



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)

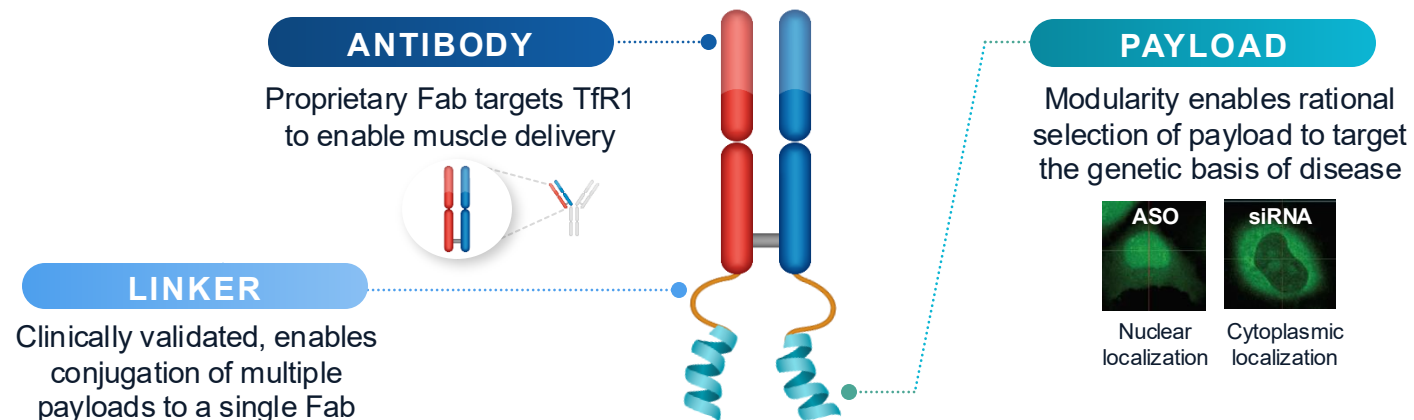


**NO
approved
therapies**

DYNE'S APPROACH

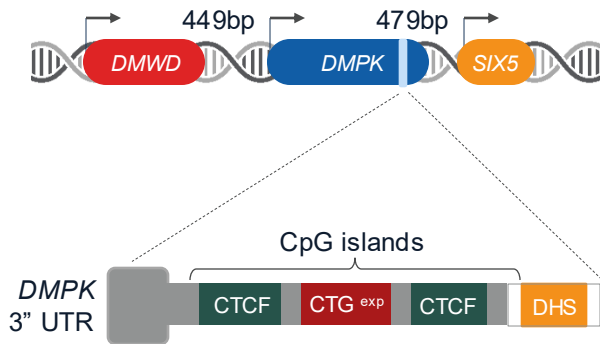
Disease-Modifying Nuclear *DMPK* Knockdown

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

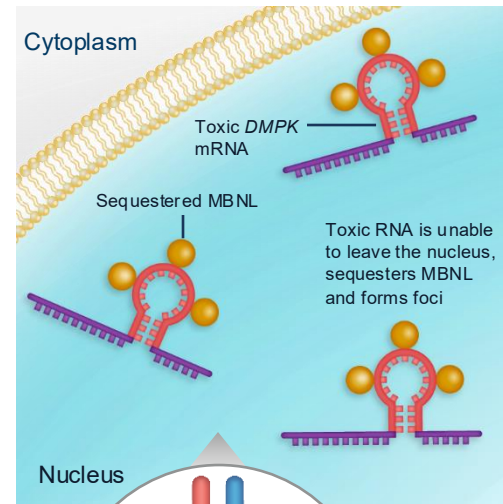


FORCE Targets the Genetic Basis of DM1 to Correct Splicing

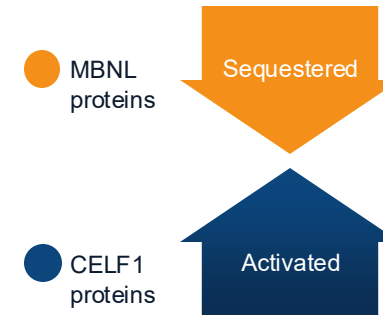
DNA Triplet Repeats



Toxic RNA Forms Foci in Nucleus



RNA Binds Splicing Proteins

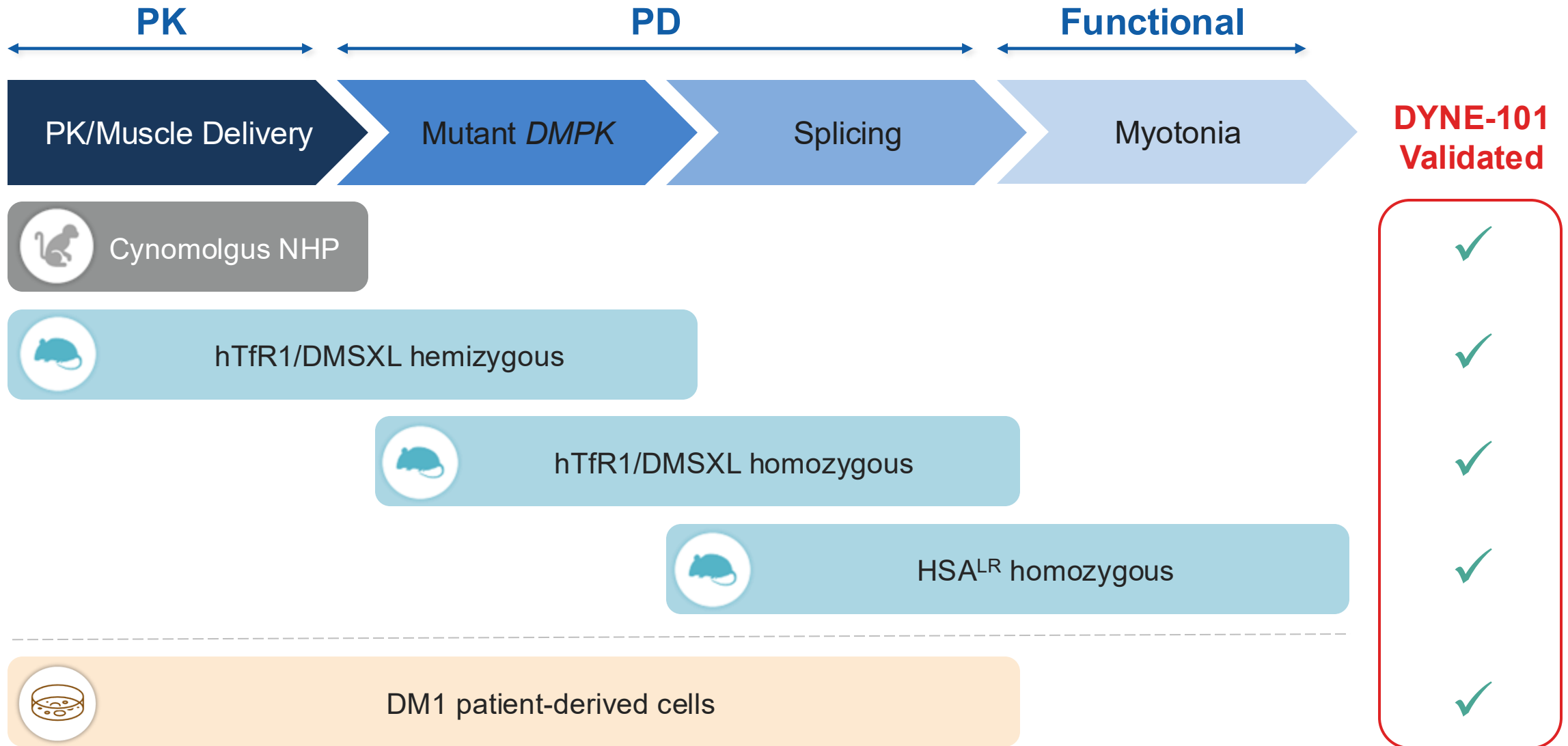


Clinical Presentation

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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



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



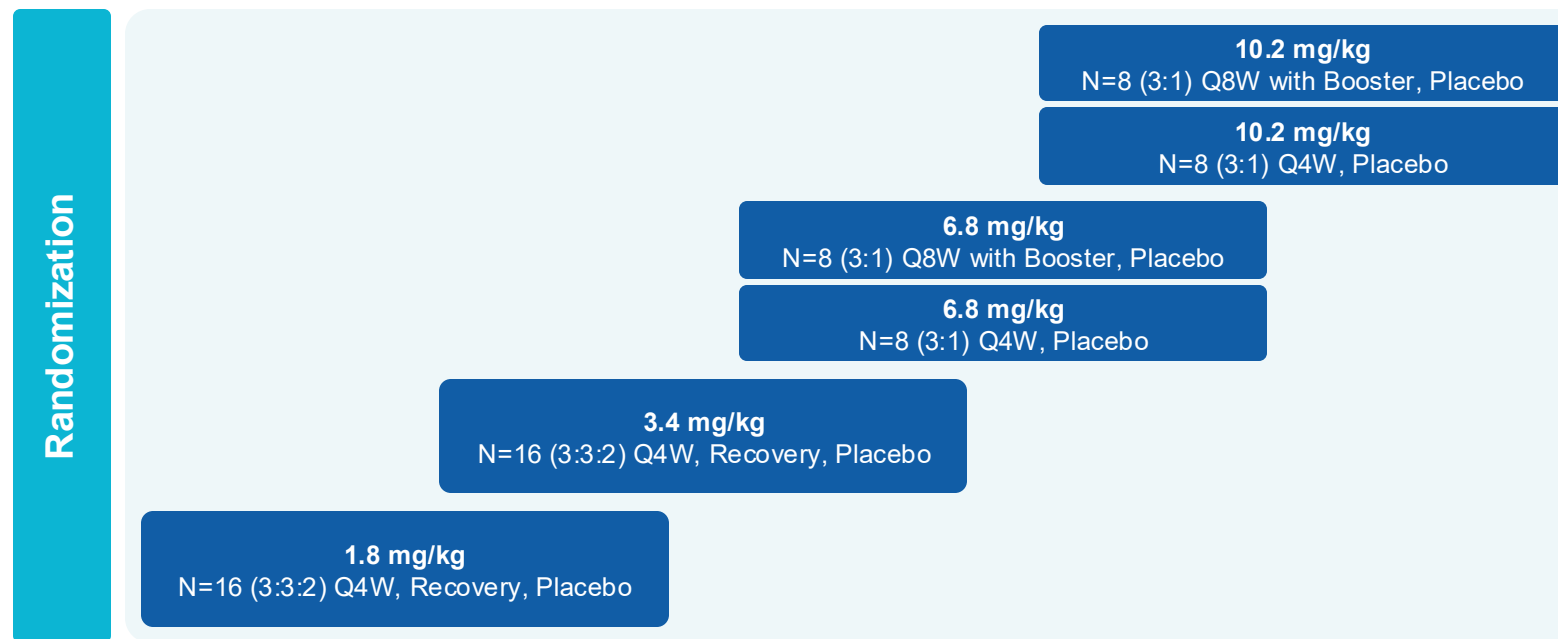
Population	Primary Endpoints	Key Secondary Endpoints	Stages of ACHIEVE
• Adult patients living with DM1 • Ages 18 to 49 years • ~64 adult participants	• Safety and tolerability	• Pharmacokinetics • Change from baseline of: – Splicing – <i>DMPK</i> RNA expression – Multiple assessments of muscle strength and function	• 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**

Multiple Ascending Dose Stage of 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

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