Design Therapeutics Announces Positive Preclinical Data Highlighting Disease-Modifying Potential of its Novel DM1 GeneTACs as a Treatment for Myotonic Dystrophy Type-1

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Data to be Presented during the 2021 Virtual Myotonic Dystrophy Foundation Annual Conference

CARLSBAD, Calif., Sept. 08, 2021 (GLOBE NEWSWIRE) -- Design Therapeutics, Inc. (Nasdaq: DSGN), a biotechnology company developing small molecule treatments for degenerative genetic disorders, today announced new preclinical data from its novel DM1 GeneTAC™ program, which demonstrated a near-complete resolution of disease-causing foci and correction of splicing defects in myotonic dystrophy type-1 (DM1) patient cells. These data will be presented in a poster titled "*Small molecule GeneTACs reduce toxic nuclear foci and correct splicing defects in multiple DM1 cell types,*" at the 2021 Virtual Myotonic Dystrophy Foundation Annual Conference, being held virtually from September 10-11, 2021.

"DM1 is a devastating multi-system genetic disorder caused by a nucleotide repeat expansion in the DMPK gene that leads to progressive muscle weakness, and also affects the heart, the gastrointestinal and endocrine systems, and ultimately impairs respiration. There are currently no approved treatment options," said João Siffert, M.D., president and chief executive officer of Design Therapeutics. "Our DM1 GeneTACs are small molecules designed to address the underlying root causes of DM1 by specifically blocking transcription of the mutant DMPK gene."

"New preclinical data demonstrated the ability of our DM1 GeneTACs to potently and selectively block expression of the mutant DMPK gene in DM1 patient cells. Reduction of nuclear foci was associated with clear correction of splicing defects that are involved in the multi-system pathophysiology of DM1," added Abhi Bhat, Ph.D., head of R&D of Design Therapeutics. "We believe these data are highly meaningful both for the potential treatment of patients with DM1, as well as further validation of our GeneTAC approach to treating inherited degenerative diseases."

Design is leveraging its proprietary GeneTAC (gene targeted chimera) platform to develop therapeutic candidates for inherited diseases driven by nucleotide repeat expansions, such as DM1. DM1 is caused by an increased number of CTG triplet repeats in the DMPK gene. Transcription of the mutant DMPK gene forms pre-mRNAs with large CUG hairpin loops that trap splicing proteins in the nucleus. Specifically, the mutant DMPK pre-mRNAs trap a critical CUG-binding protein called muscle blind-like protein 1 (MBNL1), which leads to the formation of toxic nuclear foci. These foci inhibit the ability of MBNL1 to process pre-mRNAs, which when mis-spliced disrupt muscle development and function that is characteristic of DM1.

Design's DM1 GeneTAC program is designed to block transcription of the mutant DMPK gene and prevent the formation of the CUG hairpin structures that trap MBNL1, thereby addressing the underlying cause of the disease. New preclinical data being presented from studies of Design's DM1 GeneTAC showed:

- near-complete resolution of toxic nuclear foci of greater than 90% in DM1 patient fibroblasts and myoblasts, with dose-responsive resolution at concentrations less than 100 nM;
- near-complete correction of splicing defects in the MBNL1 gene of greater than 90% in DM1 patient myoblasts, also at concentrations less than 100 nM;
- highly selective knockdown of the mutant DMPK allele without affecting the normal, wild-type allele following a 72-hour treatment period in patient fibroblasts;
- resolution of CUG foci at substantially greater levels than with antisense oligonucleotide controls in both primary myotubes and primary myoblast patient cells;
- redistribution of MBNL1 from aggregates in DM1 patient-derived myotubes; and
- biodistribution to key tissues implicated in DM1, skeletal muscle and heart, at concentrations above those needed to reverse splicing defects *in vitro* at doses that were well-tolerated in rodents.

These data, supplemented by a growing body of data from the company's GeneTAC program for Friedrich ataxia, support the continued advancement of the DM1 program and rationale to evaluate the utility of the GeneTAC approach in multiple additional nucleotide repeat expansion diseases.

About Design Therapeutics
Design Therapeutics, Inc. (Nasdaq: DSGN) is a biotechnology company developing a new class of therapies based on a platform of gene targeted chimera (GeneTAC™) small molecules. The company's GeneTAC molecules are designed to either turn on or turn off a specific disease-causing gene to address the underlying cause of disease. Design's lead program is focused on the treatment of Friedreich ataxia, followed by a program in myotonic dystrophy type-1 and discovery efforts for multiple other serious degenerative disorders caused by nucleotide repeat expansions. For more information, please visit designtx.com.

Forward Looking Statements
Statements in this press release that are not purely historical in nature are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements related to: preclinical data and the relevance of such data; Design's DM1 GeneTAC program and its design and potential therapeutic benefits and advantages; and Design's GeneTAC approach. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "believes," "designed to," "anticipates," "plans," "expects," "intends," "will," "goal," "potential" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Design's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks associated with the

process of discovering, developing and commercializing therapies that are safe and effective for use as human therapeutics and operating as a development stage company; Design's ability to develop, initiate or complete preclinical studies and clinical trials for, obtain approvals for and commercialize any of its product candidates; the risk that promising early research or clinical trials do not demonstrate safety and/or efficacy in later preclinical studies or clinical trials; changes in Design's plans to develop and commercialize its product candidates; the risk that Design may not obtain approval to market its product candidates; uncertainties associated with performing clinical trials, regulatory filings and applications; risks associated with reliance on third parties to successfully conduct clinical trials and preclinical studies; changes in Design's plans to develop and commercialize its product candidates; Design's ability to raise any additional funding it will need to continue to pursue its business and product development plans; regulatory developments in the United States and foreign countries; Design's reliance on key third parties, including contract manufacturers and contract research organizations; Design's ability to obtain and maintain intellectual property protection for its product candidates; our ability to recruit and retain key scientific or management personnel; competition in the industry in which Design operates; and market conditions. For a more detailed discussion of these and other factors, please refer to Design's filings with the Securities and Exchange Commission ("SEC"), including under the "Risk Factors" heading of Design's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, as filed with the SEC on August 9, 2021. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and Design undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof, except as required by law.

Contact:
Chelcie Lister
THRUST Strategic Communications
(910) 777-3049
chelcie@thrustsc.com