Entrada Therapeutics Reports Positive Preliminary Data in Healthy Volunteers from Phase 1 ENTR-601-44-101 Trial for Duchenne Muscular Dystrophy

June 24, 2024

– ENTR-601-44 was well-tolerated in healthy volunteers with no serious adverse events, no drug-related adverse events and no clinically significant changes or trends noted in vital signs, ECGs, physical exams or laboratory assessments –

– ENTR-601-44 demonstrated significant plasma concentration, muscle concentration and exon skipping, at levels that suggest the potential for a clinically meaningful starting dose in planned upcoming patient trials –

– Phase 2 planning underway for separate ENTR-601-44 and ENTR-601-45 clinical trials with regulatory filings anticipated in Q4 2024 –

BOSTON, June 24, 2024 (GLOBE NEWSWIRE) -- Entrada Therapeutics, Inc. (Nasdaq: TRDA) is a clinical-stage biopharmaceutical company aiming to transform the lives of patients by establishing a new class of medicines that engage intracellular targets long considered inaccessible. The Company today announced positive preliminary data from its Phase 1 clinical trial, ENTR-601-44-101. Data will be featured in a presentation at the 29th Annual Congress of the World Muscle Society, taking place in Prague, Czechia from October 8-12, 2024.

“We are excited to present the first clinical data from our Duchenne franchise, led by ENTR-601-44. ENTR-601-44 was well tolerated in healthy volunteers and we are pleased to see significant plasma concentration, muscle concentration and exon skipping. We achieved the goals of the ENTR-601-44-101 trial, including the identification of a clinically relevant starting dose for the planned Phase 2 global patient study. Based on the cumulative data to date, we expect to see a significant accumulation of exon skipping and dystrophin production in patients, which we believe will lead to an improvement in functional outcomes after multiple doses,” said Dipal Doshi, Chief Executive Officer at Entrada Therapeutics.

He continued, “Patients are at the core of our mission at Entrada. We believe that the flexibility of our EEV-based approach will allow the therapeutic to be tailored to meet the changing needs of growing pediatric and young adult patients via dosing and other important parameters. Today’s update represents a clear validation and differentiation of Entrada’s approach and brings us one step closer to providing a potential treatment for this relentlessly progressive neuromuscular disease.”

The primary objective of Entrada’s Phase 1 clinical trial was to evaluate the safety and tolerability of a single dose of ENTR-601-44. ENTR-601-44-101 also evaluated pharmacokinetics and target engagement, as measured by exon skipping in the skeletal muscle. The study included a total of 32 healthy male volunteers across four cohorts, with each cohort consisting of six participants receiving ENTR-601-44 and two participants receiving a placebo control. The doses administered across the cohorts were 0.75 mg/kg, 1.5 mg/kg, 3 mg/kg and 6 mg/kg.

There were no serious adverse events, no drug-related adverse events and no clinically significant changes or trends noted in vital signs, ECGs, physical exams or laboratory assessments observed in the trial. The study demonstrated target engagement as measured by exon skipping on a ng/g of tissue adjusted basis supporting the importance of endosomal escape to therapeutic index optimization. Muscle concentration was detected in all six subjects in the 6 mg/kg dose cohort (mean of 53.8 ng/g, range 40 ng/g-73.5 ng/g) and mean target engagement as measured by exon skipping was 0.44% (range 0.3-0.65%). Exon skipping was statistically significant compared to the placebo control ($p<0.005$) in the 6 mg/kg dose cohort. These results are based upon data collected to date and are aggregated based upon the placebo and study drug groups.

“I am encouraged to see the preliminary results of Entrada’s Phase 1 clinical trial of ENTR-601-44. These data in healthy volunteers represent a potentially transformative treatment option for boys and young men living with Duchenne who are exon 44 skipping amenable, a population for which there are currently no exon skipping options,” said Francesco Muntoni, MD, Professor of Paediatric Neurology. “The data on safety generated so far are very encouraging. This, coupled with the possibility for Entrada’s EEV-therapeutics to allow for dosing intervals of at least six weeks, would significantly reduce the burden of the administration of this novel therapeutic compound and I am sure this information will be positively received by the patient community.”

Based on the positive preliminary data from the Phase 1 clinical trial, the Company is on track to submit regulatory applications in the fourth quarter of 2024 to initiate separate global Phase 2 clinical trials for ENTR-601-44 in patients with Duchenne who are exon 44 skipping amenable and for ENTR-601-45 in patients with Duchenne who are exon 45 skipping amenable. In addition, the Company plans to submit regulatory applications in 2025 to initiate a global Phase 2 clinical trial for its third Duchenne candidate, ENTR-601-50, in patients who are exon 50 skipping amenable.

About ENTR-601-44
ENTR-601-44, a proprietary Endosomal Escape Vehicle (EEV™)-conjugated phosphorodiamidate morpholino oligomer (PMO), is the lead product candidate within Entrada’s Duchenne muscular dystrophy franchise from its growing pipeline of EEV-therapeutics. Each EEV-PMO therapeutic candidate has an oligonucleotide sequence designed and optimized for the specific subpopulation of interest. ENTR-601-44 is designed to address the underlying cause of Duchenne due to mutated or missing exons in the DMD gene. ENTR-601-44, an investigational therapy for the potential treatment of people living with Duchenne who are exon 44 skipping amenable, is being evaluated for its potential to restore the mRNA reading frame and allow for the translation of dystrophin protein that is slightly shortened but still functional.

About Duchenne Muscular Dystrophy (DMD)
Duchenne muscular dystrophy is a rare, genetic disease that causes progressive muscle degeneration and weakness throughout the body. DMD is caused by mutations in the DMD gene, which leads to inadequate production of dystrophin, a protein essential to maintaining the structural integrity and function of muscle cells. DMD causes progressive loss of muscle function throughout the body, which limits mobility and causes heart and respiratory complications in the later stages of the disease. Currently approved therapies for DMD seek to improve dystrophin production, but to date,

the clinical benefits of these products have not been confirmed.

About Entrada Therapeutics
Entrada Therapeutics is a clinical-stage biopharmaceutical company aiming to transform the lives of patients by establishing a new class of medicines that engage intracellular targets that have long been considered inaccessible. The Company's Endosomal Escape Vehicle (EEV™)-therapeutics are designed to enable the efficient intracellular delivery of a wide range of therapeutics into a variety of organs and tissues, resulting in an improved therapeutic index. Through this proprietary, versatile and modular approach, Entrada is advancing a robust development portfolio of RNA-, antibody- and enzyme-based programs for the potential treatment of neuromuscular, ocular, metabolic and immunological diseases, among others. The Company's lead oligonucleotide programs are in development for the potential treatment of people living with Duchenne who are exon 44, 45 and 50 skipping amenable. Entrada has partnered to develop a clinical-stage program, VX-670, for myotonic dystrophy type 1.

For more information about Entrada, please visit our website, www.entradatx.com, and follow us on LinkedIn.

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 Entrada's strategy, future operations, prospects and plans, objectives of management, the validation and differentiation of Entrada's approach and its ability to provide a potential treatment for patients, the translatability of the preliminary ENTR-601-44-101 data to the complete data set, expectations regarding the starting dose for Entrada's planned Phase 2 clinical trial for ENTR-601-44, expectations regarding significant accumulation of exon skipping and dystrophin production in patients, expectations regarding improvement in functional outcomes for patients after multiple doses of ENTR-601-44, expectations regarding the importance of endosomal escape to therapeutic index optimization, expectations regarding the timing of regulatory filings for the planned Phase 2 clinical trials for ENTR-601-44 and ENTR-601-45 in the fourth quarter of 2024, and ENTR-601-50 in 2025, the ability to recruit for and complete a global Phase 2 trial for ENTR-601-44, ENTR-601-45 and ENTR-601-50, the potential of Entrada's EEV product candidates, including the potential for ENTR-601-44 to be a transformative treatment option, and EEV platform, and the continued development and advancement of ENTR-601-44, ENTR-601-45 and ENTR-601-50 for the treatment of Duchenne and the partnered product VX-670 for the treatment of myotonic dystrophy type 1, 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. Entrada 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 and the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical and clinical studies; the timing of and Entrada's ability to submit and obtain regulatory clearance and initiate clinical trials; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; whether preliminary clinical data will be predictive of final clinical data; whether Entrada's cash resources will be sufficient to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; as well as the risks and uncertainties identified in Entrada's filings with the Securities and Exchange Commission (SEC), including the Company's most recent Form 10-K and in subsequent filings Entrada may make with the SEC. In addition, the forward-looking statements included in this press release represent Entrada's views as of the date of this press release. Entrada anticipates that subsequent events and developments will cause its views to change. However, while Entrada 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 Entrada's views as of any date subsequent to the date of this press release.

Investor and Media Contact
Caileigh Dougherty
Head of Investor Relations & Corporate Communications
cdougherty@entradatx.com