Design Therapeutics Announces Favorable Phase 1 Data for DT-168 Supporting Advancement into Phase 2 Biomarker Trial for Patients with Fuchs Endothelial Corneal Dystrophy

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Phase 2 biomarker trial in FECD patients anticipated to begin in the second half of 2025

CARLSBAD, Calif., May 01, 2025 (GLOBE NEWSWIRE) -- Design Therapeutics, Inc. (Nasdaq: DSGN), a clinical-stage biotechnology company developing treatments for serious degenerative genetic diseases, today announced favorable data from a Phase 1 single- and multiple-ascending dose (SAD/MAD) trial of DT-168 in healthy volunteers, which will be presented on May 2, 2025 at Eyecelerator @ Park City 2025, an event backed by the American Academy of Ophthalmology highlighting industry advancements and innovative new products disrupting eye care.

DT-168 is a novel GeneTAC® small molecule, formulated as an eye drop, that is designed to selectively target and reduce the expression of the mutant TCF4 gene that causes corneal endothelial cell dysfunction leading to Fuchs endothelial corneal dystrophy (FECD).

“DT-168 represents a differentiated opportunity for FECD, a disease with millions of patients facing progressive vision loss and no approved disease modifying therapies,” said Pratik Shah, Ph.D., chairperson and chief executive officer of Design Therapeutics. “Leveraging a convenient eye drop formulation, DT-168 is designed to address the underlying genetic cause of FECD by targeting the repeat expansion that drives disease progression. We are excited to initiate the Phase 2 proof-of-concept trial later this year as we advance what has the potential to be the first disease-modifying medicine for a large, underserved patient population.”

Design completed a Phase 1, double-masked, placebo-controlled, randomized, SAD/MAD trial to evaluate the safety, tolerability and systemic pharmacokinetics (PK) of DT-168 ophthalmic solution. Twenty-four healthy volunteers received either placebo or single- and multiple-ascending doses of DT-168 eye drops twice daily for seven days (up to a maximum dose of two 0.5% drops twice-daily).

- DT-168 eye drops were well-tolerated in all participants.
- There were no serious adverse events, no ocular adverse events (AEs) and no treatment discontinuations due to AEs in the trial. All observed AEs were deemed not related to DT-168 by the trial investigator.
- As expected, PK analysis demonstrated systemic exposure below the limit of quantitation for all participants across all timepoints and all dose groups.

In parallel with the Phase 1 trial, Design conducted reference range studies which showed consistently different splicing in the corneal endothelium between unaffected eye donors and surgical samples from mutant TCF4 FECD patients, supporting the potential for corneal endothelium RNA biomarkers as a clinical proof-of-concept measure of drug activity.

Phase 2 Biomarker Trial of DT-168 in Patients with FECD

Based on these findings, Design plans to conduct a Phase 2 biomarker trial of DT-168 to evaluate safety, tolerability, and corneal endothelium biomarkers in patients with FECD. The trial will enroll FECD patients with the TCF4 mutation who are scheduled for corneal transplant surgery. Patients will receive 0.5% DT-168 eye drops twice-daily for approximately 4 weeks or more before corneal transplant surgery. Following surgery, tissues from the treated eyes of FECD patients will undergo testing to assess corneal endothelium RNA biomarkers, including the abnormal splicing of genes known as spliceopathy. Design plans to initiate the DT-168 Phase 2 biomarker trial in the second half of 2025, with data anticipated in 2026.

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. In addition to its GeneTAC® programs, DT-216P2, in development for patients with Friedreich ataxia, and DT-168, for Fuchs endothelial corneal dystrophy, the company is advancing programs in myotonic dystrophy type-1 and Huntington’s disease. Discovery efforts are underway for multiple genomic medicines. 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 DT-168’s ability to target the repeat expansion that leads to FECD; the opportunity and potential for DT-168 to be the first disease-modifying treatment for FECD; the potential utility of corneal endothelium biomarkers in clinical development; the planned initiation and trial design and data result of Design’s Phase 2 biomarker trial of DT-168 and the timing thereof **;** Design's ability to advance its pipeline of GeneTAC® small molecules and create long-term value; and the capabilities and potential advantages of Design’s pipeline of GeneTAC ® small 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,” “anticipates,” “capable of,” “on track to,” “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 and uncertainties associated with: the acceptance of INDs by the FDA or similar

applications by foreign regulatory agencies for the conduct of planned clinical trials of our product candidates and our proposed design of future clinical trials; pursuing a biomarker-driven clinical development strategy carries increased risks as there are currently a limited number of approved biomarker-specific therapies; nonclinical development activities and results of nonclinical studies; conducting a clinical trial and patient enrollment, which are 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; undesirable side effects or other undesirable properties, which could cause Design or regulatory authorities to suspend or discontinue clinical trials and thereby delay or prevent Design's product candidates' development or regulatory approval; Design's ability to develop, initiate or complete nonclinical studies and clinical trials for its product candidates; whether promising early research or clinical trials will demonstrate safety and/or efficacy in later nonclinical studies or clinical trials; changes in Design's plans to develop its product candidates; reliance on third parties to successfully conduct clinical trials and nonclinical studies; competitive products, which may make any products we develop or seek to develop obsolete or noncompetitive; Design's reliance on key third parties, including contract manufacturers and contract research organizations; 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 ability to obtain and maintain intellectual property protection for its product candidates; Design's ability to recruit and retain key scientific or management personnel; 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, 2024, as filed with the SEC on March 10, 2025. 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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