CRISPR Therapeutics Provides Business Update and Reports Fourth Quarter and Full Year 2021 Financial Results

- More than 70 patients have been dosed with CTX001™ across CLIMB-Thal-111 and CLIMB-SCD-121 to date; enrollment complete and regulatory submissions planned for late 2022-

-Initiated and began dosing patients in the pivotal trial of CTX110™, targeting CD19+ B-cell malignancies; additional data expected to report in 2022-

-Top-line data expected to report in 1H2022 for ongoing CTX120™ and CTX130™ clinical trials-

-First patient dosed in Phase 1 clinical trial of VCTX210 for the treatment of type 1 diabetes (T1D)-

ZUG, Switzerland and CAMBRIDGE, Mass., February 15, 2022 – 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, 2021.

"2021 was a productive year for CRISPR Therapeutics on all fronts. We and our partner Vertex completed enrollment in the CTX001 clinical trials and are on track for planned regulatory submissions in late 2022," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "Concurrently, we advanced our wholly-owned immuno-oncology pipeline, and have initiated dosing of patients in our CTX110 pivotal trial. Further, we and our partner ViaCyte, recently announced the dosing of the first patient in the Phase 1 clinical trial of VCTX210 for the treatment of type 1 diabetes. This investigational therapy has the potential to be a transformative treatment for patients with all insulin-requiring forms of diabetes. Looking ahead, we expect a productive 2022 with continued progress across our portfolio as we enter a new phase of growth for our Company. Given the breadth of our portfolio and our strong capital position, we remain well positioned to advance our pipeline and platform to develop transformative medicines for patients suffering from serious diseases."

Recent Highlights and Outlook

- **Beta Thalassemia and Sickle Cell Disease Programs**
    - More than 70 patients have been dosed with CTX001 across both trials to date. Target enrollment has been achieved in the ongoing clinical trials for CTX001 in transfusion-dependent beta thalassemia (TDT) and severe sickle cell disease (SCD), with planned regulatory submissions in late 2022.
    - In June 2021, data from 22 patients with at least three months of follow-up after CTX001 infusion were presented at the Annual European Hematology Association Virtual Congress (EHA) and continued to build the profile of a potentially functional cure for patients with TDT and SCD, showing consistent and durable benefit with longer term data from a larger population of patients.

- In April 2021, CRISPR Therapeutics and Vertex announced an amendment to their collaboration for CTX001. In connection with the completion of the transaction in June, Vertex made a $900 million upfront payment to CRISPR Therapeutics.

- In April 2021, CRISPR Therapeutics and Vertex announced that the European Medicines Agency (EMA) granted Priority Medicines (PRIME) designation to CTX001 for the treatment of TDT. CTX001 was granted PRIME designation for the treatment of SCD in 2020.

- **Immuno-Oncology Programs**

  - CRISPR Therapeutics has begun dosing patients in the pivotal trial of CTX110, its wholly-owned allogeneic chimeric antigen receptor T cell (CAR-T) investigational therapy targeting CD19+ B-cell malignancies. Enrollment is ongoing and the Company expects to report additional data in 2022. The U.S. Food and Drug Administration (FDA) granted Regenerative Medicine Advanced Therapy (RMAT) designation to CTX110 in November 2021.

  - In October 2021, CRISPR Therapeutics announced positive results from its ongoing Phase 1 CARBON trial evaluating the safety and efficacy of CTX110. The data showed early evidence of a dose dependent response to CTX110, with overall response rates (ORR), complete response rates (CR) and durability similar to approved autologous CD19 CAR-T therapies on an intent-to-treat (ITT) basis. A single dose of CTX110 at DL2 and above resulted in a 58% ORR and 38% CR rate in large B-cell lymphoma (LBCL) patients on an ITT basis. The pharmacokinetic data provide a strong rationale that consolidation dosing can improve on an already competitive profile for CTX110. Based on the safety and efficacy profile, the Company has expanded the current trial into a pivotal trial that incorporates consolidation dosing and has begun dosing patients in this pivotal arm. The Company expects to report additional data in 2022.

  - In addition to CTX110, CRISPR Therapeutics has ongoing Phase 1 clinical trials assessing safety and efficacy of several dose levels for the following CAR-Ts: (i) CTX120, its wholly-owned allogeneic CAR-T investigational therapy targeting B-cell maturation antigen for the treatment of relapsed or refractory multiple myeloma; and (ii) CTX130, its wholly-owned allogeneic CAR-T investigational therapy targeting CD70 for the treatment of both solid tumors and certain hematologic malignancies. The Company expects to report top-line data in the first half of 2022.

  - In May 2021, CRISPR Therapeutics and Nkarta, Inc. announced a strategic partnership to research, develop, and commercialize CRISPR/Cas9 gene-edited cell therapies for cancer. Under the agreement, the companies will co-develop and co-commercialize two CAR-NK cell product candidates, one targeting the CD70 tumor antigen and the other target to be determined. In addition, the companies will bring together their complementary cell therapy engineering and manufacturing capabilities to advance the development of a

novel NK+T product candidate harnessing the synergies of the adaptive and innate immune systems.

- **Regenerative Medicine and *In Vivo* Programs**

    - Earlier this month, CRISPR Therapeutics and its partner ViaCyte announced the first patient had been dosed in the Phase 1 clinical trial of VCTX210 for the treatment of T1D. VCTX210 is an investigational, allogeneic, gene-edited, stem cell-derived product developed in collaboration by applying CRISPR Therapeutics' gene-editing technology to ViaCyte's proprietary stem cell capabilities for the generation of pancreatic cells designed to evade recognition by the immune system. This immune-evasive cell replacement therapy is designed to enable patients to produce their own insulin.

    - In June 2021, CRISPR Therapeutics and Capsida Biotherapeutics, Inc. announced a strategic partnership to research, develop, manufacture and commercialize *in vivo* gene editing therapies delivered with engineered AAV vectors for the treatment of familial amyotrophic lateral sclerosis (ALS) and Friedreich's ataxia. Under the agreement, CRISPR Therapeutics will lead research and development of the Friedreich's ataxia program and perform gene-editing activities for both programs, and Capsida will lead research and development of the ALS program and conduct capsid engineering for both programs.

    - The Company continues to make progress with its *in vivo* approaches for liver gene editing utilizing both viral and non-viral delivery vehicles. The Company expects to move multiple programs utilizing *in vivo* approaches into the clinic in the next 18 to 24 months.

- **Other Corporate Matters**

    - Under the June 2019 collaboration agreement with Vertex to discover and develop gene editing therapies for the treatment of Duchenne Muscular Dystrophy (DMD) and Myotonic Dystrophy Type 1 (DM1), CRISPR Therapeutics received a payment of $12.5 million from Vertex related to the achievement of a research milestone in the DM1 program. CRISPR Therapeutics is eligible to receive additional milestone payments from Vertex of up to $775 million for these two programs.

Fourth Quarter and Full Year 2021 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $2,379.1 million as of December 31, 2021, compared to $1,690.3 million as of December 31, 2020. The increase in our cash position of $688.8 million was primarily driven by an upfront payment of $900.0 million in connection with the Amended and Restated Joint Development and Commercialization Agreement with Vertex. Additionally, cash provided by financing activities was $250.9 million, primarily related to common shares issued in connection with utilizing the Company's at-the-market (ATM) financing facility as well as option exercises. These increases were offset by continuing operating expenses to support ongoing research and development

of the Company's clinical and pre-clinical programs as well as capital investments in our manufacturing facility.

- **Revenue:** Total collaboration revenue was $12.3 million for the fourth quarter of 2021 compared to $0.2 million for fourth quarter of 2020, and $913.1 million for the year ended December 31, 2021, compared to $0.5 million for the year ended December 31, 2020. The increase in collaboration revenue is primarily attributable to revenue recognized in connection with the aforementioned payments received from Vertex.
- **R&D Expenses:** R&D expenses were $134.5 million for the fourth quarter of 2021 compared to $82.4 million for the fourth quarter of 2020, and $438.6 million for the year ended December 31, 2021, compared to $266.9 million for the year ended December 31, 2020. The increase in expense for the year was driven by development activities supporting the advancement of the hemoglobinopathies program and wholly-owned immuno-oncology programs, as well as increased headcount and supporting facilities-related expenses.
- **G&A Expenses:** General and administrative expenses were $24.1 million for the fourth quarter of 2021 compared to $25.8 million for the fourth quarter of 2020, and $102.8 million for the year ended December 31, 2021, compared to $88.2 million for the year ended December 31, 2020. The increase in general and administrative expenses for the year was driven by headcount-related expense.
- **Net Income / Loss:** Net loss was $141.2 million for the fourth quarter of 2021 compared to a net loss of $107.0 million for the fourth quarter of 2020, and net income was $377.7 million for the year ended December 31, 2021, compared to a net loss of $348.9 million for the year ended December 31, 2020.

About CTX001

CTX001 is an investigational, autologous, *ex vivo* CRISPR/Cas9 gene-edited therapy that is being evaluated for patients suffering from TDT or severe SCD, in which a patient's hematopoietic stem cells are edited to produce high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. HbF is a form of the oxygen-carrying hemoglobin that is naturally present at birth, which then switches to the adult form of hemoglobin. The elevation of HbF by CTX001 has the potential to alleviate or eliminate transfusion requirements for patients with TDT and reduce or eliminate painful and debilitating sickle crises for patients with SCD. Earlier results from these ongoing trials were published as a Brief Report in *The New England Journal of Medicine* in January of 2021.

Based on progress in this program to date, CTX001 has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, Orphan Drug, and Rare Pediatric Disease designations from the U.S. Food and Drug Administration (FDA) for both TDT and SCD. CTX001 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 investigated/evaluated for TDT and SCD, CTX001 is the furthest advanced in clinical development.

About the CRISPR-Vertex Collaboration
Vertex and CRISPR Therapeutics 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. CTX001 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 CTX001 and split program costs and profits worldwide 60/40 with CRISPR Therapeutics.

About CLIMB-111
The ongoing Phase 1/2 open-label trial, CLIMB-Thal-111, is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 12 to 35 with TDT. The trial will enroll up to 45 patients and follow patients for approximately two years after infusion. Each patient will be asked to participate in a long-term follow-up trial.

About CLIMB-121
The ongoing Phase 1/2 open-label trial, CLIMB-SCD-121, is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 12 to 35 with severe SCD. The trial will enroll up to 45 patients and follow patients for approximately two years after infusion. Each patient will be asked to participate in a long-term follow-up trial.

About CLIMB-131
This is a long-term, open-label trial to evaluate the safety and efficacy of CTX001 in patients who received CTX001 in CLIMB-111 or CLIMB-121. The trial is designed to follow participants for up to 15 years after CTX001 infusion.

About CTX110
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 trial.

About CARBON
The ongoing Phase 1 single-arm, multi-center, open label clinical trial, CARBON, is designed to assess the safety and efficacy of several dose levels of CTX110 for the treatment of relapsed or refractory B-cell malignancies.

About CTX120
CTX120, a wholly-owned program of CRISPR Therapeutics, is a healthy donor-derived gene-edited allogeneic CAR-T investigational therapy targeting B-cell maturation antigen, or BCMA. CTX120 is being investigated in an ongoing Phase 1 single-arm, multi-center, open-label clinical trial designed to assess the safety and efficacy of several dose levels of CTX120 for the treatment of relapsed or refractory multiple myeloma. CTX120 has been granted Orphan Drug designation from the FDA.

About CTX130

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 both solid tumors, such as renal cell carcinoma, and T-cell and B-cell hematologic malignancies. CTX130 is being investigated in two ongoing independent Phase 1, single-arm, multi-center, open-label clinical trials that are designed to assess the safety and efficacy of several dose levels of CTX130 for the treatment of relapsed or refractory renal cell carcinoma and various subtypes of lymphoma, respectively.

About VCTX210

VCTX210 is an investigational, allogeneic, gene-edited, immune-evasive, stem cell-derived therapy for the treatment of T1D. VCTX210 is being developed under a co-development and co-commercialization agreement between CRISPR Therapeutics and ViaCyte, Inc.

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 collaborations 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 Cambridge, Massachusetts, and business offices in San Francisco, California and 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) the safety, efficacy and clinical progress of CRISPR Therapeutics' various clinical programs, including CTX001, CTX110, CTX120, CTX130, and VCTX210; (ii) the status of clinical trials (including, without limitation, expectations regarding the data that is being presented, the expected timing of data releases and development, as well as completion of clinical trials) and development timelines for CRISPR Therapeutics' product candidates; (iii) 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, including expectations regarding the CTX001 and CTX110 data that was previously presented; (iv) its in vivo programs; (v) the actual or potential benefits of regulatory designations; (vi) the intellectual property coverage and positions of CRISPR Therapeutics, its licensors and third parties as well as the status and potential outcome of proceedings involving any such intellectual property; (vii) the sufficiency of CRISPR Therapeutics' cash resources; (viii) the expected benefits of CRISPR Therapeutics' collaborations; and (ix) 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 initial and preliminary data from any clinical trial and initial data from a limited number of patients not to be indicative of final trial results; the potential that clinical trial results may not be favorable; that one or more of CRISPR Therapeutics' 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 CRISPR Therapeutics' product candidates; uncertainties inherent in the initiation and completion of preclinical studies for CRISPR Therapeutics' product candidates (including, without limitation, availability and timing of results and whether such results will be predictive of future results of the future trials); uncertainties about regulatory approvals to conduct trials or to market products; the potential impacts due to the coronavirus pandemic such as (x) delays in regulatory review, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy; (y) the timing and progress of clinical trials, preclinical studies and other research and development activities; and (z) the overall impact of the coronavirus pandemic on its business, financial condition and results of operations; uncertainties regarding the intellectual property protection for CRISPR Therapeutics' 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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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,	
	2021	2020	2021	2020
Revenue:				
Collaboration revenue	$ 12,348	$ 194	$ 913,081	$ 543
Grant revenue	551	176	1,882	176
Total revenue	$ 12,899	$ 370	$ 914,963	$ 719
Operating expenses:				
Research and development	134,470	82,365	438,633	266,946
General and administrative	24,127	25,766	102,802	88,208
Total operating expenses	158,597	108,131	541,435	355,154
(Loss) income from operations	(145,698)	(107,761)	373,528	(354,435)
Total other income, net	2,197	575	6,003	6,379
Net (loss) income before income taxes	(143,501)	(107,186)	379,531	(348,056)
Benefit (provision) for income taxes	2,253	147	(1,870)	(809)
Net (loss) income	(141,248)	(107,039)	377,661	(348,865)
Foreign currency translation adjustment	3	37	(11)	40
Unrealized loss on marketable securities	(4,300)	14	(4,973)	(130)
Comprehensive (loss) income	$ (145,545)	$ (106,988)	$ 372,677	$ (348,955)
Net (loss) income per common share — basic	$ (1.84)	$ 1.50	$ 4.97	$ (5.29)
Basic weighted-average common shares outstanding	76,649,727	71,282,096	75,948,686	65,949,672
Net (loss) income per common share — diluted	$ (1.84)	$ 1.50	$ 4.70	$ (5.29)
Diluted weighted-average common shares outstanding	76,649,727	71,282,096	80,393,496	65,949,672

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

	As of	
	December 31, 2021	December 31, 2020
Cash	$ 923,031	$ 1,168,620
Marketable securities	1,456,098	521,713
Working capital	2,297,630	1,622,361
Total assets	2,751,877	1,827,966
Total shareholders' equity	2,399,460	1,664,234