Design Therapeutics to Present Preclinical Data Highlighting the Potential of its GeneTAC™ Small Molecule, DT-216, for the Treatment of Friedreich Ataxia at ICAR 2022

October 17, 2022

Company On-track to Report Initial Data from Friedreich Ataxia Phase 1 Trial of DT-216 in the Fourth Quarter of 2022

CARLSBAD, Calif., Oct. 17, 2022 (GLOBE NEWSWIRE) -- Design Therapeutics, Inc. (Nasdaq: DSGN), a clinical-stage biotechnology company developing treatments for serious degenerative genetic diseases, today announced that preclinical data for the company's novel GeneTAC™ small molecule, DT-216, as a potential treatment for Friedreich ataxia (FA) will be presented during an oral session at the International Congress for Ataxia Research (ICAR) 2022. The data were included in the company's Investigational New Drug (IND) application for DT-216, which is currently being evaluated in a Phase 1 clinical trial. The conference will be held in Dallas, Texas from November 1-4, 2022.

FA is a devastating multisystem degenerative disease caused by a mutation characterized by a GAA repeat expansion in the frataxin (FXN) gene that impairs FXN transcription and reduces gene expression. Reduced FXN transcription results in mitochondrial and cellular dysfunction and leads to all FA disease manifestations, including neurological deficits such as loss of balance and coordination, cardiomyopathy, arrhythmias, diabetes and other serious symptoms. DT-216 is a GeneTAC™ small molecule designed to specifically target the GAA repeat expansion mutation and restore endogenous FXN transcription.

The preclinical data support the potential for DT-216 to restore FXN gene expression, improve mitochondrial function and address the root cause of FA. Key findings of the presentation include:

- DT-216 dose-dependently increased FXN in peripheral white blood cells from multiple FA donors and in multiple FA patient cell models
    - Administration of DT-216 increased FXN mRNA by approximately 10-fold in peripheral blood mononuclear cells (PBMCs) collected directly from FA patients (N=23 donors with >100 to > 1500 GAA repeats)
    - Administration of DT-216 at ~ 10nM, the 90% maximal effective concentration (EC90) for the molecule, for 14 days in FA patient-derived neurons restored FXN protein to levels comparable to non-FA neurons
- DT-216 improved mitochondrial respiration in FA B-lymphoblastoid cells and patient-derived cardiomyocytes as measured using a Seahorse XFp Analyzer

Design is currently evaluating DT-216 in a Phase 1 clinical trial in adult patients with FA. The company plans to report initial data, including safety, tolerability, pharmacokinetics and FXN expression levels from the single-ascending dose portion of the trial in the fourth quarter of 2022.

Details of the oral presentation are as follows:

Title: GeneTAC™ small molecules increase frataxin in a mouse model of Friedreich ataxia, restore FXN and improve mitochondrial function in patient-derived cells, and achieve sustained biodistribution in CNS and heart in rats and non-human primates
Session Title: Plenary Session: Emerging and Existing Therapeutics
Date/Time: Thursday, Nov. 3, 2022, at 9:15 a.m. CDT

About Design Therapeutics
Design Therapeutics is a clinical-stage biotechnology company developing a new class of therapies based on its platform of GeneTAC™ gene targeted chimera small molecules. The company's GeneTAC™ molecules are designed to either dial up or dial down the expression of 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 projections from preclinical data, including the potential for DT-216 to restore FXN gene expression, improve mitochondrial function, and address the root cause of FA; Design's expectations for reporting data and the timing thereof; the potential benefits of FXN restoration; and the capabilities and potential advantages of Design's pipeline of GeneTAC™ molecules. 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 "designed to," "on track to," "plans," "expects," "will," "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 conducting a clinical trial and patient enrollment, which is affected by many factors, and any difficulties or delays encountered with such clinical trial or patient enrollment may delay or otherwise adversely affect Design's ongoing Phase 1 clinical trial for DT-216; the process of discovering and developing 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 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 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; 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; Design's ability to recruit and retain key scientific or management personnel; competition in the industry in which Design operates, which may result in others discovering, developing or commercializing competitive products before or more successfully than Design; 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, 2022, as filed with the SEC on August 8, 2022. 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:
Investors:
Chelcie Lister
THRUST Strategic Communications
chelcie@thrustsc.com

Media:
Amanda Sellers
Verge Scientific Communications
asellers@vergescientific.com