CRISPR Therapeutics Provides Business Update and Reports Fourth Quarter and Full Year 2022 Financial Results

-Regulatory submissions complete for exagamglogene autotemcel (exa-cel) in Europe for transfusion-dependent beta thalassemia (TDT) and sickle cell disease (SCD); U.S. rolling Biologics Licensing Application (BLA) submission on track for completion by end of Q1 2023-

-Enrollment and dosing ongoing for CTX110®, targeting CD19+ B-cell malignancies, and CTX130™, targeting CD70 for the treatment of T cell lymphomas-

-Initiating Phase 1/2 clinical trials for next generation CAR T products, CTX112™ targeting CD19+ B-cell malignancies and CTX131™, targeting CD70+ solid tumors-

-Enrollment and dosing ongoing in a Phase 1/2 clinical trial of VCTX211™ for the treatment of Type 1 Diabetes (T1D)-

-Expects to advance its lead in vivo program, CTX310™, targeting angiopoietin-related protein 3 (ANGPTL3) into clinical trials this year-

ZUG, Switzerland and Boston, Mass., February 21, 2023 – CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today reported financial results for the fourth quarter and full year ended December 31, 2022.

"2022 marked a significant year of progress toward our goal of delivering innovative gene edited therapies to patients. Exa-cel has the potential to be the first approved CRISPR-based therapy in the world, with regulatory submissions complete in Europe and underway in the United States," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "At the same time, we continue to expand our pipeline and drive forward our programs across the immuno-oncology, diabetes and cardiovascular disease verticals. Based on encouraging data reported in 2022 at EHA and ASH conferences, we continue to advance both CTX110 and CTX130 in larger clinical trials. We are also initiating clinical trials for our next generation CAR T cell programs, CTX112 and CTX131, which have the potential to be best-in-class cell therapies. We continue to progress our regenerative medicine portfolio with the advancement of VCTX211, an immune-evasive cell replacement therapy designed to enable patients with T1D to produce their own insulin, to the clinic following clearance of our CTA by Health Canada. Finally, we expect to move our first *in vivo* program, CTX310, into the clinic this year, while advancing additional *in vivo* programs into IND-enabling studies. We are well-positioned to continue expanding our portfolio of transformative medicines while continuously improving our editing and delivery platform throughout 2023."

Recent Highlights and Outlook

- **Hemoglobinopathies**
    - In December 2022, CRISPR Therapeutics and Vertex completed regulatory submissions for exa-cel, formerly known as CTX001™, with the European Medicines Agency (EMA) and

the Medicines and Healthcare products Regulatory Agency (MHRA) in the EU and the U.K., respectively. Both the EMA and the MHRA have validated the Marketing Authorization Application (MAA). Exa-cel has been granted Priority Medicines (PRIME) designation in the EU and Orphan Drug designation (ODD) in the EU. The companies initiated the rolling submission of their Biologics Licensing Application (BLA) in the U.S. in November 2022 and expect to complete the submission by the end of Q1 2023. In the U.S., exa-cel has been granted Fast Track, Regenerative Medicine Advanced Therapy (RMAT), Orphan Drug and Rare Pediatric Disease designations.

- The Phase 1/2/3 CLIMB-111 and CLIMB-121 studies and the CLIMB-131 long-term follow-up study are ongoing in patients 12 years of age and older.

- Two additional Phase 3 studies of exa-cel in pediatric patients with TDT and SCD continue to enroll patients.

- CRISPR Therapeutics continues to advance its anti-CD117 (c-Kit) antibody-drug conjugate (ADC), its internal targeted conditioning program, in pre-clinical studies. This targeted conditioning agent has the potential to significantly expand the patient population that can benefit from exa-cel.

- **Immuno-Oncology**

  - In December, CRISPR Therapeutics provided an update for both Part A (single dose with optional re-dosing) and Part B (consolidation dosing) of its ongoing Phase 1 CARBON trial evaluating the safety and efficacy of CTX110®, its wholly-owned allogeneic chimeric antigen receptor T cell (CAR T) candidate targeting CD19+ B-cell malignancies. Part A data, presented at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition, showed the potential for CTX110 to achieve long-term durable complete remissions (CRs) with a positively differentiated safety profile in heavily pre-treated patients, and emerging data from Part B showed an encouraging efficacy profile with the potential to improve the efficacy with the use of a consolidation dose. Based on these data, and discussions with regulatory agencies, the Company initiated a Phase 2 single-arm potentially registrational clinical trial which incorporates consolidation dosing.

  - CRISPR Therapeutics will initiate clinical trials for CTX112™, its next generation CAR T candidate targeting CD19+ B-cell malignancies, in the first half of 2023, following the previously-announced clearance of its Investigational New Drug (IND) application by the U.S. Food and Drug Administration (FDA). CTX112 incorporates the edits in CTX110 plus additional edits to the genes encoding Regnase-1 and TGFBRII, which have been shown to increase the potency of the CAR T cells in pre-clinical studies.

  - In June, CRISPR Therapeutics presented positive results from the Company's ongoing Phase 1 COBALT™-LYM trial evaluating the safety and efficacy of CTX130™, its wholly-

owned allogeneic CAR T cell therapy targeting CD70 for the treatment of relapsed or refractory T cell malignancies. Based on these early data, CTX130 was granted the RMAT designation by the FDA. Given the encouraging early results, the Company continues to advance CTX130 for these difficult-to-treat T cell lymphomas in its COBALT-LYM trial.

- In November, CRISPR Therapeutics presented data at the Society for Immunotherapy of Cancer (SITC) 37th Annual Meeting for CTX130 for the treatment of relapsed or refractory renal cell carcinoma (RCC). In this presentation, CRISPR disclosed the first reported complete response in a solid tumor setting using an allogeneic CAR T. In a Phase 1 trial in clear cell RCC (ccRCC), CTX130 showed a tolerable safety profile with encouraging anti-tumor activity and a 77% disease control rate in heavily pretreated patients. Based on the encouraging activity, the Company is advancing its next generation CAR T cell candidate targeting CD70, CTX131™, into the clinic this year following clearance of its IND application by the FDA in February 2023. CTX131 incorporates the edits in CTX130 plus additional edits to the genes encoding Regnase-1 and TGFBRII, which have been shown to increase the potency of the CAR T cells in pre-clinical studies.

- **Regenerative Medicine**

  - Following the previously-announced clearance of the Clinical Trial Application (CTA) by Health Canada for VCTX211™, a Phase 1/2 clinical trial of VCTX211 has been initiated and enrollment and dosing are ongoing. VCTX211 is an investigational, allogeneic, gene-edited, stem cell-derived product candidate for Type 1 Diabetes (T1D), which originated under the CRISPR Therapeutics and ViaCyte collaboration. In the third quarter of 2022, Vertex announced it had acquired ViaCyte.

  - The Phase 1 clinical trial investigating safety and tolerability of VCTX210 for the treatment of T1D, the first-generation allogeneic, gene-edited, stem cell-derived product candidate, has completed dosing. The VCTX210 trial was designed to demonstrate the safety of implanting devices containing the stem cell-derived cells into patients.

- ***In Vivo***

  - CRISPR Therapeutics continues to advance a number of programs which utilize its *in vivo* gene editing approach targeted to the liver using a lipid nanoparticle (LNP) delivery platform. Based upon the ongoing progress of its editing and delivery platform, the Company expects to advance its lead *in vivo* program, CTX310™, targeting angiopoietin-related protein 3 (ANGPTL3) into clinical trials this year. ANGPTL3 has been identified as an important therapeutic target for lowering plasma low-density lipoprotein (LDL) cholesterol and triglycerides which are important risk factors for the development of atherosclerotic cardiovascular disease. Beyond CTX310, the Company expects to advance additional programs directed towards cardiovascular risk reduction into the clinic in the next 12-18 months.

- CRISPR Therapeutics continues its discovery efforts related to *in vivo* approaches utilizing viral delivery methods for neuromuscular indications such as Amyotrophic Lateral Sclerosis (ALS) and Friedreich's Ataxia in collaboration with its partner, Capsida Therapeutics.

- **Other Corporate Matters**

  - In December, CRISPR Therapeutics announced the appointment of Alex Harding, M.D., M.B.A., as Senior Vice President and Head of Business Development. Dr. Harding brings extensive leadership experience in biopharma business development and corporate strategy and joins CRISPR Therapeutics to lead the Company's business development operations.

Fourth Quarter and Full Year 2022 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $1,868.4 million as of December 31, 2022, compared to $2,379.1 million as of December 31, 2021. The decrease in cash of $510.7 million was primarily driven by cash used in operating activities to support ongoing research and development.

- **Revenue:** Total collaboration revenue was not material for the quarter and year ended December 31, 2022. Collaboration revenue for the fourth quarter of 2021 was $12.3 million and collaboration revenue for the year ended December 31, 2021 was $913.1 million. Collaboration revenue recognized in 2021 was primarily attributable to revenue recognized in connection with an upfront and milestone payment.

- **R&D Expenses:** R&D expenses were $103.6 million for the fourth quarter of 2022, compared to $103.1 million for the fourth quarter of 2021, and $461.6 million for the year ended December 31, 2022, compared to $340.6 million for the year ended December 31, 2021. The increase in annual expense was driven by development activities supporting the advancement of our pipeline programs and reallocation of internal resources from our partnered programs to our wholly-owned programs.

- **G&A Expenses:** General and administrative expenses were $21.2 million for the fourth quarter of 2022, compared to $23.7 million for the fourth quarter of 2021, and $102.5 million for the year ended December 31, 2022, compared to $99.7 million for the year ended December 31, 2021.

- **Collaboration Expense:** Collaboration expense, net, was $6.8 million for the fourth quarter of 2022, compared to $31.8 million for the fourth quarter of 2021, and $110.3 million for the year ended December 31, 2022, compared to $101.2 million for the year ended December 31, 2021. The decrease in collaboration expense, net, for the fourth quarter was due to the fact that we exercised our option to defer specified costs on the exa-cel program in excess of $110.3 million

for the year ended December 31, 2022 in accordance with the amended collaboration agreement. Any such deferred amounts are only recoverable by Vertex as an offset against future profitability of the exa-cel program, subject to annual limits in accordance with the amended collaboration agreement. The increase in collaboration expense, net, for the full year was driven by the clinical development and commercial preparation for the exa-cel program.

- **Net (Loss) Income:** Net loss was $110.6 million for the fourth quarter of 2022, compared to a net loss of $141.2 million for the fourth quarter of 2021, and a net loss of $650.2 million for the year ended December 31, 2022, compared to net income of $377.7 million for the year ended December 31, 2021.

About exagamglogene autotemcel (exa-cel)
Exa-cel, formerly known as CTX001™, is an investigational, autologous, *ex vivo* CRISPR/Cas9 gene-edited therapy that is being evaluated for patients with TDT or SCD characterized by recurrent VOCs, in which a patient's own hematopoietic stem cells are edited to produce high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. 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. The elevation of HbF by exa-cel has the potential to alleviate transfusion requirements for patients with TDT and reduce painful and debilitating sickle crises for patients with SCD. Earlier results from these ongoing trials were published in *The New England Journal of Medicine* in January of 2021.

Based on progress in this program to date, exa-cel has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, Orphan Drug, and Rare Pediatric Disease designations from the FDA for both TDT and SCD. Exa-cel has also been granted Orphan Drug Designation from the European Commission, as well as Priority Medicines (PRIME) designation from the European Medicines Agency (EMA), for both TDT and SCD.

Among gene-editing approaches being evaluated for TDT and SCD, exa-cel is the furthest advanced in clinical development.

About CLIMB-111 and CLIMB-121
The ongoing Phase 1/2/3 open-label trials, CLIMB-111 and CLIMB-121, are designed to assess the safety and efficacy of a single dose of exa-cel in patients ages 12 to 35 years with TDT or with SCD, characterized by recurrent VOCs, respectively. The trials are now closed for enrollment. Patients will be followed for approximately two years after exa-cel infusion. Each patient will be asked to participate in CLIMB-131, a long-term follow-up trial.

About CLIMB-131
This is a long-term, open-label trial to evaluate the safety and efficacy of exa-cel in patients who received exa-cel in CLIMB-111, CLIMB-121, CLIMB-141 or CLIMB-151. The trial is designed to follow participants for up to 15 years after exa-cel infusion.

About CLIMB-141 and CLIMB-151

The ongoing Phase 3 open-label trials, CLIMB-141 and CLIMB-151, are designed to assess the safety and efficacy of a single dose of exa-cel in patients ages 2 to 11 years with TDT or with SCD, characterized by recurrent VOCs, respectively. The trials are now open for enrollment and currently enrolling patients ages 5 to 11 years of age and will plan to extend to patients 2 to less than 5 years of age at a later date. Each trial will enroll approximately 12 patients. Patients will be followed for approximately two years after infusion. Each patient will be asked to participate in CLIMB-131, a long-term follow-up- trial.

About the CRISPR-Vertex Collaboration

CRISPR Therapeutics and Vertex Pharmaceuticals 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 potential treatment to emerge from the joint research program. Under a recently amended collaboration agreement, Vertex will lead global development, manufacturing and commercialization of exa-cel and split program costs and profits worldwide 60/40 with CRISPR Therapeutics.

About CTX110 and CTX112

CTX110, a wholly owned program of CRISPR Therapeutics, is a healthy donor-derived gene-edited allogeneic CAR T investigational therapy targeting cluster of differentiation 19, or CD19. CTX110 is being investigated in the ongoing CARBON clinical trial, which is designed to assess the safety and efficacy of CTX110 in adult patients with relapsed or refractory CD19-positive B-cell malignancies who have received at least two prior lines of therapy. CTX110 has been granted RMAT designation by the FDA. In addition, CTX112, a next-generation allogeneic CAR T cell therapy targeting CD19, is being investigated in a clinical trial. CTX112 includes two additional edits beyond CTX110 that are designed to enhance the potency of the CAR T cells.

About CTX130 and CTX131

CTX130, a wholly owned program of CRISPR Therapeutics, is a healthy donor-derived gene-edited allogeneic CAR T investigational therapy targeting cluster of differentiation 70, or CD70, an antigen expressed on various solid tumors and hematologic malignancies. CTX130 is being developed for the treatment of relapsed or refractory T-cell hematologic malignancies in the COBALT-LYM trial. CTX130 has been granted Orphan Drug designation for the treatment of T-cell lymphoma by the FDA and RMAT designation for the treatment of relapsed or refractory Mycosis Fungoides and Sézary Syndrome (MF/SS), types of cutaneous T-cell lymphoma (CTCL). In addition, CTX131, a next-generation allogeneic CAR T cell therapy targeting CD70, is being assessed for safety and efficacy in a clinical trial investigating a basket of select solid tumors. CTX131 includes two additional edits beyond CTX130 that are designed to enhance the potency of the CAR T cells.

About VCTX210 and VCTX211

VCTX210 is an investigational, allogeneic, gene-edited, immune-evasive, stem cell-derived investigational therapy for the treatment of T1D. VCTX210 is being developed under a co-development and co-commercialization agreement between CRISPR Therapeutics and ViaCyte, Inc. VCTX211 is an allogeneic, gene-edited, stem cell-derived investigational therapy for the treatment of T1D, which incorporates additional gene edits that aim to further enhance cell fitness. This immune-evasive cell replacement therapy is designed to enable patients to produce their own insulin in response to glucose.

About CRISPR Therapeutics
CRISPR Therapeutics is a leading gene editing company focused on developing transformative gene-based medicines for serious diseases using its proprietary CRISPR/Cas9 platform. CRISPR/Cas9 is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. CRISPR Therapeutics has established a portfolio of therapeutic programs across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine and rare diseases. To accelerate and expand its efforts, CRISPR Therapeutics has established strategic partnerships with leading companies including Bayer, Vertex Pharmaceuticals and ViaCyte, Inc. 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. For more information, please 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 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 preclinical studies, clinical trials and pipeline products and programs, including, without limitation, status of such studies and trials, expected timing of data releases, timing of regulatory submissions and the regulatory filings for exa-cel; (ii) the sufficiency of its cash resources; (iii) the expected benefits of its collaborations; 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 potential for preliminary data from any clinical trial not to be indicative of final trial results; the potential that clinical trial results may not be favorable; that one or more of its internal or external product candidate programs will not proceed as planned for technical, scientific or commercial reasons; that 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; 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. CRISPR

Investor Contact:
Susan Kim
+1-617-307-7503
susan.kim@crisprtx.com

Media Contact:
Rachel Eides
+1-617-315-4493
rachel.eides@crisprtx.com

CRISPR Therapeutics AG
Condensed Consolidated Statements of Operations
(Unaudited, In thousands except share data and per share data)

	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Revenue:				
Collaboration revenue	$ 6	$ 12,348	$ 436	$ 913,081
Grant revenue	—	551	762	1,882
Total revenue	$ 6	$ 12,899	$ 1,198	$ 914,963
Operating expenses:				
Research and development	103,555	103,095	461,645	340,567
General and administrative	21,169	23,678	102,464	99,690
Collaboration expense, net	6,823	31,824	110,250	101,178
Total operating expenses	131,547	158,597	674,359	541,435
Total operating expenses	(131,541)	(145,698)	(673,161)	373,528
Total other income, net	11,490	2,197	22,661	6,003
Net (loss) income before income taxes	(120,051)	(143,501)	(650,500)	379,531
Benefit (provision) for income taxes	9,476	2,253	325	(1,870)
Net (loss) income	(110,575)	(141,248)	(650,175)	377,661
Foreign currency translation adjustment	115	3	(80)	(11)
Unrealized loss on marketable securities	6,501	(4,300)	(10,500)	(4,973)
Comprehensive (loss) income	$ (103,959)	$ (145,545)	$ (660,755)	$ 372,677
Net (loss) income per common share — basic	$ (1.41)	$ (1.84)	$ (8.36)	$ 4.97
Basic weighted-average common shares outstanding	78,336,506	76,649,727	77,746,575	75,948,686
Net (loss) income per common share — diluted	$ (1.41)	$ (1.84)	$ (8.36)	$ 4.70
Diluted weighted-average common shares outstanding	78,336,506	76,649,727	77,746,575	80,393,496

CRISPR Therapeutics AG
Condensed Consolidated Balance Sheets Data
(Unaudited, in thousands)

	As of	
	December 31, 2022	December 31, 2021
Cash	$ 211,885	$ 923,031
Marketable securities	1,603,433	1,456,098
Marketable securities, non-current	53,130	—
Working capital	1,731,919	2,297,630
Total assets	2,243,057	2,751,877
Total shareholders' equity	1,875,479	2,399,460