Design Therapeutics Announces Preclinical Data Highlighting Novel GeneTAC™ Therapy for the Treatment of Fuchs Endothelial Corneal Dystrophy to be Presented at ARVO 2022

March 9, 2022

Treatment with GeneTAC™ Small Molecules Reduced Nuclear Foci and Restored Normal Splicing In Vitro, Supporting Further Development

CARLSBAD, Calif., March 09, 2022 (GLOBE NEWSWIRE) -- Design Therapeutics, Inc. (Nasdaq: DSGN), a biotechnology company developing treatments for degenerative genetic disorders, today announced that preclinical data supporting the potential of the company's novel GeneTAC™ small molecules to correct the most common underlying genetic cause of Fuchs endothelial corneal dystrophy (FECD) will be presented at the Association for Research in Vision and Ophthalmology 2022 Annual Meeting (ARVO 2022). The *in vitro* data in corneal endothelial cells derived from patients with FECD showed that the company's FECD GeneTAC™ molecules reduced toxic nuclear foci and restored normal splicing. The data will be presented at ARVO 2022, which is being held in Denver, Colorado from May 1- 4, 2022 and virtually from May 11-12, 2022.

FECD is characterized by progressive degeneration of the corneal endothelium and subsequent loss of vision. This genetic eye disease affects more than one million people in the U.S., with approximately 75% of cases caused by a CTG trinucleotide repeat expansion within the transcription factor 4 (*TCF4*) gene, leading to the formation of toxic RNA foci, global splicing dysregulation, cellular dysfunction, and eventual death of corneal endothelial cells. Due to the lack of disease-modifying therapies approved for FECD, corneal transplantation is the only procedure currently used to restore vision.

Design's approach utilizes its FECD GeneTAC™ molecules to selectively target the expanded CTG repeats in the *TCF4* gene to reduce RNA foci formation and mis-splicing. Design conducted preclinical studies to evaluate its FECD GeneTAC™ molecules in corneal endothelial cells, which contained nuclear foci, derived from patients with FECD. When tested *in vitro,* FECD GeneTAC™ molecules led to robust reductions in toxic nuclear RNA foci of up to 99% in a time- and concentration-dependent manner. The FECD GeneTAC™ molecules also corrected key mis-spliced transcripts in FECD corneal endothelial cells to levels observed in unaffected corneal endothelial cells.

"FECD is the leading indication for corneal transplantation, which is usually reserved for more advanced stages of the disease. GeneTAC™ molecules are designed to target specific genomic sequences and modulate transcription without requiring invasive procedures or gene editing, potentially offering a novel option for earlier medical treatment across a significantly larger portion of the affected population than current standard of care," said João Siffert, M.D., president and chief executive officer of Design Therapeutics. "These early data are encouraging and suggest that our FECD GeneTAC™ molecules may be able to correct the underlying genetic cause of FECD in the majority of patients. With a growing body of preclinical data across a range of indications, we believe our GeneTAC™ molecules can play a meaningful role in the future treatment for both rare and prevalent genetic diseases."

These findings support the potential for FECD GeneTAC™ molecules to correct the molecular hallmarks of FECD, and Design plans to advance this research program through additional preclinical studies.

Details of the poster presentation are as follows:

Title: GeneTAC™ small molecules reduce toxic nuclear foci and restore normal splicing in corneal endothelial cells derived from patients with Fuchs endothelial corneal dystrophy (FECD) harboring repeat expansions in transcription factor 4 (*TCF4*)
Session Title: Corneal Endothelium
Session Abbreviation: 334
Date/Time: Tuesday, May 3, 2022 at 1:00 p.m. MST

About Design Therapeutics
Design Therapeutics is a 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, statements related to: Design's FECD GeneTAC ™ program and its design and potential therapeutic benefits and advantages, including that Design's FECD GeneTAC™ molecules may be able to correct the underlying genetic cause of FECD in the majority of patients; the potential advancement of Design's pipeline and ability to bring forward a new class of treatments for patients living with devastating genetic diseases; and the potential advantages of these GeneTAC™ programs. 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," "planned," "expects," "estimate," "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 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; 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 September 30, 2021, as filed with the SEC on November 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.

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