May 20, 2024

A Letter to the Myotonic Dystrophy Community

From Dyne Therapeutics

At Dyne we are working to advance our proprietary FORCE™ platform to overcome the limitations of muscle tissue delivery, with the stated mission to deliver life-transforming therapies for people living with serious muscle diseases. Our initial focus includes programs for myotonic dystrophy type 1 (DM1), Duchenne muscular dystrophy (DMD) and facioscapulohumeral muscular dystrophy (FSHD), with the hope of delivering on a shared goal with the community- stopping or reversing disease progression. You can learn more about the FORCE™ platform and our pipeline priorities here: https://www.dyne-tx.com/our-forcetm-platform/. Our purpose and passion are fueled by our continuous engagement and active dialogue with the communities we serve.

In January we shared initial clinical data for DYNE-101 from the earliest cohorts (study groups) as part of the Phase 1/2 ACHIEVE multiple ascending dose (MAD) trial design. Upon the release of that early data, we partnered with patient advocacy organizations and the patient community to share our data and our program progress, as well as to answer questions. We value transparency to build trust.

Recognizing a shared sense of urgency with the Myotonic Dystrophy community to accelerate potential therapies, we are pleased to now share new clinical data from the ongoing DYNE-101 ACHIEVE trial. This is in advance of our anticipated plan to provide data in the second half of 2024. Our clinical data continues to demonstrate the promise of the FORCE™ platform. The most recent data shares efficacy data from 40 adult DM1 patients enrolled in the randomized, placebo-controlled multiple ascending dose (MAD) portion of the DYNE-101 ACHIEVE trial, including 12-month data from the 1.8 mg/kg Q4W (approximate ASO dose) cohort, 6-month data from the 3.4 mg/kg Q4W cohort, and 3-month data from the 5.4 mg/kg Q8W cohort.

Key findings from ACHIEVE include:

Splicing

- DYNE-101 continued to show dose dependent splicing correction as seen in earlier cohorts in ACHIEVE. Patients in the 5.4 mg/kg Q8W cohort had a 27% mean splicing correction from baseline across a broad, 22-gene panel at 3 months, with all

participants demonstrating splicing correction. As a reminder, based on our preclinical work, input from others in the field and natural history, we believe 20-25% splicing correction is needed to drive functional benefit for patients. The most recent data shared today on function reinforce this belief that changes in splicing will translate into functional benefits for patients.

Function

- **Myotonia (vHOT):** DYNE-101 demonstrated an improvement in myotonia as measured by video hand opening time (vHOT) in all reported cohorts.
- **Strength & Timed Assessments:** DYNE-101 demonstrated an improvement in muscle strength as measured by Quantitative Myometry Testing (QMT), a test of muscle strength and fatigue, and early and sustained potential benefit in 10-Meter Walk/Run Test and 5 Times Sit to Stand Test.

Patient Reported Outcomes (PROs)

- **Myotonic Dystrophy Health Index (MDHI):** DYNE-101 demonstrated an overall improvement in the MDHI and benefit in all 17 subscales, including those that assess peripheral muscles, central nervous system, and gastrointestinal measures. These represent some of the most burdensome manifestations of DM1 and daily quality of life issues for patients and their families.
- **Myotonic Dystrophy Type 1 Activity and Participation Scale (DM1-ACTIV^{C})**: Treatment with DYNE-101 resulted in an improvement in assessment of various activities of daily living as measured by DM1-ACTIV^{C}. .

Safety & Tolerability Data

- DYNE-101 has demonstrated a favorable safety profile[1], inclusive of the 56 patients enrolled through the 6.8 mg/kg Q8W cohort of the MAD portion of the ACHIEVE trial. The majority of treatment-emergent adverse events were mild or moderate and no related serious treatment-emergent adverse events have been identified.

We look forward to sharing this data and our program-updates in more detail with the community over the coming weeks. Similarly, as the study progresses and additional data report out, we anticipate additional opportunities to collectively advance our understanding of DYNE-101 as a potential therapy for DM1.

Thank You

Our therapy development efforts and the other critical studies being conducted to better understand serious muscle diseases, progression and symptom burden would not be possible without the generous participation of community members like you. The insights and expertise provided by you have contributed to the development of our science and the design of our programs. Our recent publication in the journal Research Involvement and Engagement, *Patient Engagement in Clinical Trial Design for Rare Neuromuscular Disorders: Impact on the DELIVER and ACHIEVE Clinical Trials (* https://rdcu.be/du0ID*),* delivered on this commitment by documenting how your input enabled our ACHIEVE trial of DYNE-101 for DM1. We recognize and acknowledge the time, hard work and thought provided by community participants and we are deeply grateful. Thank you.

With gratitude,

Dyne Therapeutics

Q4W: dosing once every four weeks; Q8W: dosing once every eight weeks

[1] DYNE-101 safety data as of May 8, 2024