CRISPR Therapeutics Highlights Strategic Priorities and 2024 Outlook

ZUG, Switzerland and BOSTON, Mass., January 8, 2024 – CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today highlighted its strategic priorities and 2024 outlook as the Company enters its next phase of growth.

"We had a landmark year in 2023, marked by the first-ever approval of a CRISPR-based gene-editing therapy in addition to entering the clinic with our *in vivo* therapies," said Samarth Kulkarni, Ph.D., Chairman and Chief Executive Officer of CRISPR Therapeutics. "As we look ahead to 2024, we continue to drive forward our programs and expand our pipeline with the goal of delivering paradigm-shifting gene editing therapies to patients. We are well positioned to execute on our clinical trials across various therapeutic areas, including oncology, autoimmune, cardiovascular and diabetes, setting up a catalyst-rich 12-18 months for the company. In parallel, we are continuously innovating on our platform with next-generation gene editing and delivery technologies that could enable us to address even more diseases with potentially curative medicines. Even in this challenging macroeconomic environment for biotech companies, our strong capital position and efficient operating model provides us with a competitive advantage to expand upon our leadership in the space."

Strategic Priorities and 2024 Outlook

CASGEVY™ (exagamglogene autotemcel [exa-cel])

- Received regulatory approvals for CASGEVY in the fourth quarter of 2023 in the U.S. for sickle cell disease (SCD) and in Great Britain and Bahrain for the treatment of SCD and transfusion-dependent beta thalassemia (TDT); also received a positive opinion from the European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) for CASGEVY for both SCD and TDT from the European Medicines Agency (EMA). Exa-cel is the first therapy to emerge from a strategic partnership between CRISPR Therapeutics and Vertex Pharmaceuticals. Vertex leads global development, manufacturing, regulatory and commercialization of CASGEVY with support from CRISPR Therapeutics.

- The FDA has assigned a Prescription Drug User Fee Act (PDUFA) action date of March 30, 2024, for CASGEVY in TDT. Additional regulatory submissions for CASGEVY are currently under review in Switzerland and the Kingdom of Saudi Arabia, with the submission in Canada planned for the first half of 2024.

- Completed enrollment in two global Phase 3 studies of CASGEVY in patients 5 to 11 years of age with SCD or TDT.

- Vertex is engaging with experienced hospitals to establish a network of authorized treatment centers (ATCs) throughout the U.S. to offer CASGEVY to patients. Nine ATCs have been activated in the U.S. and three in Europe, with the goal of activating approximately 50 ATCs in the U.S. and 25 in the EU. Additionally, Vertex announced an agreement with a major medication contracting

organization, Synergie Medication Collective, which covers nearly 100 million lives in the U.S., to provide access to CASGEVY through an outcomes-based contract.

Hemoglobinopathies

- CRISPR Therapeutics has two next-generation research focuses that each have the potential to expand the addressable population with SCD and TDT significantly. First, the Company continues to advance its internal targeted conditioning program, an anti-CD117 (c-Kit) antibody-drug conjugate (ADC), through preclinical studies.

- Second, the Company has ongoing research efforts to enable *in vivo* editing of hematopoietic stem cells. This work, supported in part by a $14.5 million grant from the Bill & Melinda Gates Foundation, could obviate the need for conditioning altogether, expand geographic reach, and enable the treatment of multiple additional other diseases beyond SCD and TDT.

Immuno-Oncology and Autoimmune Disease

- CRISPR Therapeutics' next-generation allogeneic CAR T candidates reflect the Company's mission of innovating continuously to bring potentially transformative medicines to patients as quickly as possible. Clinical trials are ongoing for CRISPR Therapeutics' next-generation CAR T product candidates, CTX112™ and CTX131™, targeting CD19 and CD70, respectively. Emerging pharmacology data, including pharmacokinetics, indicate that the novel potency gene edits in CTX112 and CTX131 can lead to significantly higher CAR T cell expansion and functional persistence in patients compared to the first-generation candidates. Focusing efforts on these candidates will enable the Company to advance these potentially best-in-class CAR T therapies more efficiently and rapidly. The Company expects to provide a clinical update in 2024 for these next-generation candidates.

- CRISPR Therapeutics plans to initiate a clinical trial of CTX112 in systemic lupus erythematosus (SLE) in the first half of 2024, with the potential to expand into additional autoimmune indications in the future. Early clinical studies have shown that CD19-directed autologous CAR T therapy can produce long-lasting remissions in multiple autoimmune indications.

- CRISPR Therapeutics is expanding trials of CTX131 into hematologic malignancies, including T- and B-cell malignancies, in addition to the ongoing clinical trial in solid tumors.

In Vivo

- CRISPR Therapeutics is advancing a pipeline of *in vivo* gene editing programs using lipid nanoparticle (LNP) delivery of Cas9 mRNA and a guide RNA (gRNA) to the liver. Its first two *in vivo* programs, CTX310™ and CTX320™, each aim to reduce expression of a validated target for

cardiovascular disease. Beginning with these programs, CRISPR Therapeutics aims to transform the treatment paradigm for cardiovascular indications and beyond with potential one-time therapies that could recapitulate the proven benefit of targets validated by natural human genetics and other therapeutic modalities.

- A Phase 1 clinical trial is ongoing for CTX310, targeting angiopoietin-like 3 protein (ANGPTL3). In humans, naturally occurring loss-of-function variants in *ANGPTL3* are associated with reduced levels of serum lipids and reduced risk of atherosclerotic cardiovascular disease. The Phase 1 trial is enrolling patients with mixed dyslipidemias, homozygous familial hypercholesterolemia, and severe hypertriglyceridemia.

- CRISPR Therapeutics has initiated a Phase 1 clinical trial for CTX320™, an investigational program targeting lipoprotein(a) (Lp(a)). Elevated Lp(a), which is associated with an increased risk of atherosclerotic cardiovascular disease, is present in approximately one in five people in the United States and around the world.

- CRISPR Therapeutics expects to nominate additional *in vivo* programs targeting both rare and common diseases this year, to be disclosed in mid-2024.

Regenerative Medicine

- CRISPR Therapeutics announced today that ViaCyte, Inc. (a subsidiary of Vertex Pharmaceuticals, Inc.) has elected to opt-out of the collaboration with CRISPR Therapeutics for the co-development and co-commercialization of gene-edited stem cell therapies for the treatment of diabetes. Per the opt-out terms, the on-going collaboration assets will now be wholly owned by CRISPR Therapeutics, subject to a royalty on future sales owed to ViaCyte. The opt-out will become effective in early February. The ViaCyte collaboration assets include CTX211™ (formerly VCTX211™), an allogeneic, gene-edited, immune-evasive, stem cell derived product candidate that is transplanted into patients in a device and intended to produce insulin in a glucose-dependent manner. CRISPR Therapeutics continues to advance a Phase 1 clinical trial for CTX211 for the treatment of Type 1 Diabetes (T1D). CRISPR Therapeutics remains committed to its goal of developing a beta-cell replacement product that does not require chronic immunosuppression.

- Separate from the ViaCyte collaboration, Vertex continues to have non-exclusive rights to certain CRISPR Therapeutics' CRISPR/Cas9 technology to accelerate development of potentially curative cell therapies for T1D. Vertex paid $170 million to CRISPR Therapeutics in upfront and milestone payments in 2023 as part of that licensing agreement, and CRISPR Therapeutics remains eligible for an additional $160 million in research and development milestones and would receive royalties on any future products resulting from this agreement.

Manufacturing

- CRISPR Therapeutics' state-of-the-art Good Manufacturing Practice (GMP) facility located in Framingham, MA is fully operational, and continues to support the production of the Company's

various investigational therapies. Potential benefits of this facility include significantly lower cost of goods, increased flexibility and greater scalability.

- The Company's next-generation allogeneic CAR T candidates manufactured at its internal GMP facility exhibit increased manufacturing robustness, yield and scalability.

Cash Position and Operating Efficiencies

- CRISPR Therapeutics begins 2024 in a strong financial position with approximately $1.9 billion in cash, cash equivalents and marketable securities, which is inclusive of a $200 million milestone payments received in January related to the FDA approval of CASGEVY.

- CRISPR Therapeutics continues to focus on resource efficiency and return on invested capital as it advances multiple clinical programs across its pipeline.

About CASGEVY™ (exagamglogene autotemcel [exa-cel])
CASGEVY is a genome-edited cellular therapy consisting of autologous CD34+ hematopoietic stem cells (HSCs) edited by CRISPR/Cas9 technology at the erythroid-specific enhancer region of the *BCL11A* gene. CASGEVY is intended for one time administration via a hematopoietic stem cell transplant procedure where the patient's own CD34+ cells are modified to reduce *BCL11A* expression in erythroid lineage cells, leading to increased fetal hemoglobin (HbF) production. HbF is the form of the oxygen-carrying hemoglobin that is naturally present during fetal development, which then switches to the adult form of hemoglobin after birth. CASGEVY has been shown to reduce or eliminate vaso-occlusive crises for patients with SCD.

CASGEVY is approved in the U.S. to treat people aged 12 years and older with SCD who have recurrent VOCs. CASGEVY was granted a conditional marketing authorization in Great Britain by the U.K. Medicines and Healthcare products Regulatory Agency and by the National Health Regulatory Authority in Bahrain for patients 12 years of age and older with SCD characterized by recurrent vaso-occlusive crises or transfusion-dependent beta thalassemia (TDT), for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related hematopoietic stem cell donor is not available. CASGEVY is currently under review by the European Medicines Agency and the Saudi Food and Drug Authority for both SCD and TDT.

The use of CASGEVY for the treatment of TDT in the U.S. remains investigational. Vertex has submitted a BLA to the U.S. FDA for the potential use of CASGEVY for patients 12 years and older with TDT and has been assigned a Prescription Drug User Fee Act (PDUFA) target action date of March 30, 2024.

About the CRISPR Collaboration and Vertex
CRISPR Therapeutics and Vertex entered into a strategic research collaboration in 2015 focused on the use of CRISPR/Cas9 to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. Exa-cel represents the first treatment to emerge from the joint research

program. Under an amended collaboration agreement, Vertex now leads global development, manufacturing and commercialization of exa-cel and splits program costs and profits worldwide 60/40 with CRISPR Therapeutics.

About CD19 Candidates
CTX112 is a next-generation, wholly-owned, allogeneic CAR T product candidate targeting Cluster of Differentiation 19, or CD19, which incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion. CTX112 is being investigated in an ongoing clinical trial designed to assess safety and efficacy of the product candidate in adult patients with relapsed or refractory CD19-positive B-cell malignancies who have received at least two prior lines of therapy.

About CD70 Candidates
CTX131 is a next-generation, wholly-owned, allogeneic CAR T product candidate targeting Cluster of Differentiation 70, or CD70, an antigen expressed on various solid tumors and hematologic malignancies. CTX112 incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion. CTX131 is being investigated in a clinical trial designed to assess the safety and efficacy of the product candidate in adult patients with relapsed or refractory solid tumors.

About CTX211 (to be renamed CTX211™ once the opt-out is effective)
CTX211 is an allogeneic, gene-edited, stem cell-derived investigational therapy for the treatment of T1D, which incorporates gene edits that aim to enhance cell fitness. This immune-evasive cell replacement therapy is designed to enable patients to produce their own insulin in response to glucose.

About *in vivo*
Our lead investigational *in vivo* programs, CTX310 and CTX320, target angiopoietin-related protein 3 (ANGPTL3) and lipoprotein(a) (Lp(a)), respectively, two validated targets for cardiovascular disease, and we have initiated a Phase 1 clinical trial for CTX310 targeting ANGPTL3.

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 with a diverse portfolio of product candidates across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine, cardiovascular and rare diseases. 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.

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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 made by Dr. Kulkarni in this press release, as well as statements regarding CRISPR Therapeutics' expectations about any or all of the following: (i) its plans for and its 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 generally; (ii) the data that will be generated by ongoing and planned clinical trials, and the ability to use that data for the design and initiation of further clinical trials; (iii) plans and expectations for the commercialization of, and anticipated benefits of, CASGEVY, including the anticipated patient population eligible for CASGEVY in the United States and patient access to CASGEVY; (iv) timelines for and expectations regarding additional regulatory agency decisions for exa-cel; (v) the sufficiency of its cash resources; (vi) the expected benefits of its collaborations and (vii) 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 clinical trials will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory submissions; regulatory authorities may not approve exa-cel on a timely basis or at all; adequate pricing or reimbursement may not be secured to support continued development or commercialization of exa-cel following regulatory approval; clinical trial results may not be favorable; 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; initiation and completion of preclinical studies for its product candidates is uncertain and results from such studies may not be predictive of future results of future studies or clinical trials; regulatory approvals to conduct trials or to market products are uncertain; uncertainties inherent in the operation of a manufacturing facility; it may not realize the potential benefits of its collaborations; 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, quarterly report on Form 10-Q 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. 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. 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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