Dyne Therapeutics Announces New Clinical Data from Phase 1/2 DELIVER Trial of DYNE-251 in Duchenne Muscular Dystrophy Demonstrating Unprecedented Dystrophin Expression and Functional Improvement in Multiple Cohorts

September 3, 2024

- Initiating Registrational Cohorts with Update on Path to Registration by Year-End 2024 -
- Virtual Investor Event Today at 8:00 a.m. ET -

WALTHAM, Mass., Sept. 03, 2024 (GLOBE NEWSWIRE) -- Dyne Therapeutics, Inc. (Nasdaq: DYN), a clinical-stage muscle disease company focused on advancing innovative life-transforming therapeutics for people living with genetically driven diseases, today announced new clinical data from its ongoing Phase 1/2 DELIVER trial of DYNE-251 in patients with Duchenne muscular dystrophy (DMD) who are amenable to exon 51 skipping demonstrating unprecedented dystrophin expression and functional improvement in multiple cohorts.

"We believe these data reinforce the opportunity to transform the treatment paradigm for individuals living with Duchenne. In DELIVER, DYNE-251 achieved the highest level of dystrophin expression reported for an exon 51 skipping therapy and improvement in multiple functional endpoints across multiple cohorts that continued with time on therapy," said Wildon Farwell, M.D., MPH, chief medical officer of Dyne. "Our goal has always been to drive dystrophin levels that lead to functional benefit for patients – these data suggest that the distribution across cardiac, diaphragm and other skeletal muscles observed preclinically with the FORCE platform is translating in the clinic. Importantly, treatment with DYNE-251 resulted in meaningful improvements in SV95C, a digital outcome measure approved as a primary endpoint for Duchenne clinical trials in Europe. With these exciting data, we are moving quickly to initiate registrational cohorts in DELIVER, and we continue to pursue expedited approval pathways and plan to provide an update on our path to registration by the end of this year."

This assessment of the DELIVER trial evaluating DYNE-251 includes 6-month biomarker and functional data from 8 male patients enrolled in the 20 mg/kg (approximate PMO dose) cohort who were randomized to receive DYNE-251 or placebo once every four weeks, and 12-month functional data from 6 participants in the 10 mg/kg cohort.[1] DYNE-251 demonstrated dose dependent exon skipping and dystrophin expression and improvement in multiple functional endpoints in both cohorts. Key findings include:

- **Dystrophin expression:** DYNE-251 demonstrated unprecedented dystrophin expression as measured by Western blot. Patients treated with 20 mg/kg of DYNE-251 Q4W had a mean absolute dystrophin expression of 3.71% of normal (unadjusted for muscle content), more than 10-fold higher than the 0.3% reported in a clinical trial of the weekly standard of care, eteplirsen.[2] When adjusting for muscle content, the DYNE-251 treated group reached 8.72% mean absolute dystrophin, which is greater than levels reported by peptide conjugate PMOs in clinical development.[3]
- **Function:** Meaningful improvements in multiple functional endpoints were observed in both the 20 mg/kg and 10 mg/kg DYNE-251 Q4W groups, including North Star Ambulatory Assessment (NSAA), Stride Velocity 95th Centile (SV95C), 10-Meter Walk/Run Time (10-MWR), Time to Rise from Floor. The 10 mg/kg cohort showed continued improvement in all reported measures from 6 months to 12 months.[1]
    - SV95C is a digital objective outcome measure of ambulatory performance in patients' normal daily environment and is approved as a primary endpoint for Duchenne clinical trials in Europe. The change from baseline observed in both the 10 mg/kg and 20 mg/kg cohorts of DELIVER met the published minimal clinically important difference (MCID) as defined by the European Medicines Agency.
- **Safety and Tolerability:** Safety and tolerability data are 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.[4] No related serious treatment emergent adverse events have been identified other than in two participants at the 40 mg/kg dose level with events potentially related to study drug and both participants have recovered. Approximately 675 doses have been administered to date in the DELIVER trial, representing over 50 patient-years of follow-up.

Key Milestones for DELIVER and ACHIEVE Trials

- Based on these data and regulatory interactions, Dyne is initiating registrational cohorts in the DELIVER trial and plans to provide an update on the path to registration by the end of 2024.
- Dyne is also executing its ongoing Phase 1/2 ACHIEVE clinical trial of DYNE-101 in myotonic dystrophy type 1. The safety profile of DYNE-101 continues to be favorable and includes safety data up to the 6.8 mg/kg Q8W cohort.[5] The company continues to engage with global regulators, including the U.S. Food and Drug Administration, and plans to provide an update on the path to registration for DYNE-101, including additional clinical data, by the end of 2024.

Virtual Investor Event

Dyne will host a video webcast event to discuss these DELIVER data today, September 3, 2024, at 8:00 a.m. ET and a replay will be accessible for 90 days following the presentation. An accompanying slide presentation for the event and an updated corporate presentation will also be available. To access these presentations and register for the live webcast and replay, please visit the Investors & Media section of Dyne's website at https://investors.dyne-tx.com/news-and-events/events-and-presentations and the live event may also be accessed here.

About the DELIVER Trial

DELIVER is a Phase 1/2 global clinical trial evaluating DYNE-251, consisting of a 24-week multiple ascending dose (MAD) randomized placebo-controlled period, a 24-week open-label extension and a 96-week long-term extension. The trial, which is designed to be registrational, is enrolling ambulant and non-ambulant males with Duchenne muscular dystrophy (DMD) who are ages 4 to 16 and have mutations amenable to exon 51 skipping. The primary endpoints are safety, tolerability and change from baseline in dystrophin levels as measured by Western blot. Secondary endpoints include measures of muscle function, exon skipping and pharmacokinetics. For more information on the DELIVER trial, visit https://www.clinicaltrials.gov/ (NCT05524883).

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 a clinical-stage muscle disease company focused on advancing innovative life-transforming therapeutics for people living with genetically driven diseases. With its proprietary FORCE™ platform, Dyne is developing modern oligonucleotide therapeutics that are designed to overcome limitations in delivery to muscle tissue. Dyne has a broad pipeline for serious muscle diseases, including clinical programs for myotonic dystrophy type 1 (DM1) and Duchenne muscular dystrophy (DMD) and a preclinical program for facioscapulohumeral muscular dystrophy (FSHD). 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 anticipated timelines for reporting additional data from the ACHIEVE and DELIVER clinical trials and initiating 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 plans to provide future updates on pipeline programs, 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 the Company'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. During the OLE period, all participants in 10 mg/kg cohort were dose escalated to 20 mg/kg Q4W regimen.
2. No head-to-head trials have been conducted comparing DYNE-251 to eteplirsen. Eteplirsen data may not be directly comparable due to differences in trial protocols, dosing regimens and patient populations. Accordingly, these cross-trial comparisons may not be reliable. Eteplirsen data from J Neuromuscul Dis. 2021; 8(6): 989–1001.

3. No head-to-head trials have been conducted comparing DYNE-251 to SRP-5051. SRP-5051 data may not be directly comparable due to differences in trial protocols, dosing regimens, methodologies for calculating muscle content adjusted dystrophin and patient populations. Accordingly, these cross-trial comparisons may not be reliable. SRP-5051 data from Clinical Update: MOMENTUM (Study SRP-5051-201, Part B) Jan. 29, 2024.
4. DYNE-251 safety data as of August 21, 2024.
5. DYNE-101 safety data as of August 20, 2024.

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