Dyne Therapeutics Reports New Clinical Data Showing Compelling Impact on Multiple Measures of Myotonic Dystrophy Type 1 (DM1); Dyne Plans to Initiate Registrational Expansion Cohort to Support Potential Submission for U.S. Accelerated Approval for DYNE-101 in DM1 in H1 2026

January 10, 2025

- DYNE-101 in DM1: Dyne plans to initiate global Registrational Expansion Cohort of ACHIEVE trial with registrational dose of 6.8 mg/kg Q8W following study data showing splicing correction and robust and sustained functional improvements; potential to support H1 2026 submission for U.S. Accelerated Approval -

- DYNE-251 in Exon 51 DMD: Based on recent FDA feedback, pursuing U.S. Accelerated Approval with dystrophin as surrogate endpoint; data from ongoing Registrational Expansion Cohort in DELIVER trial expected late 2025 with potential to support early 2026 regulatory submission -

- Investor event today, January 10th at 8:00 a.m. ET -

WALTHAM, Mass., Jan. 10, 2025 (GLOBE NEWSWIRE) -- Dyne Therapeutics, Inc. (Nasdaq: DYN) (Dyne), a clinical-stage neuromuscular disease company focused on advancing life-transforming therapeutics for people living with genetically driven diseases, today announced new clinical data from its ongoing Phase 1/2 ACHIEVE trial of DYNE-101 in patients with myotonic dystrophy type 1 (DM1). DYNE-101 continued to demonstrate a compelling impact on key disease biomarkers, including *DMPK* and splicing correction, reversal of disease progression across multiple functional endpoints, and a favorable safety profile. Dyne plans to initiate a global Registrational Expansion Cohort with the potential to support a submission for U.S. Accelerated Approval based on biomarker and functional data in H1 2026.

“The data from the ACHIEVE trial in DM1 show substantial functional benefit across a range of clinical measures, and we are excited to have selected the dose for our Registrational Expansion Cohort,” said Doug Kerr, M.D., Ph.D., chief medical officer of Dyne. “DM1 is a heterogenous and potentially devastating disease, marked by a wide range of symptoms involving the muscle and other tissues. We believe our preclinical and clinical data provide evidence showing that our FORCE™ platform can deliver medicines broadly and deeply into relevant tissues, enabling DYNE-101 to uniquely address the broad manifestations of the disease. Supported by our robust results, we are advancing the development of DYNE-101 rapidly, recognizing the urgency to bring the potential first treatment to people living with DM1.”

“We have the potential to deliver a best-in-class therapy for DM1 patients with a broad range of clinical benefits. Additionally, we are excited about the emerging, highly differentiated profile of DYNE-251 for Duchenne muscular dystrophy which is the first exon 51 skipping treatment candidate to demonstrate a meaningful functional benefit. With both programs, we remain on track to complete enrollment in our Registrational Expansion Cohorts in 2025 with the goal to submit applications for accelerated approvals in 2026 in hopes of transforming the treatment paradigm for patients,” said John Cox, president and chief executive officer of Dyne.

“The ACHIEVE trial data represent a significant step forward and underscore the potential of DYNE-101 to address many of the most challenging symptoms experienced by individuals living with DM1,” said Dr. James Lilleker, Neurologist, UK, and principal investigator in the ACHIEVE trial. “In addition to the favorable safety profile, I am particularly excited by the improvements observed in measures of strength and mobility, as well as effects on CNS manifestations suggested by the trends seen in the MDHI data. These data reflect clinically meaningful aspects of patients’ functional abilities and daily lives.”

Phase 1/2 ACHIEVE Trial of DYNE-101 in DM1

ACHIEVE is a randomized, placebo-controlled, double-blind, Phase 1/2 clinical trial designed with a Multiple Ascending Dose (MAD) portion to evaluate the safety and efficacy of DYNE-101 in DM1. The study was designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of DYNE-101 administered intravenously. The study protocol also allows for the creation of a Registrational Expansion Cohort to support a submission for U.S. Accelerated Approval.

Activity of DYNE-101 was assessed using key biomarkers including *DMPK* and the Composite Alternative Splicing Index (CASI-22). Myotonia, muscle strength, timed function tests, and patient reported outcomes, including CNS-related disease manifestations, were also assessed in the trial. CASI-22 was used to assess the utility of splicing correction to serve as surrogate endpoint and to support selection of a dose for the Registrational Expansion Cohort.

Dyne measured splicing in all study participants using CASI-22 to quantify the splicing abnormalities that directly lead to the hallmark and multi-organ symptoms of DM1, including myotonia, loss of muscle strength and function, cardiac arrhythmias, gastrointestinal problems, and cognitive impairments.

Dyne has completed the MAD portion of the study and selected the 6.8 mg/kg Q8W dose (approximate ASO dose) to be evaluated in the Registrational Expansion Cohort based on its potential to demonstrate broad functional benefit.

DYNE-101 Efficacy Data

Today, Dyne reported efficacy data from adult DM1 patients enrolled in the randomized, placebo-controlled MAD portion of the DYNE-101 ACHIEVE trial, including data from the 6.8 mg/kg Q8W cohort (n=8) at up to 6 months.

At the 6.8 mg/kg Q8W dose, DYNE-101 resulted in significant splicing correction at 3 months compared to baseline, which was associated with improvement in multiple functional endpoints, beginning at 3 months and continuing at 6 months.

Key findings from ACHIEVE include:

Biomarker Data and Functional Improvements

- ***DMPK***: Analysis of muscle biopsy data for the 6.8 mg/kg Q8W cohort demonstrated a substantial knockdown of *DMPK* (DYNE-101 molecular target) RNA levels.
- **Composite Alternative Splicing Index (CASI-22):** Splicing correction at 3 months for the 6.8 mg/kg Q8W cohort was robust and was associated with improvement in multiple functional endpoints, supporting CASI-22 at 3 months as a surrogate endpoint for potential U.S. Accelerated Approval.
- **Myotonia (vHOT):** Early and sustained improvement in myotonia as measured by video hand opening time (vHOT) was seen in the 6.8 mg/kg Q8W cohort, as well as at low doses with modest splicing correction, deepening with more time on drug.
- **Strength and Timed Assessments:** Functional measures such as 5 Times Sit to Stand Test, reflective of muscle strength and dynamic balance, Quantitative Myometry Testing (QMT), a test of muscle strength and fatigue, and the 10-Meter Walk/Run Test (10MWR) showed early and sustained clinical benefit at the 6.8 mg/kg Q8W dose.

Patient Reported Outcomes (PROs)

- **Myotonic Dystrophy Health Index (MDHI):** DYNE-101 at the 6.8 mg/kg Q8W doses showed encouraging trends on the MDHI patient reported outcome (PRO) measure, including those subscales that assess central nervous system disease manifestations. These represent some of the most burdensome manifestations of DM1 and daily quality of life issues for patients and their families.

DYNE-101 Safety and Tolerability Data[1]

- Dyne also reported safety and tolerability data from 56 patients enrolled through the 6.8 mg/kg Q8W cohort of the ACHIEVE trial. DYNE-101 demonstrated a favorable safety profile. The majority of treatment emergent adverse events were mild or moderate, and no related serious treatment emergent adverse events have been identified.
    - Approximately 855 doses have been administered, representing over 72-patient years of follow-up, with some patients being followed for up to 2.1 years.

Clinical Plan to Support DYNE-101 Product Registration and Upcoming Milestones

- Based on previous dialogue with the Center for Drug Evaluation and Research (CDER) division of the U.S. Food and Drug Administration (FDA), Dyne continues to pursue accelerated approval in the U.S. based on splicing as a surrogate endpoint.

- Dyne plans to initiate a global placebo-controlled Registrational Expansion Cohort in ACHIEVE that includes approximately 32 patients at the 6.8 mg/kg Q8W dose. The primary endpoint for this cohort will be mean splicing correction at 3 months as measured by the composite alternative splicing index (CASI-22), supported by clinically meaningful measures of muscle strength and function. The Registrational Expansion Cohort will also assess various quality of life and CNS-related endpoints (e.g., fatigue, daytime sleepiness). Dyne intends that the data from the approximately 32-patient Registrational Expansion Cohort and the 56 patients from the long-term extension portion of ACHIEVE will support a submission for U.S. Accelerated Approval. Dyne is also pursuing expedited approval pathways globally for DYNE-101.

- Dyne anticipates completion of enrollment of the Registrational Expansion Cohort in mid-2025 and submission for U.S. Accelerated Approval in H1 2026.

Phase 1/2 DELIVER Trial of DYNE-251 in DMD

- DELIVER is a Phase 1/2 clinical trial designed to study the safety and efficacy of DYNE-251 in patients with DMD who are amenable to exon 51 skipping. DELIVER was designed to be a registrational trial, and Dyne is pursuing expedited approval pathways globally for DYNE-251.

- Dyne previously reported that DYNE-251 demonstrated unprecedented dystrophin expression and functional improvement on multiple measures including Stride Velocity 95th Centile (SV95C).

- Dyne reported today updated safety and tolerability data based on 54 participants enrolled in the DELIVER trial. DYNE-251 demonstrated a favorable safety profile, and the majority of treatment emergent adverse events were mild or moderate.[2] The safety profile remains unchanged, and no new treatment-related serious adverse events have been observed since the prior update provided as of August 21, 2024. Approximately 837 doses have been administered to date in the DELIVER trial, representing over 65 patient-years of follow-up, with some patients followed for up to 2.2 years.
- Based on recent feedback from the FDA, Dyne continues to pursue U.S. Accelerated Approval based on dystrophin as a surrogate endpoint.

- Dyne is currently enrolling a 20 mg/kg (approximate PMO dose) Q4W Registrational Expansion Cohort of approximately 32 participants as part of the DELIVER trial. Dyne anticipates completion of enrollment in Q1 2025 with data from this cohort expected in late 2025.

Investor Conference Call and Webcast

Dyne will host a live conference call and webcast event today, January 10, 2025, at 8:00 a.m. ET. The live webcast will be available on the Events & Presentations page of the Investors & Media section of Dyne's website and a replay will be accessible for 90 days following the presentation. An accompanying slide presentation and an updated corporate presentation will also be available. To access the presentation, register for the live webcast and replay, please visit https://investors.dyne-tx.com/news-and-events/events-and-presentations.

About DYNE-101

DYNE-101 is an investigational therapeutic being evaluated in the Phase 1/2 global ACHIEVE clinical trial for people living with DM1. DYNE-101 consists of an antisense oligonucleotide (ASO) conjugated to a fragment antibody (Fab) that binds to the transferrin receptor 1 (TfR1) which is highly expressed on muscle. It is designed to enable targeted muscle tissue delivery with the goal of reducing toxic *DMPK* RNA in the nucleus, releasing splicing proteins, allowing normal mRNA processing and translation of normal proteins, and potentially stopping or reversing the disease progression. DYNE-101 has been granted orphan drug designation by the U.S. Food and Drug Administration and the European Medicines Agency for the treatment of DM1.

About Myotonic Dystrophy Type 1 (DM1)

DM1 is a rare, progressive, genetic disease that affects skeletal, cardiac and smooth muscle. It is a monogenic, autosomal dominant disease caused by an abnormal trinucleotide expansion in a region of the *DMPK* gene. This expansion of CTG repeats causes toxic RNA to cluster in the nucleus, forming nuclear foci and altering the splicing of multiple proteins essential for normal cellular function. This altered splicing, or spliceopathy, results in a wide range of symptoms. People living with DM1 typically experience myotonia and progressive weakness of major muscle groups, which can affect mobility, breathing, heart function, speech, digestion and vision as well as cognition. DM1 is estimated to affect more than 40,000 people in the United States and over 74,000 people in Europe, but there are currently no approved disease-modifying therapies.

About DYNE-251

DYNE-251 is an investigational therapeutic being evaluated in the Phase 1/2 global DELIVER clinical trial for people living with DMD who are amenable to exon 51 skipping. DYNE-251 consists of a phosphorodiamidate morpholino oligomer (PMO) conjugated to a fragment antibody (Fab) that binds to the transferrin receptor 1 (TfR1) which is highly expressed on muscle. It is designed to enable targeted muscle tissue delivery and promote exon skipping in the nucleus, allowing muscle cells to create a truncated, functional dystrophin protein, with the goal of stopping or reversing disease progression. DYNE-251 has been granted fast track, orphan drug and rare pediatric disease designations by the U.S. Food and Drug Administration for the treatment of DMD mutations amenable to exon 51 skipping.

In addition to DYNE-251, Dyne is building a global DMD franchise and has preclinical programs targeting other exons, including 53, 45 and 44.

About Duchenne Muscular Dystrophy (DMD)

DMD is a rare disease caused by mutations in the gene that encodes for dystrophin, a protein critical for the normal function of muscle cells. These mutations, the majority of which are deletions, result in the lack of dystrophin protein and progressive loss of muscle function. DMD occurs primarily in males and affects an estimated 12,000 to 15,000 individuals in the U.S. and 25,000 in Europe. Loss of strength and function typically first appears in pre-school age boys and worsens as they age. As the disease progresses, the severity of damage to skeletal and cardiac muscle often results in patients experiencing total loss of ambulation by their early teenage years and includes worsening cardiac and respiratory symptoms and loss of upper body function by the later teens. There is no cure for DMD and currently approved therapies provide limited benefit.

About Dyne Therapeutics

Dyne Therapeutics is focused on discovering and advancing innovative life-transforming therapeutics for people living with genetically driven neuromuscular diseases. Leveraging the modularity of its FORCE™ platform, Dyne is developing targeted therapeutics that are designed to overcome limitations in delivery to muscle tissue and the central nervous system (CNS). Dyne has a broad pipeline for neuromuscular diseases, including clinical programs for myotonic dystrophy type 1 (DM1) and Duchenne muscular dystrophy (DMD) and preclinical programs for facioscapulohumeral muscular dystrophy (FSHD) and Pompe disease. For more information, please visit https://www.dyne-tx.com/, and follow us on X, LinkedIn and Facebook.

Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this press release, including statements regarding Dyne's strategy, future operations, prospects and plans, objectives of management, the potential of the FORCE platform, the therapeutic potential of DYNE-101 and DYNE-251, the anticipated timelines for reporting additional data from the ACHIEVE and DELIVER clinical trials and initiating and enrolling registrational cohorts, expectations regarding the timing and outcome of interactions with global regulatory authorities and the availability of accelerated approval pathways for DYNE-101 and DYNE-251 and expectations regarding the timing of filing applications for U.S. Accelerated Approval, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," or "would," or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Dyne may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the identification and development of product candidates, including the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; the timing of and Dyne's ability to enroll patients in clinical trials; whether results from preclinical studies and initial data from early clinical trials will be predictive of the final results of the clinical trials or future trials; uncertainties as to the FDA's and other regulatory authorities' interpretation of the data from Dyne's clinical trials and acceptance of Dyne's clinical programs and the regulatory approval process;

whether Dyne's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; as well as the risks and uncertainties identified in Dyne's filings with the Securities and Exchange Commission (SEC), including Dyne's most recent Form 10-Q and in subsequent filings Dyne may make with the SEC. In addition, the forward-looking statements included in this press release represent Dyne's views as of the date of this press release. Dyne anticipates that subsequent events and developments will cause its views to change. However, while Dyne may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Dyne's views as of any date subsequent to the date of this press release.

[1] DYNE-101 safety data as of December 6, 2024

[2] DYNE-251 safety data as of November 21, 2024

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