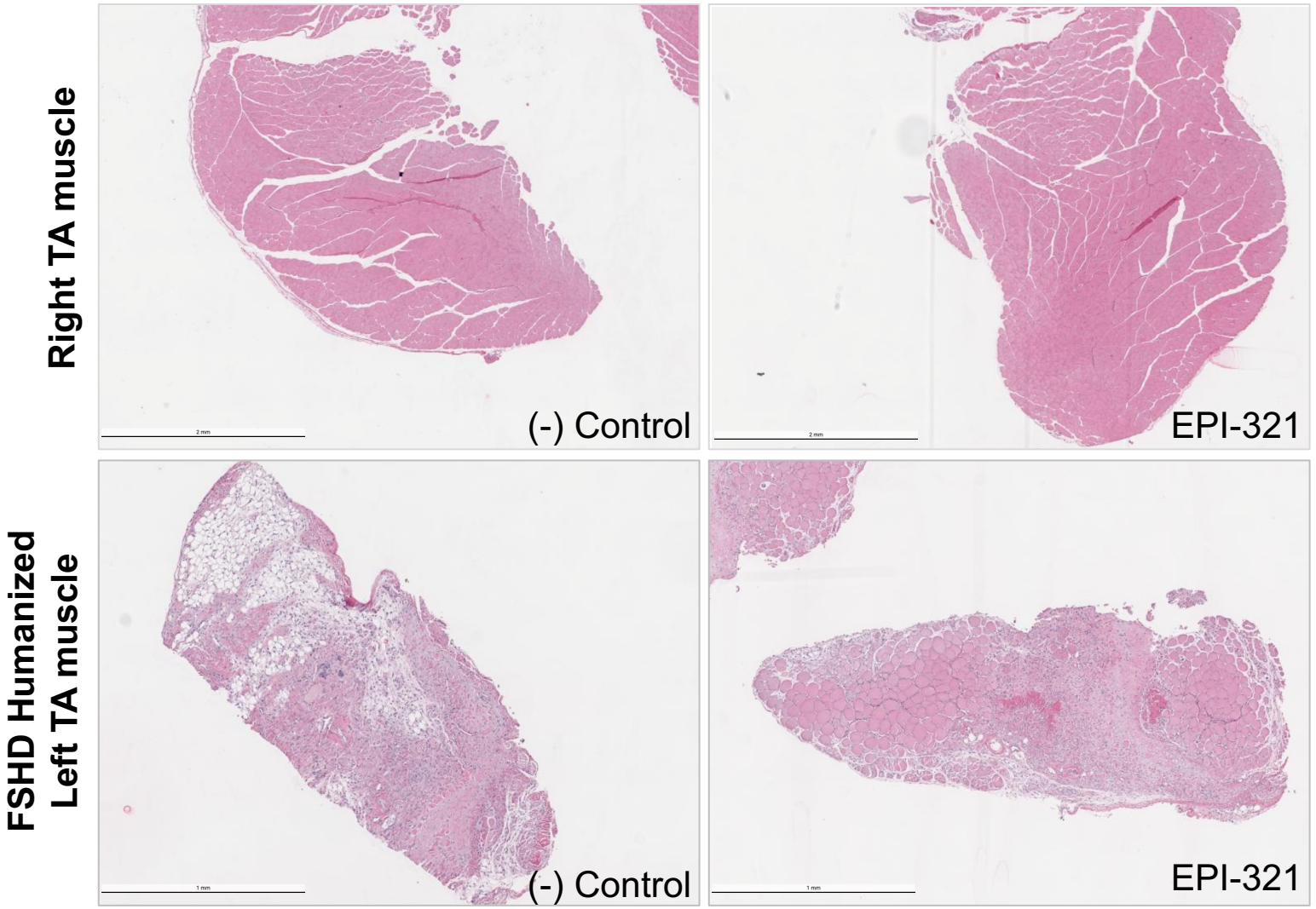
EPI-321 Improves Human FSHD Muscle Cells Survival In Vivo

FSHD cell survival

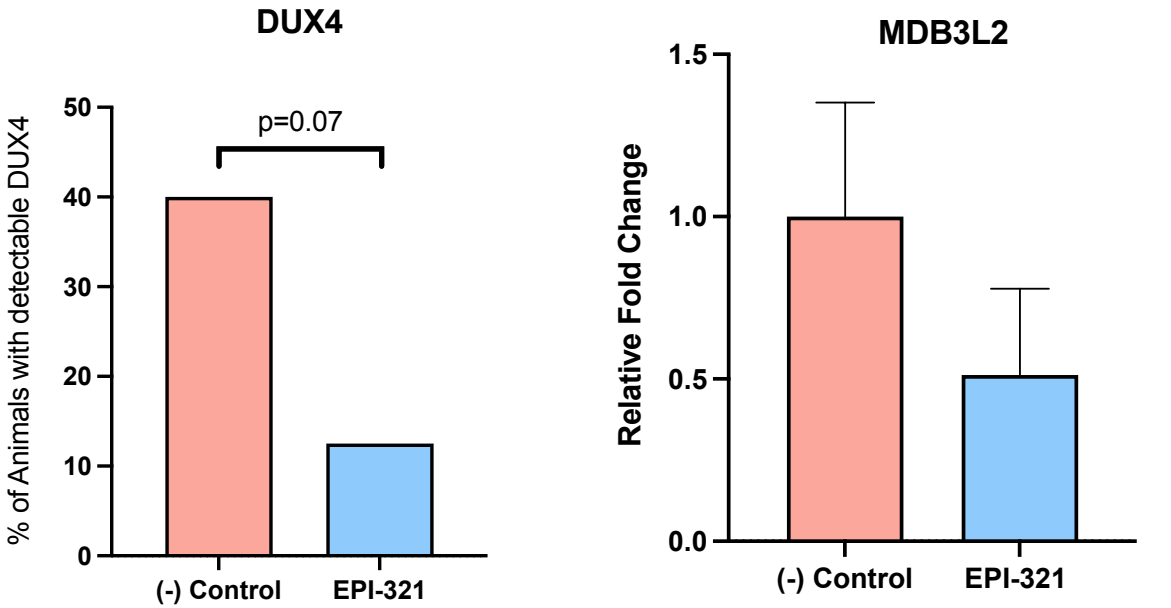


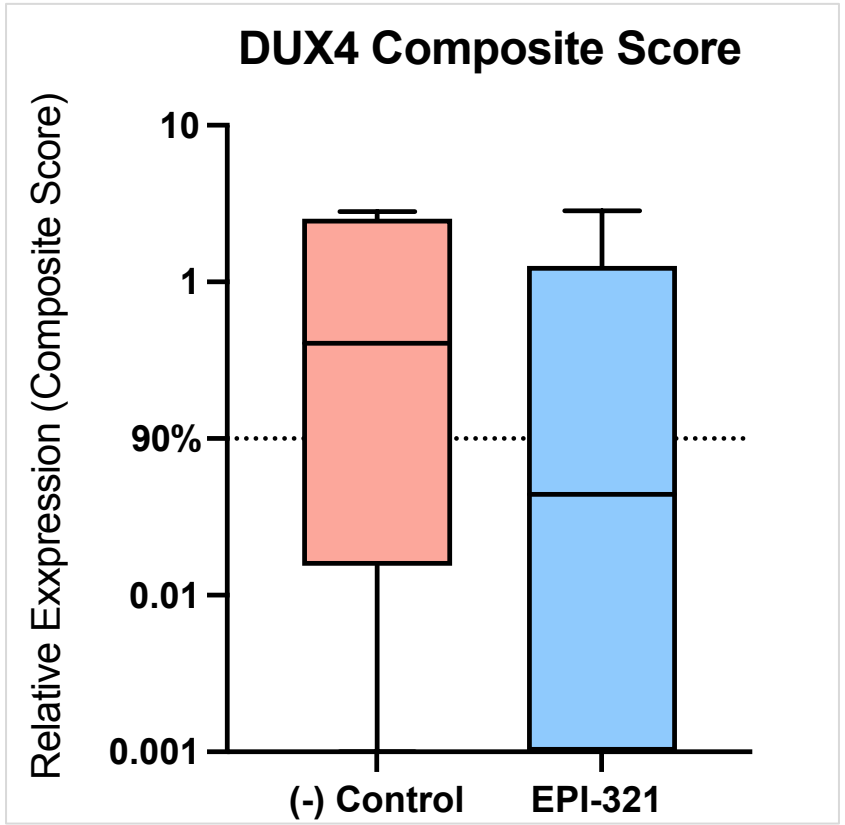
55% Improved *human FSHD muscle cells survival in vivo 4 weeks post EPI-321 administration*

Histology of TA muscle



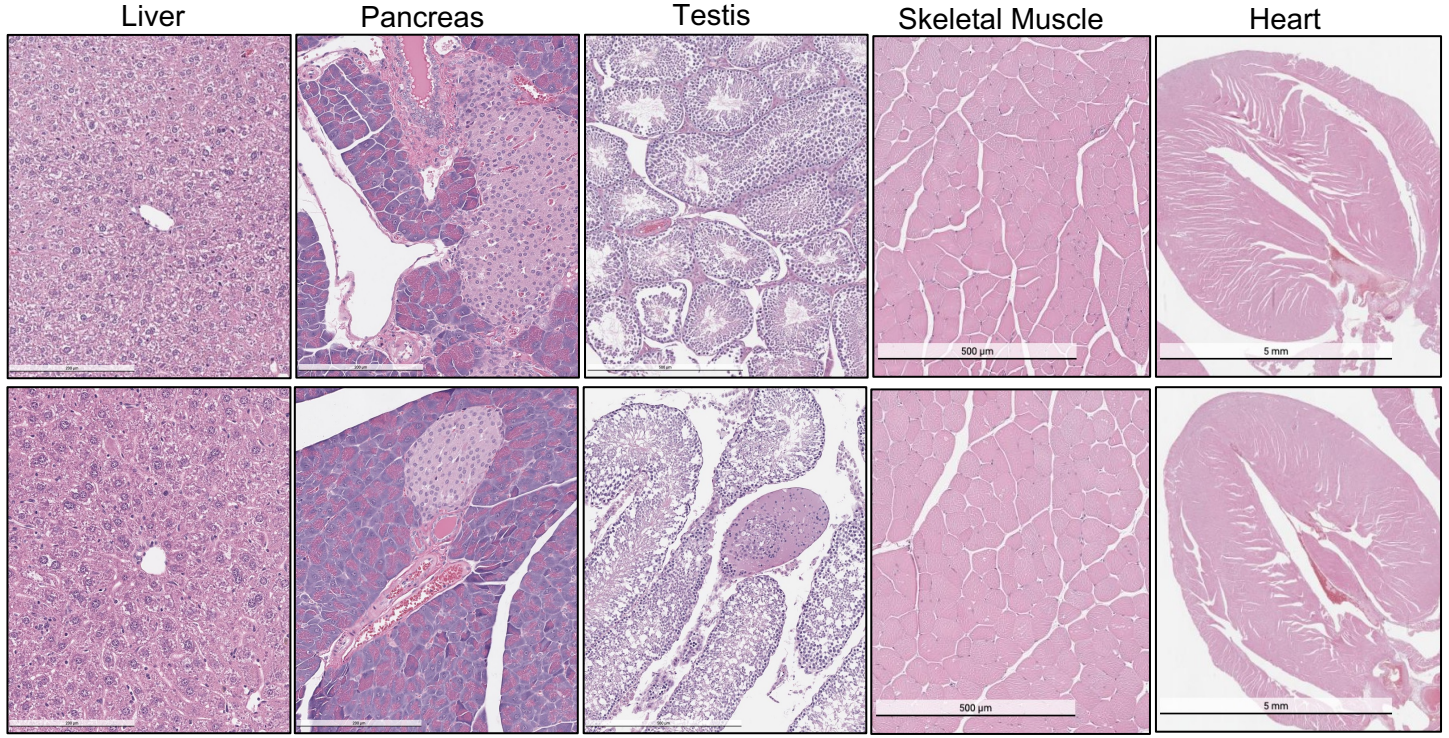
EPI-321 Suppresses DUX4 Pathway in Humanized FSHD Mice Model



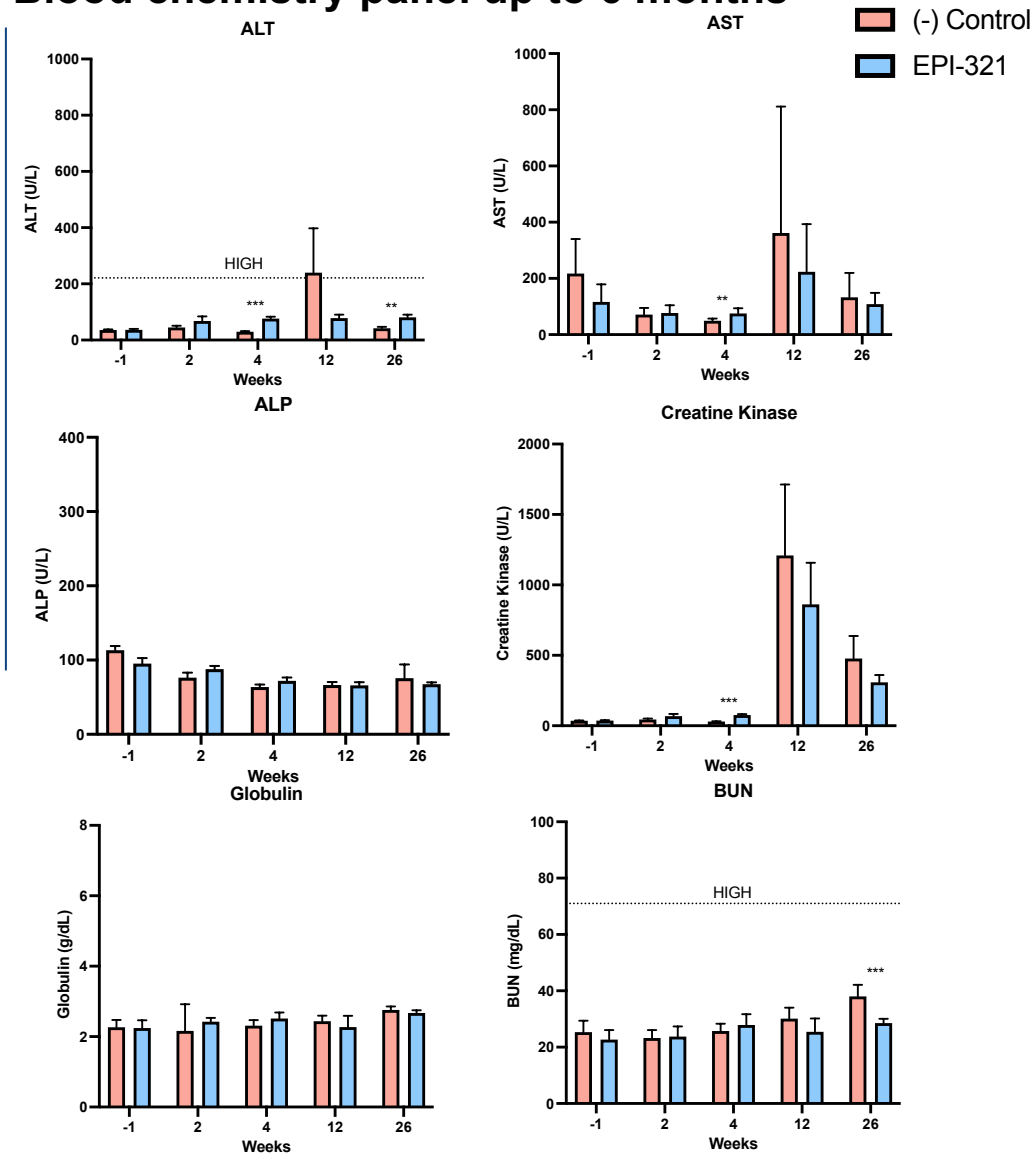


6 Months Study on Immunocompetent Mice Indicates Safety of EPI-321

Hematoxylin and eosin (H&E) staining at 3 months

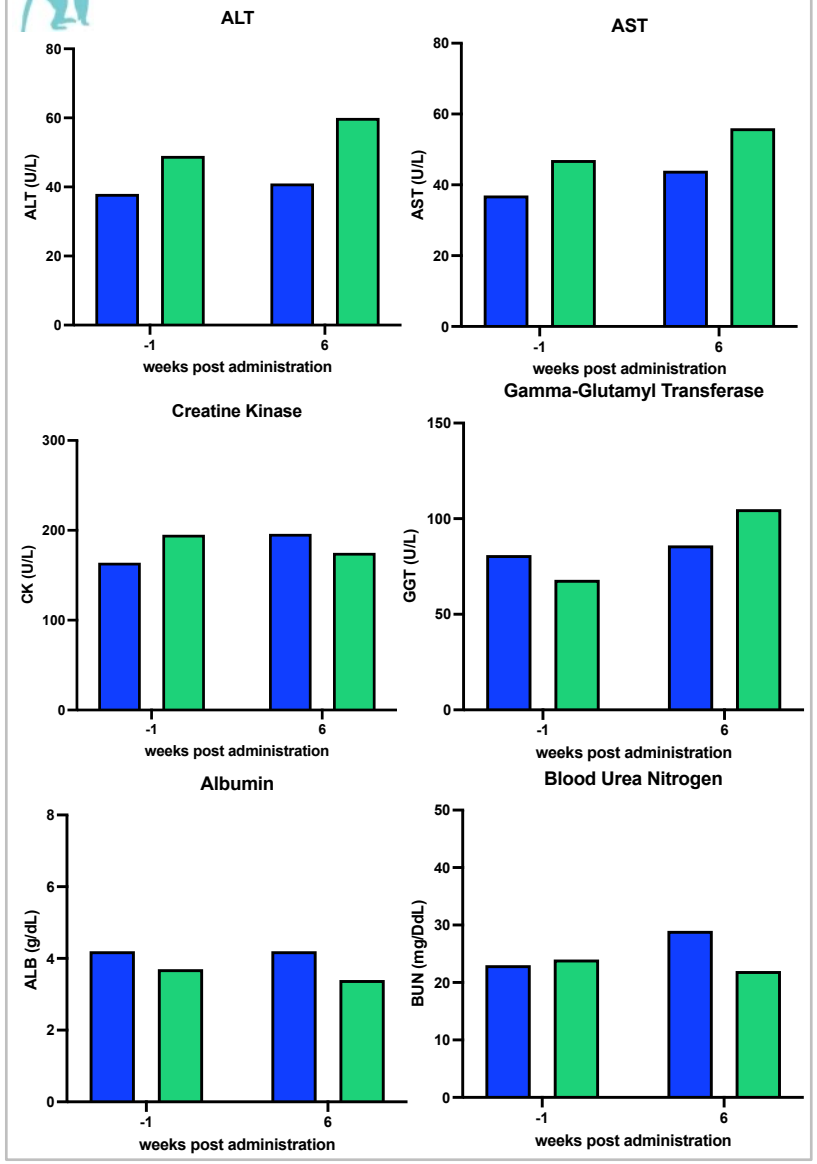


Blood chemistry panel up to 6 months

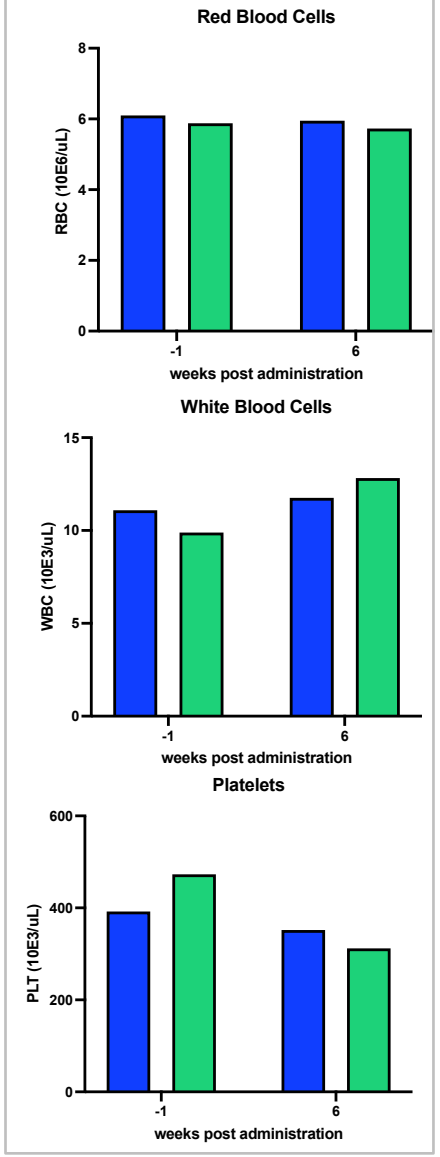


3 Months Study on Immunocompetent NHP: *Blood chemistry & hematology data indicate safety of EPI-321*

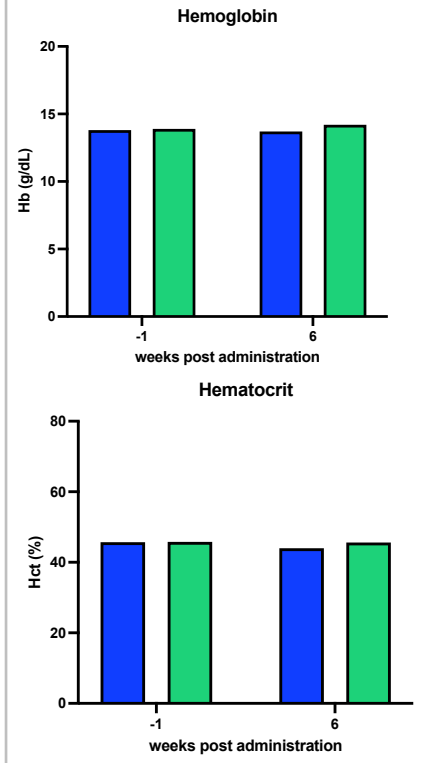
Blood Chemistry



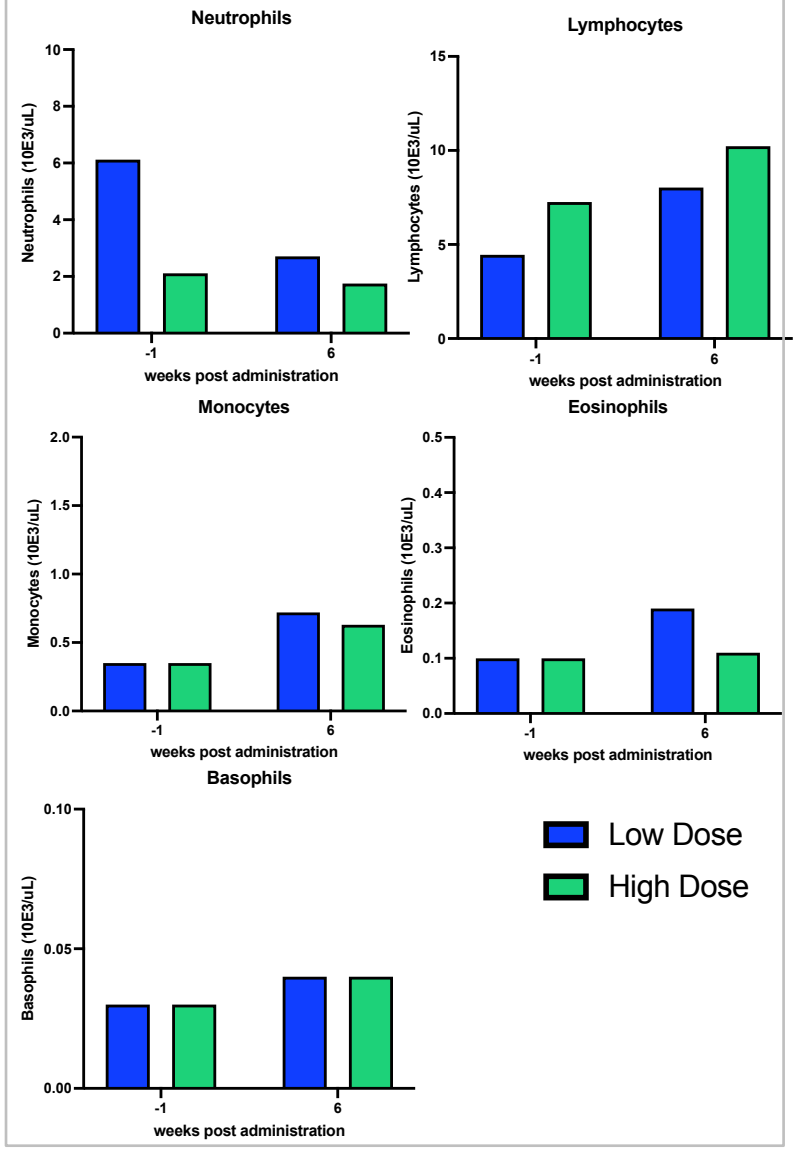
Complete Blood Count



Hemoglobin & Hematocrit

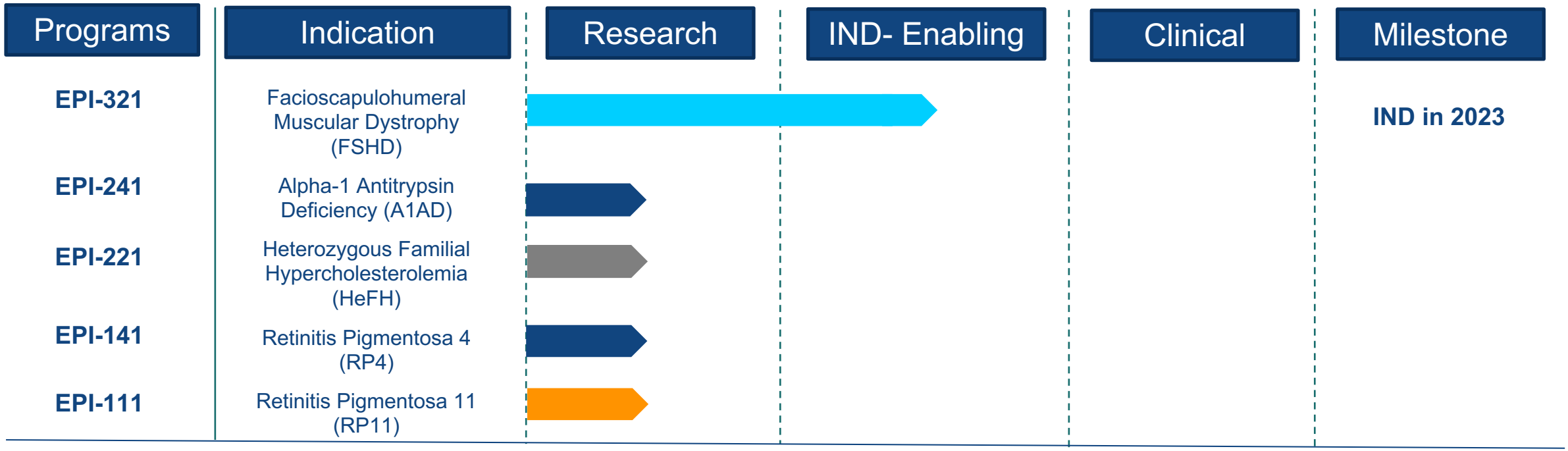


White Blood Differential



Pipeline - First IND Planned for 2023

Well positioned to file an IND every 12-18 months



- **Suppress:** Suppress the endogenous gene either by downregulation or by permanently turning off the expression of a gene
- **Suppress and replace:** Suppress the endogenous mutated gene and replace it with exogenous wildtype version of gene
- **Activate**: Upregulate the expression of a gene either to physiological levels or above physiological levels (i.e., to restore haploinsufficiency gene activity)
- **Undisclosed**

De-risked Pipeline with Rapid Path to the Clinic

- Disease pathology is well validated
- Clinical precedent accessing the tissue of interest
- Measurable endpoints support early clinical validation

EPIC BIO

Thank you!

May 19, 2023