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'-aminolevulinate 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'-aminolevulinate 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.

CRISPR Therapeutics Forward-Looking Statement

This press release may contain a number of "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding CRISPR Therapeutics' expectations about any or all of the following: (i) its ongoing and/or planned preclinical studies, clinical trials and pipeline products and programs, including, without limitation, the status of such studies and trials, potential expansion into new indications and expectations regarding data generally (including expected timing of data releases) as well as the data that is being presented as described above; (ii) the safety, efficacy and clinical progress of its various clinical and preclinical programs including the program described in the oral presentation and poster; (iii) the data that will be generated by ongoing and planned preclinical studies and/or clinical trials, and the ability to use that data for the design and initiation of further preclinical studies and/or clinical trials; and (iv) the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and therapies. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects" and similar expressions are intended to identify forward-looking statements. You are cautioned that forward-looking statements are inherently uncertain. Although CRISPR Therapeutics believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: the efficacy and safety results from ongoing pre-clinical studies and/or clinical trials will not continue or be repeated in ongoing or planned pre-clinical studies and/or clinical

trials or may not support regulatory submissions; pre-clinical study and/or clinical trial results may not be favorable or support further development; one or more of its product candidate programs will not proceed as planned for technical, scientific or commercial reasons; future competitive or other market factors may adversely affect the commercial potential for its product candidates; uncertainties inherent in the initiation and completion of preclinical studies for its product candidates and whether results from such studies will be predictive of future results of future studies or clinical trials; uncertainties about regulatory approvals to conduct trials or to market products; uncertainties regarding the intellectual property protection for its technology and intellectual property belonging to third parties, and the outcome of proceedings (such as an interference, an opposition or a similar proceeding) involving all or any portion of such intellectual property; and those risks and uncertainties described 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, which are available on the SEC's website at www.sec.gov. CRISPR Therapeutics disclaims 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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