Design Therapeutics to Present Preclinical Data on its GeneTAC™ Small Molecule, DT-168, for the Treatment of Fuchs Endothelial Corneal Dystrophy at ARVO 2023

April 24, 2023

Treatment with DT-168 Eye Drops Reduced Nuclear Foci and Significantly Improved Mis-Splicing In Vitro

Company On-track to Submit Investigational New Drug Application for DT-168 in the Second Half of 2023

CARLSBAD, Calif., April 24, 2023 (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-168, an eye drop being developed for the treatment of Fuchs endothelial corneal dystrophy (FECD), will be presented during an oral session at the Association for Research in Vision and Ophthalmology 2023 Annual Meeting (ARVO 2023), which is being held in New Orleans from April 23-27, 2023.

FECD is characterized by progressive corneal degeneration leading to vision loss and affects millions of people in the U.S. Approximately 75% of cases are caused by a mutation in the *transcription factor 4* (*TCF4*) gene, consisting of a CTG trinucleotide repeat expansion that leads to the formation of pathogenic RNA foci in the nucleus and the mis-splicing of multiple transcripts. There are no disease-modifying therapies approved for FECD, and advanced cases generally require ocular surgery, including corneal transplant.

DT-168 is designed to selectively target the expanded CTG repeats in the *TCF4* gene to reduce RNA foci formation and mis-splicing. In preclinical studies, DT-168 reduced foci in patient-derived primary corneal endothelial cells (CECs) to levels seen in cells from healthy individuals with low nanomolar IC50 values. Treatment with DT-168 also significantly improved mis-splicing in patient-derived CECs across a panel of genes. Additionally, in animal studies DT-168 eye drops were well-tolerated after multiple doses and distributed throughout the cornea with micromolar levels of DT-168 observed in the cornea 24 hours after dosing.

The preclinical data support the potential for DT-168 to address the most common genetic cause of FECD and support the continued development of DT-168 as a potential disease-modifying therapy. Design remains on-track to submit an Investigational New Drug application for DT-168 for the treatment of FECD in the second half of 2023.
Details of the oral presentation are as follows:

Title: Pharmacological and molecular features of DT-168, a topical GeneTAC™ small molecule being developed as potential treatment for Fuchs Endothelial Corneal Dystrophy caused by CTG repeat expansions in the TCF4 gene
Presentation Number: 1333
Session Title: Corneal Endothelium
Session Number: 209
Date & Time: Monday, April 24, 2023, 12:30-12:45 p.m.
Location: Room 244

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 is currently evaluating its lead GeneTAC™ small molecule, DT-216, in an ongoing Phase 1 clinical trial in patients with Friedreich ataxia. The company is also advancing programs in Fuchs endothelial corneal dystrophy and myotonic dystrophy type-1. Discovery efforts for multiple other serious degenerative disorders caused by nucleotide repeat expansions are also underway, including for fragile X syndrome, spinocerebellar ataxias, Huntington disease, spinobulbar muscular atrophy, and C9orf72-amyotrophic lateral sclerosis/frontotemporal dementia. 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 early-stage programs, preclinical data and early-stage clinical data; Design's FECD GeneTAC ™ small molecule DT-168 and its design and potential therapeutic benefits and advantages, including that DT-168 may address the most common genetic cause of FECD and has the potential to be a disease-modifying therapy; Design's anticipated timeline to submit an IND for DT-168 in the second half of 2023; the potential of Design's GeneTAC™ small molecules to be a new class of therapies for patients suffering from devastating genetic diseases; 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 "believes," "designed to," "on-track to," "anticipates," "aims," "plans to," "expects," "estimate," "intends," "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 clinical development plans; 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 Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as filed with the SEC on March 14, 2023. 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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