# Dyne Therapeutics Myotonic Dystrophy Type 1 Program Achieves Robust RNA Knock Down of Toxic Human Nuclear DMPK in Preclinical Study

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*- In Vivo Model Developed by Dyne Sets New Standard for Evaluating Pharmacodynamics in DM1 -*

*- Preclinical Data Further Validate FORCE™ Platform; IND Submissions Planned for DM1, DMD and FSHD Programs Between Q4'21 and Q4'22 -*

WALTHAM, Mass., Jan. 10, 2021 (GLOBE NEWSWIRE) -- Dyne Therapeutics, Inc. (Nasdaq: DYN), a muscle disease company focused on advancing innovative life-transforming therapeutics for people living with genetically driven diseases, today announced new preclinical data from its myotonic dystrophy type 1 (DM1) program demonstrating robust RNA knockdown of toxic human nuclear *DMPK*, the genetic basis of the disease.

Dyne's FORCE™ platform leverages the importance of transferrin 1 receptor, TfR1, in muscle biology as the foundation for its novel approach. TfR1, which is highly expressed on the surface of muscle cells, is required for iron transport into muscle cells. Dyne links therapeutic payloads to its TfR1-binding fragment antibody (Fab) to develop targeted therapeutics for muscle diseases. Dyne's DM1 lead candidate consists of a Fab conjugated to an antisense oligonucleotide (ASO) to enable targeted delivery to muscle tissue to reduce accumulation of toxic *DMPK* RNA in the nucleus, release splicing proteins, allow normal mRNA processing and translation of normal proteins, and potentially stop or reverse the disease.

These new preclinical data build on previous results showing significant reduction in cytoplasmic wild type *DMPK* RNA in a mouse model that expresses human TfR1(hTfR1). To assess the ability of its lead DM1 candidate to reduce toxic human nuclear *DMPK* RNA, Dyne developed an innovative hTfR1/DMSXL mouse model that expresses the human TfR1 and carries a human *DMPK* gene that represents a severe DM1 phenotype with more than 1,000 CTG repeats. In this model, two doses (2 x 10 mg/kg) of Dyne's candidate resulted in significant toxic human nuclear *DMPK* knockdown at 14 days: 60 percent in the heart; 56 percent in the diaphragm; 54 percent in the tibialis anterior and 39 percent in the gastrocnemius. In the study, Dyne's candidate was well tolerated. Dyne expects to share data from the hTfR1/DMSXL model at a scientific meeting during 2021.

"At Dyne we are focused on developing therapies designed to target the genetic basis of the disease with the goal of delivering disease modification for patients," said Romesh Subramanian, Ph.D., chief scientific officer of Dyne. "Multiple genetic studies in DM1 have suggested that a 30 to 50 percent knockdown of toxic human *DMPK* has the potential to be disease modifying. We are very pleased with the robust toxic human *DMPK* reduction observed in the hTfR1/DMSXL model, which, along with our previous preclinical data showing correction of splicing and reversal of myotonia, indicates the potential to have an impact for patients living with a disease with no approved therapies. We intend to utilize this novel model to conduct IND-enabling work as we progress toward the clinic."

"In DM1, it is critical to target the nucleus where the disease-causing toxic *DMPK* resides and forms foci," said Valeria Sansone, M.D., Ph.D., Clinical and Scientific Director, Clinical Center NeMO, Milan; Associate Professor of Neurology, University of Milan. "The innovative preclinical model used in this study has the potential for translation into human disease. The data demonstrate compelling reduction in levels of *DMPK* RNA and suggest this approach may be effective in targeting nuclear *DMPK* and delivering a therapeutic to muscle for diseases such as DM1."

The new preclinical data from the hTfR1/DMSXL model are included in an updated corporate presentation available in the Investors & Media section of the Company's website and add to the robust *in vitro* and *in vivo* findings generated previously in Dyne's DM1 program:

- Reduction in nuclear foci and correction of splicing in DM1 patient cells
- Correction of splicing and reversal of myotonia in well-validated $HSA^{LR}$ model
- Enhanced muscle distribution as evidenced by reduced levels of cytoplasmic wild type *DMPK* RNA in non-human primates (NHPs)
- Durability of response of up to 12 weeks after a single dose in a wild type mouse model
- Favorable tolerability observed in multiple NHP studies

"Today's exciting data further validate our FORCE platform which drives our efforts to deliver targeted, modern oligonucleotide therapies with the potential to be life-transforming for patients with serious muscle diseases," said Joshua Brumm, president and chief executive officer of Dyne. "We remain on track to submit INDs for our three programs between the fourth quarter of 2021 and the fourth quarter of 2022, with DM1 and DMD submissions anticipated in the earlier part of that window, followed later by FSHD."

**About Myotonic Dystrophy Type 1 (DM1)**

DM1 is a rare, progressive, genetic disease that affects skeletal, cardiac and smooth muscles. It is a monogenic, autosomal dominant disease caused by an abnormal expansion in a region of the *DMPK* gene. The expansion in the number of CTG triplet 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 results in a wide range of symptoms. People living with DM1 typically experience 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 Therapeutics**

Dyne Therapeutics is building a leading muscle disease company focused on advancing innovative life-transforming therapeutics for people living with genetically driven diseases. The Company is utilizing its proprietary FORCE™ platform to overcome the current limitations of muscle tissue delivery

with modern oligonucleotide therapeutic candidates. Dyne is developing a broad portfolio of therapeutics for muscle diseases, including programs in myotonic dystrophy type 1 (DM1), Duchenne muscular dystrophy (DMD) and facioscapulohumeral muscular dystrophy (FSHD). For more information, please visit www.dyne-tx.com, and follow us on Twitter, 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, plans, objectives of management, the expected timeline for submitting investigational new drug applications, the potential advantages of Dyne's FORCE platform and programs, expectations regarding the translation of preclinical findings to human disease and plans to conduct additional preclinical studies, 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 conduct of research activities, the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies; the timing of and Dyne's ability to submit and obtain regulatory approval for investigational new drug applications; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; Dyne's ability to obtain sufficient cash resources to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; the impact of the COVID-19 pandemic on Dyne's business and operations; 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.

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