CRISPR Therapeutics Presents Phase 1a Data for CTX310® Demonstrating Deep and Durable ANGPTL3 Editing, Triglyceride and LDL Lowering at ESC Congress 2026

-Data presented in a late-breaking presentation at the European Society of Cardiology (ESC) Congress 2026-

-Phase 1a clinical data for CTX310® continued to demonstrate robust, dose-dependent reductions in circulating ANGPTL3 with a mean reduction from baseline of 79% (maximum 89%), a mean reduction in triglycerides (TG) of 48% (maximum 78%), and a mean reduction of low-density lipoprotein (LDL) of 53% (maximum 84%) at the highest dose-

-CTX310 was well tolerated with no treatment-related serious adverse events, no ≥Grade 3 changes in liver transaminases, and no additional treatment-related adverse events since the previous update-

-Findings simultaneously published in The New England Journal of Medicine *entitled "Durability of CRISPR-Cas9 Gene Editing Targeting ANGPTL3 with CTX310"-*

ZUG, Switzerland and BOSTON, Aug. 28, 2026 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (Nasdaq: CRSP) today presented durability data from its Phase 1a clinical trial evaluating CTX310®, an investigational, *in vivo* CRISPR/Cas9 gene editing therapy targeting ANGPTL3. A single-course treatment with CTX310 produced deep and durable reductions in circulating ANGPTL3, triglycerides (TG), and low-density lipoprotein (LDL) that were sustained through one year of follow-up. At the highest dose, mean reductions from baseline were 79% (maximum 89%) for ANGPTL3, 48% (maximum 78%) for TG, and 53% (maximum 84%) for LDL. These extended follow-up data demonstrate the durability of CTX310's effect and support its potential to deliver long-lasting lipid lowering after a single intravenous (IV) infusion.

These data were presented today during a late breaking session at the European Society of Cardiology (ESC) Congress 2026 and extend the Phase 1 results previously presented. The data were also published today in *The New England Journal of Medicine (NEJM)* in a peer reviewed article entitled "Durability of CRISPR-Cas9 Gene Editing Targeting ANGPTL3 with CTX310." CRISPR Therapeutics is advancing CTX310 in a Phase 1b clinical trial, with U.S. and ex-U.S. trials ongoing, and expects to provide an additional update on the CTX310 program in the second half of 2026.

"These durability data mark an important next step for the CTX310 program and for the field of *in vivo* gene editing," said Naimish Patel, M.D., Chief Medical Officer, CRISPR Therapeutics. "Evidence that a single dose can produce lasting lipid lowering is central to our goal of developing one-time treatments for cardiometabolic diseases. These results provide strong support for continued advancement of CTX310 and our broader cardiovascular gene editing portfolio, and we look forward to sharing new data from the severe hypertriglyceridemia cohort of the CTX310 Phase 1b trial in the second half of this year."

"For patients at high cardiovascular risk, the biggest challenge is often not starting therapy but staying on it, since daily medications require lifelong adherence that many patients are unable to maintain," said Luke Laffin, M.D., principal investigator and Medical Director of the Cleveland Clinic Coordinating Center for Clinical Research. "A single infusion producing durable reductions at one-year is an encouraging signal that a one-time approach could help close that adherence gap."

"What is compelling about this update is that the reductions in ANGPTL3, triglycerides, and LDL from a single infusion have persisted out to one-year, suggesting a sustained biological effect," said Steven E. Nissen, M.D., senior author of the study and Chief Academic Officer at the Cleveland Clinic Heart, Vascular and Thoracic Institute. "A one-time treatment with this degree of durability could represent a meaningful advance in how we manage lifelong lipid disorders."

Phase 1a Clinical Trial Design

The Phase 1a portion of the study was an open label, dose-escalation trial evaluating single-course IV doses of CTX310 ranging from 0.1 to 0.8 mg/kg (lean body weight) targeting *ANGPTL3* in four patient groups: homozygous familial hypercholesterolemia (HoFH), severe hypertriglyceridemia (sHTG), heterozygous familial hypercholesterolemia (HeFH), or mixed dyslipidemias (elevated TG and LDL). Eligible participants had uncontrolled TG levels >150 mg/dL and/or LDL cholesterol >100 mg/dL (or >70 mg/dL for those with established ASCVD) despite background standard of care per local guidelines.

The majority of participants were receiving statins and/or ezetimibe, while 40% were taking PCSK9 inhibitors. The trial was designed to evaluate safety and tolerability as primary endpoints, with changes in circulating ANGPTL3 protein, TG, and LDL as

secondary endpoints.

Safety and Tolerability

Single-course ascending doses of CTX310 were administered to 15 participants across sequential cohorts, and all participants completed at least one-year of follow-up as of the data cutoff. CTX310 was generally well tolerated, and no dose-limiting toxicities or serious adverse events related to treatment. Adverse events were generally mild to moderate.

As previously reported in Laffin et al. (2025), one participant experienced an allergic reaction that resolved the following day with supportive care. Infusion-related reactions occurred in three participants (two at 0.6 mg/kg and one at 0.8 mg/kg dose), all Grade 2. All events resolved, and all participants completed their infusions. Beyond the transient aminotransferases elevation previously reported in one participant shortly after treatment, there were no liver function test elevations throughout the remainder of the trial.

The safety events described above were previously reported in Laffin et al. (New England Journal of Medicine, 2025) and reflect the initial treatment period of the Phase 1a clinical trial. No new treatment-related safety events were observed during extended follow-up.

Efficacy Highlights

These new results build upon previously disclosed clinical data from 15 participants across four sequential cohorts, corresponding to lean body weight-based doses of DL1 [0.1 mg/kg], DL2 [0.3 mg/kg], DL3 [0.6 mg/kg], DL3.5 [0.7 mg/kg] and DL4 [0.8 mg/kg]. All participants had at least one-year of follow-up.

- Dose dependent reductions in circulating ANGPTL3 protein were sustained through one-year following CTX310 infusion.
- Among participants treated at 0.8 mg/kg, ANGPTL3 reductions of up to 89% were observed, with a mean reduction of 79% at one-year following CTX310 infusion.

Next Steps

The Phase 1b portion of the trial examines a fixed flat dose regimen of CTX310 equivalent to the most efficacious dose in Phase 1a (0.8mg/kg). CRISPR Therapeutics continues to anticipate sharing an update from the CTX310 Phase 1b clinical trial in the second half of 2026, focused on severe hypertriglyceridemia patients.

About *In Vivo* Liver Editing Programs

CRISPR Therapeutics has established a proprietary lipid nanoparticle (LNP) delivery platform to enable gene editing in the liver using both CRISPR/Cas9 and its novel, proprietary SyNTase™ editing technology. The Company's *in vivo* portfolio includes three cardiovascular programs: CTX310, targeting angiopoietin-related protein 3 (ANGPTL3), in development for heterozygous and homozygous familial hypercholesterolemia, mixed dyslipidemias, and severe hypertriglyceridemia; CTX340™, targeting angiotensinogen (AGT), in development for refractory hypertension; and CTX321™, targeting LPA, in development for patients with elevated lipoprotein(a) [Lp(a)]. In addition, the Company's disclosed development candidates also include CTX460™, targeting SERPINA1 using SyNTase editing, for the treatment of alpha-1 antitrypsin deficiency (AATD).

About CRISPR Therapeutics

CRISPR Therapeutics is a leading biopharmaceutical company focused on developing transformative gene-based medicines for serious human diseases. Founded over a decade ago as an early pioneer in CRISPR/Cas9 gene editing, the Company has evolved from a pioneering research-stage organization into an industry leader, marking a historic milestone with the approval of CASGEVY® (exagamglogene autotemcel [exa-cel]), the world's first CRISPR-based therapy, for eligible patients with sickle cell disease and transfusion-dependent beta thalassemia. Today, CRISPR Therapeutics is advancing a broad, diversified pipeline spanning hemoglobinopathies, cardiovascular disease, autoimmune disease, oncology, regenerative medicine and rare diseases. The Company is also expanding its gene editing toolkit through SyNTase™ editing, its novel, proprietary platform designed to enable precise, efficient, and scalable gene correction. To accelerate its impact, CRISPR Therapeutics has established strategic collaborations with leading biopharmaceutical partners, including Vertex Pharmaceuticals. CRISPR Therapeutics AG is headquartered in Zug, Switzerland, with its wholly-owned U.S. subsidiary, CRISPR Therapeutics, Inc., and R&D operations based in Boston, Massachusetts and San Francisco, California. To learn more, visit www.crisprtx.com.

Reference

1. Laffin L, et al. Phase 1 Trial of CRISPR-Cas9 Gene Editing Targeting ANGPTL3. The New England Journal of Medicine. 2025.

CRISPR Special Note Regarding Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding any or all of the following: (i) CRISPR Therapeutics preclinical studies, clinical trials and pipeline products and programs, including, without limitation, manufacturing capabilities, status of such studies and trials, potential expansion into new indications and expectations regarding data, safety and efficacy generally; (ii) data included in the above-described oral presentation and any associated abstracts or posters, data included in the above-described article in The New England Journal of Medicine, as well as the ability to use data from ongoing and planned clinical trials for the design and initiation of further clinical trials; and (iii) the therapeutic value, development, and commercial potential of gene editing technologies and therapies, including CRISPR/Cas9 and SyNTase, as well as other technologies. Risks that contribute to the uncertain nature of the forward-looking statements include, without limitation, the risks and uncertainties discussed under the heading "Risk Factors" in CRISPR Therapeutics most recent annual report on Form 10-K and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. We disclaim any obligation or undertaking to update or revise any forward-looking statements contained in this press release, other than to the extent required by law.

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