



## **CRISPR Therapeutics Highlights ASGCT Oral Presentation and Announces New Programs Utilizing In Vivo Gene Editing Approach**

- ASGCT presentation demonstrates lipid nanoparticle (LNP) mediated delivery to the eye in the context of editing of the myocilin (MYOC) gene as a potential treatment for glaucoma -
- Expands pipeline with new pre-clinical programs utilizing LNP mediated delivery to the liver for refractory hypertension targeting angiotensinogen (AGT) and acute hepatic porphyria (AHP) targeting 5'-aminolevulinic acid synthase 1 (ALAS1) -
- CTX340™, targeting AGT in the liver, achieved durable editing of AGT and sustained ~30 mmHg blood pressure (BP) reduction out to 3 months in the spontaneously hypertensive rat (SHR) model, demonstrating its potential as a one-time therapeutic intervention -
- CTX450™, targeting ALAS1 in the liver, achieved ~70% editing of ALAS1 and normalizes disease-associated biomarkers in acute porphyria mouse model, demonstrating its potential as a one-time therapeutic intervention -
- Plans to initiate clinical trials for CTX340 and CTX450 in the second half of 2025 -

ZUG, Switzerland and BOSTON, May 08, 2024 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today announced new preclinical data presented at the 27th Annual Meeting of the American Society of Cell and Gene Therapy (ASGCT) highlighting the Company's approach to developing lipid nanoparticle (LNP) based delivery for *in vivo* ocular gene editing. In addition, CRISPR Therapeutics announced the expansion of its *in vivo* pipeline with two new programs. CTX340™ and CTX450™ utilize LNP-based delivery of CRISPR/Cas9 gene editing cargo to the liver, targeting angiotensinogen (AGT) for refractory hypertension and 5'-aminolevulinic acid synthase 1 (ALAS1) for acute hepatic porphyria (AHP), respectively.

"Over the past two years, we have made significant progress on the development of our lipid nanoparticle platform for the delivery of CRISPR/Cas9 to the liver and are now in clinical trials with CTX310 and CTX320," said Samarth Kulkarni, Chief Executive and Chairman of the Board of CRISPR Therapeutics. "The expansion of our *in vivo* pipeline speaks to the scalability of the platform and the exceptional translation capabilities of our team. We continue to add programs to treat both common and rare diseases, as we look to broaden the number of areas where CRISPR could have transformational impact."

### **In Vivo Pipeline Expansion**

- CRISPR Therapeutics has established a proprietary LNP platform for the delivery of CRISPR/Cas9 to the liver. The first two *in vivo* programs utilizing this proprietary platform, CTX310™ and CTX320™, are directed towards validated therapeutic targets associated with cardiovascular disease, and are in on-going clinical trials. The addition of two more programs, CTX340 and CTX450, utilizing this LNP delivery technology demonstrates the modularity and scalability of the platform.
- Refractory hypertension is a serious unmet medical need affecting approximately 1.5 million patients in the U.S. alone. CTX340 is designed to inhibit production of hepatic angiotensinogen (AGT), a validated target to modulate the renin-angiotensin-aldosterone system (RAAS) and normalize blood pressure durably with a one-time treatment. In preclinical studies, CTX340 showed ~60% liver editing and ~90% AGT protein reduction, resulting in sustained ~30 mmHg blood pressure (BP) reduction out to 3 months in the spontaneously hypertensive rat (SHR) model.
- Acute hepatic porphyria (AHP) is a group of rare genetic diseases of heme biosynthesis. Symptomatic patients have acute attacks, characterized by debilitating neurovascular symptoms, as well as multiple chronic symptoms, such as pain. There are approximately 5,000 patients diagnosed with AHP in the U.S., although the disease remains underdiagnosed. CTX450 is specifically designed to inhibit production of ALAS1 in the liver, preventing accumulation of neurotoxic aminolevulinic acid (ALA) and porphobilinogen (PBG). In preclinical studies, CTX450 showed ~70% liver editing and ~97% ALAS1 protein reduction, resulting in reduction of ALA and PBG disease biomarkers to normal levels in an AHP mouse model.
- CRISPR Therapeutics has initiated IND/CTA-enabling studies for CTX340 and CTX450 and expects to initiate both clinical trials in the second half of 2025.

## ASGCT Presentation

- In addition to expanding the liver-targeted *in vivo* pipeline, CRISPR Therapeutics reported initial data demonstrating its proprietary capabilities to deliver to and edit genes in the eye, opening a potential new focus area. The data will be presented today, May 8, 2024, from 3:00 p.m. – 3:15 p.m. ET at ASGCT in an oral presentation entitled “Development of an *In Vivo* Non-Viral Ocular Editing Platform and Application to Potential Treatments for Glaucoma.”
- Glaucoma is the second leading cause of blindness worldwide. Mutations in the myocilin (MYOC) gene represent the most common genetic cause of glaucoma that affects approximately 150,000 people in the U.S. alone. In these patients, defective myocilin protein aggregates in the trabecular meshwork (TM) cells, leading to impaired outflow of aqueous humor from the anterior segment of the eye, resulting in elevated intraocular pressure. Patients with MYOC-associated glaucoma typically have an earlier onset and more rapidly progressive disease course than is seen with other causes of glaucoma. Pharmaceutical interventions carry a significant treatment burden resulting in reduced adherence to therapy and surgical interventions frequently do not lead to a durable resolution of elevated intraocular pressure (IOP). The Company has developed an LNP platform capable of delivering gene editing cargo to the TM cells in the eye. In today's presentation, the Company presented data demonstrating efficient and specific delivery to TM cells in mouse, non-human primate, and *ex vivo* human eyes. The Company showed >90% editing of the MYOC gene *in vitro* with prioritized guide RNA, and ~90% reduction of surrogate protein expression in a mouse *in vivo* model after a single injection.

### About *In Vivo* Programs

CRISPR Therapeutics has established a proprietary LNP platform for the delivery of CRISPR/Cas9 to the liver. The Company's *in vivo* portfolio includes its lead investigational *in vivo* programs, CTX310 (directed towards angiopoietin-related protein 3 (ANGPTL3)) and CTX320 (directed towards lipoprotein(a) (Lp(a)), two validated therapeutic targets for cardiovascular disease, are in on-going clinical trials. In addition, the Company's research and pre-clinical development candidates include CTX340 and CTX450, targeting angiotensinogen (AGT) for refractory hypertension and 5'-aminolevulinate synthase 1 (ALAS1) for acute hepatic porphyria (AHP), respectively.

### About CRISPR Therapeutics

Since its inception over a decade ago, CRISPR Therapeutics has transformed from a research-stage company advancing programs in the field of gene editing, to a company that recently celebrated the historic approval of the first-ever CRISPR-based therapy and has a diverse portfolio of product candidates across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine, cardiovascular, autoimmune, and rare diseases. CRISPR Therapeutics advanced the first-ever CRISPR/Cas9 gene-edited therapy into the clinic in 2018 to investigate the treatment of sickle cell disease or transfusion-dependent beta thalassemia, and beginning in late 2023, CASGEVY™ (exagamglogene autotemcel) was approved in some countries to treat eligible patients with either of those conditions. The Nobel Prize-winning CRISPR science has revolutionized biomedical research and represents a powerful, clinically validated approach with the potential to create a new class of potentially transformative medicines. To accelerate and expand its efforts, CRISPR Therapeutics has established strategic partnerships with leading companies including Bayer and 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, and business offices in London, United Kingdom. To learn more, visit [www.crisprtx.com](http://www.crisprtx.com).

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