ACHIEVE Trial, a Randomized, Placebo-Controlled, Multiple Ascending Dose Study of DYNE-101 in Individuals with Myotonic Dystrophy Type 1 (DM1)

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DM1 Is a Progressive Neuromuscular Disease with Multisystem Involvement with no Disease-Modifying Treatment Approved

Overview

- Mutation in the *DMPK* gene
- Onset at any point, depending on DM1 phenotype
- Life expectancy of 45 - 60 years

Clinical Presentation

- Myotonia
- Muscle weakness
- Cardiac arrhythmia
- Pulmonary abnormalities

Population

- >40,000 (US)
- >74,000 (Europe)

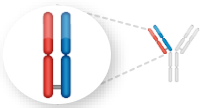
DYNE'S APPROACH

Disease-Modifying Nuclear *DMPK* Knockdown

Targeting toxic gain of function *DMPK* RNA to potentially **stop or reverse** disease progression

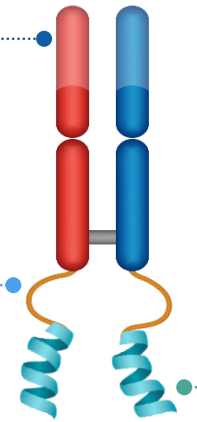
ANTIBODY

Proprietary Fab targets TfR1 to enable muscle delivery



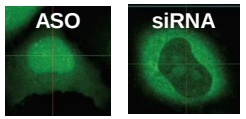
LINKER

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



PAYLOAD

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

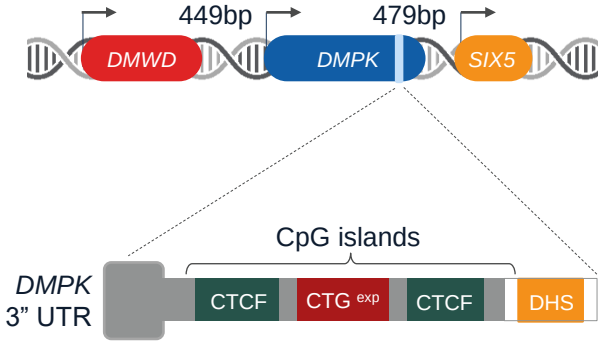


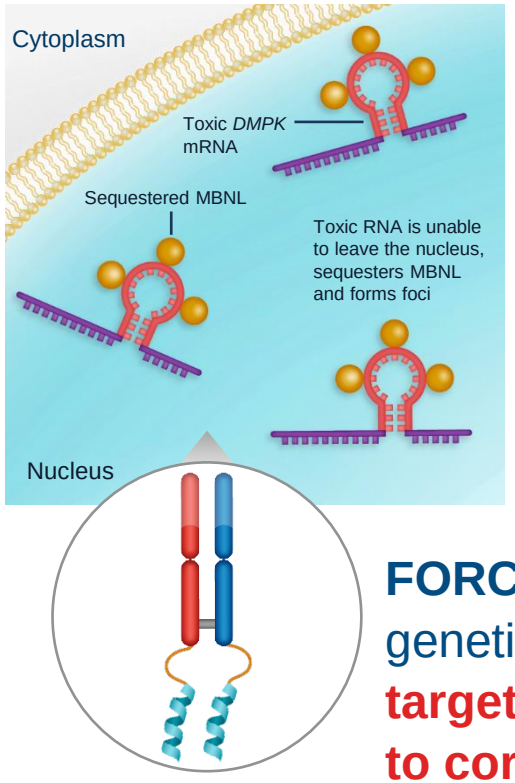
Nuclear localization | Cytoplasmic localization

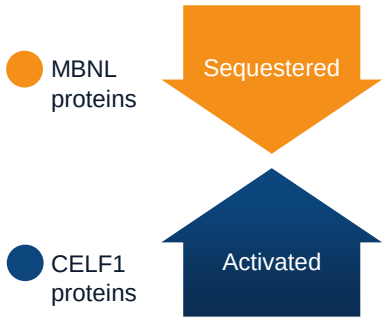
DMPK, dystrophia myotonica protein kinase

FORCE Targets the Genetic Basis of DM1 to Correct Splicing

DNA Triplet Repeats → **Toxic RNA Forms Foci in Nucleus** → **RNA Binds Splicing Proteins** → **Clinical Presentation**



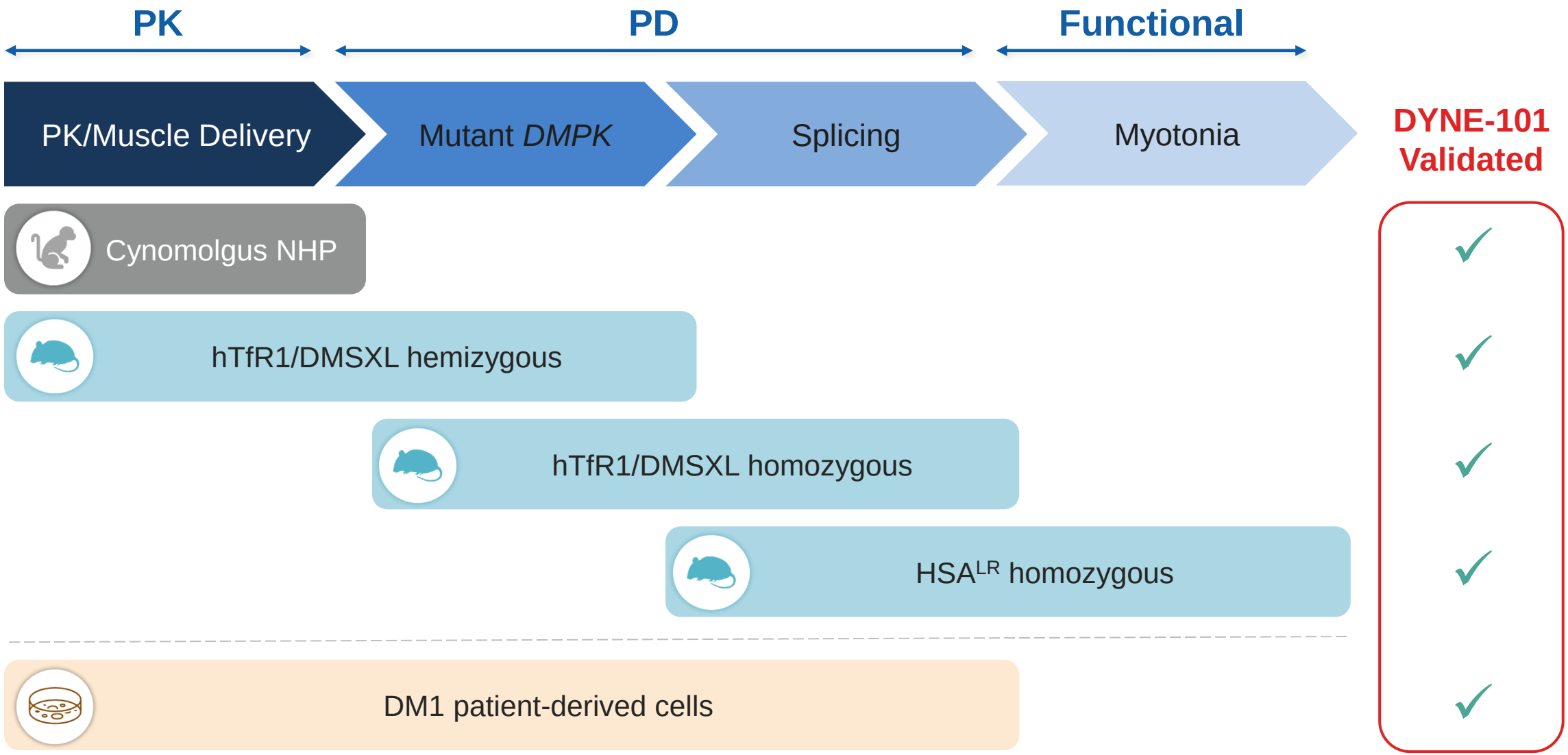




- Myotonia
- Muscle weakness
- Cardiac arrhythmia
- Pulmonary abnormalities

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

Robust Preclinical Data Support the Potential of DYNE-101 to Drive Disease Modification in the Clinic



NHP, non-human primate; hTfR1, human TfR1; HSA^{LR}, human skeletal actin-long repeat

Phase 1/2 Clinical Trial to Evaluate DYNE-101 in Adults with DM1

Population

- Adult patients living with DM1
- Ages 18 to 49 years
- ~64 adult participants

Primary Endpoints

- Safety and tolerability

Key Secondary Endpoints

- Pharmacokinetics
- Change from baseline of:
  - Splicing
  - *DMPK* RNA expression
  - Multiple assessments of muscle strength and function

Stages of ACHIEVE

- Multiple Ascending Dose (MAD): 24 weeks
- Open-Label Extension (OLE): 24 weeks
- Long-Term Extension (LTE): 96 weeks

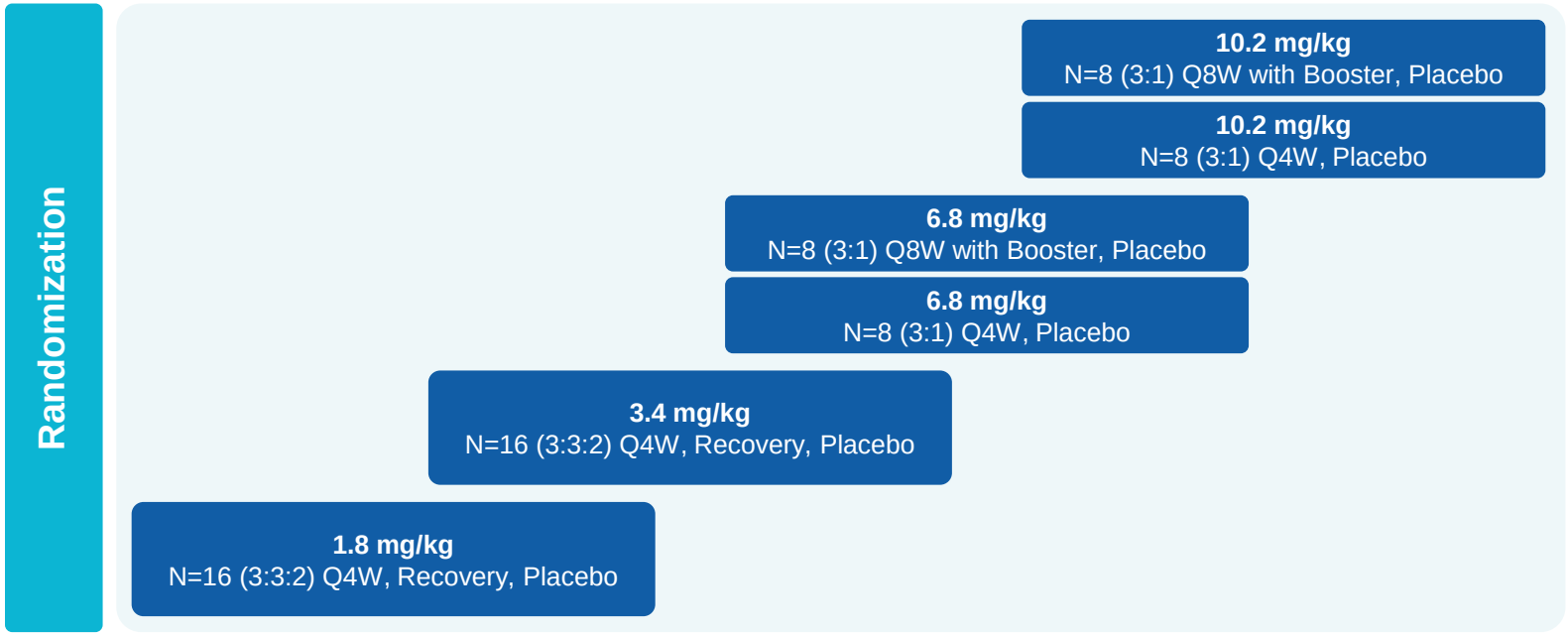
Initial Safety, Tolerability & Splicing Data Expected in H2 2023

ClinicalTrials.gov, NCT05481879

Multiple Ascending Dose Stage of ACHIEVE

ACHIEVE

Global, Randomized, Placebo-Controlled Stage Evaluating Once Monthly or Less Frequent Administration of DYNE-101 in ~64 Adult Patients Living with DM1



MAD Study Details

- IV administration of DYNE-101 or placebo every 4 weeks or every 8 weeks
- Muscle biopsies: Baseline, 12 weeks, 24 weeks
- Patients in MAD study escalated to highest tolerable dose in OLE and LTE

Q4W, every 4 weeks dosing; Q8W, every 8 weeks dosing
Doses provided refer to ASO component of DYNE-101. Recovery cohort Q4W x 2 doses then placebo for the remainder of the 24W placebo-controlled period. Q8W with booster includes Q4W x 3 doses then Q8W dosing.
ClinicalTrials.gov, NCT05481879

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