CRISPR Therapeutics Provides Business Update and Reports Second Quarter 2022 Financial Results

-CLIMB-111 and CLIMB-121 fully enrolled; completed regulatory discussions for exagamglogene autotemcel (exa-cel), formerly known as CTX001™, with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA); discussions with the U.S. Food and Drug Administration (FDA) ongoing-

-Initiated two additional Phase 3 clinical trials of exa-cel for the treatment of transfusion-dependent beta thalassemia (TDT) or severe sickle cell disease (SCD) in pediatric patients-

-Enrollment and dosing ongoing for CTX110®, targeting CD19+ B-cell malignancies; expecting to report additional data in 2022-

-Enrollment and dosing ongoing for CTX130™, targeting CD70 for the treatment of both solid tumors and certain hematologic malignancies-

-Expects to submit Investigational New Drug Applications (INDs) for two next generation chimeric antigen receptor T cell (CAR-T) candidates by year-end-

-Expects to submit a Clinical Trials Application (CTA) for VCTX211™ for the treatment of Type 1 Diabetes (T1D) in 2H 2022-

ZUG, Switzerland and BOSTON, Mass., August 8, 2022 – CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today reported financial results for the second quarter ended June 30, 2022.

"Strong progress continues across our broad portfolio of gene edited therapies and we remain on track to achieve important 2022 milestones," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "We and our partner Vertex presented new clinical data at EHA highlighting the potentially transformative profile of exa-cel in patients with TDT or SCD. We also presented encouraging new clinical data for CTX130 for the treatment of both solid tumors and certain hematologic malignancies, and we expect to report data from our ongoing trial of CTX110 targeting CD19+ B-cell malignancies later this year. In addition, we and our partner ViaCyte continue to enroll and dose patients in the Phase 1 clinical trial of VCTX210™ for T1D. We remain well positioned and well capitalized to bring transformative medicines for patients suffering from serious diseases."

Dr. Kulkarni further added, "During our Innovation Day in June, we presented the depth and breadth of our pipeline and highlighted our platform innovations to create the next generation of genomic medicines. We are poised to significantly expand our pipeline programs of potentially curative therapies with the addition of new development candidates as we continue to innovate our genome editing, delivery, and cell engineering capabilities."

Recent Highlights and Outlook

- **Hemoglobinopathies**

- In June, CRISPR Therapeutics and Vertex Pharmaceuticals presented new clinical data at the European Hematology Association (EHA) Congress on exagamglogene autotemcel (exa-cel), formerly known as CTX001, highlighting the potentially transformative profile of this investigational therapy for people with transfusion-dependent beta thalassemia (TDT) or severe sickle cell disease (SCD). Data from 75 patients (44 with TDT, 31 with SCD) from the CLIMB-111, CLIMB-121 and CLIMB-131 studies with follow-up ranging from 1.2 to 37.2 months after exa-cel infusion continued to demonstrate that exa-cel has the potential to be a durable, one-time functional cure. All 31 patients with severe SCD, characterized by recurrent vaso-occlusive crises (VOCs), were free of VOCs after exa-cel infusion through the duration of follow-up, with follow-up ranging from 2.0 to 32.3 months. Of the 44 patients with TDT, 42 were transfusion-free with follow-up ranging from 1.2 to 37.2 months. Two patients who were not yet transfusion-free had 75% and 89% reductions in transfusion volume, respectively. The safety profile was generally consistent with myeloablative conditioning with busulfan and autologous stem cell transplant. The CLIMB-111 and CLIMB-121 trials are in Phase 3 and fully enrolled.

- CRISPR Therapeutics and Vertex have initiated two additional Phase 3 clinical trials, CLIMB-131 and CLIMB-141, for exa-cel in pediatric patients with TDT or SCD.

- CRISPR Therapeutics and Vertex have completed discussions with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) on the submission package for exa-cel and are on track to submit for regulatory approvals of exa-cel for SCD and TDT in Europe and the U.K. by the end of 2022. Discussions with the FDA are ongoing.

- In June, CRISPR Therapeutics hosted an Innovation Day focused on research and development, during which it presented preclinical data on its anti-CD117 (c-Kit) antibody-drug conjugate (ADC). The Company plans to advance this internal targeted conditioning program towards clinical studies.

- **Immuno-Oncology**

  - CRISPR Therapeutics continues to enroll and dose 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. The Company expects to report additional data in 2022.

  - In June, CRISPR Therapeutics presented new T-cell lymphoma clinical data at the EHA Congress from the Company's ongoing Phase 1 COBALT™-LYM trial evaluating the safety and efficacy of CTX130, its wholly-owned allogeneic CAR-T investigational therapy targeting CD70, for both solid tumors and certain hematologic malignancies. The preliminary data demonstrate that CTX130 has the potential to provide meaningful

clinical benefit with a well-tolerated safety profile. The Company continues to enroll and dose patients in the dose expansion trial.

- In June, at CRISPR Therapeutics' Innovation Day, the Company provided the following updates regarding its wholly-owned oncology programs:
  - Presented new clinical data from the Company's ongoing Phase 1 COBALT-RCC trial evaluating the safety and efficacy of CTX130 for the treatment of relapsed or refractory renal cell carcinoma (RCC). The preliminary data demonstrates the first signs of meaningful activity in solid tumors with an allogeneic cell therapy and a well-tolerated safety profile.
  - Announced plans to advance next-generation investigational therapies with additional gene edits that have the potential to improve upon first-generation programs. The Company expects to advance two next-generation constructs to IND by year end: CTX131™ and CTX112™ targeting CD70 and CD19, respectively.
  - Announced plans for a next-generation allogeneic CAR-T therapy targeting B-cell maturation antigen (BCMA) that incorporates proprietary edits to enhance the potency of the CAR-T cells.
  - Announced collaborations with top cancer centers on new targets. One with Moffitt Cancer Center will seek to advance a first-in-human trial for an autologous CAR-T investigational therapy targeting CD83 for the potential treatment of acute myeloid leukemia (AML) and other oncology and autoimmune indications. A second with Roswell Park Comprehensive Cancer Center will seek to advance an initial trial for an autologous, gene-edited CAR-T therapy targeting GPC3 for the potential treatment of solid tumors.

- **Regenerative Medicine**

  - Enrollment and dosing are ongoing 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 with ViaCyte that applies 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, at CRISPR Therapeutics' Innovation Day, the Company provided the following updates regarding its regenerative medicine programs:
    - Announced plans to expand its regenerative medicine pipeline with two next-generation approaches. The first, VCTX211™, features novel edits to promote cell survival. The Company plans to file a CTA for VCTX211 in the second half of 2022. The second program, VCTX212™, is in early-stage development for the treatment of Type 1 and Type 2 diabetes.

- ***In Vivo***

- In June, at CRISPR Therapeutics' Innovation Day, the Company provided the following updates regarding its *in vivo* programs:
  - Based upon ongoing progress with its *in vivo* approaches for liver gene editing utilizing both viral and non-viral delivery vehicles, CRISPR Therapeutics continues to expect to move multiple programs utilizing *in vivo* approaches into the clinic in the next 12 to 18 months, including programs in cardiovascular disease. The Company's lead program, CTX310™, targeting angiopoietin-related protein 3 (ANGPTL3) is currently in IND-enabling studies.
  - Announced the establishment of CRISPR-X, a dedicated group within CRISPR Therapeutics focused on emerging technologies, including those to allow HDR-independent and/or AAV-free whole gene correction and insertion.

- **Other Corporate Matters**

  - In May, CRISPR Therapeutics announced the appointment of Phuong Khanh (P.K.) Morrow, M.D., FACP, as Chief Medical Officer. Dr. Morrow brings more than a decade of leadership experience in global drug development and joined CRISPR Therapeutics to lead the Company's global clinical development and regulatory operations.

Second Quarter 2022 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $2,073.7 million as of June 30, 2022, compared to $2,379.1 million as of December 31, 2021. The decrease in cash of $305.4 million was primarily driven by cash used in operating activities to support ongoing research and development of the Company's clinical and pre-clinical programs.

- **Revenue:** Total collaboration revenue was $0.2 million for the second quarter of 2022, compared to $900.2 million for the second quarter of 2021. Revenue for the second quarter of 2021 was primarily associated with the $900.0 million upfront payment from Vertex in connection with the Amended and Restated Joint Development and Commercialization Agreement.

- **R&D Expenses:** R&D expenses were $123.2 million for the second quarter of 2022, compared to $82.3 million for the second quarter of 2021. The increase in expense was driven by development activities supporting the advancement of our wholly-owned immuno-oncology programs, as well as expenses related to our new U.S. research and development headquarters.

- **G&A Expenses:** General and administrative expenses of $26.3 million for the second quarter of 2022 were consistent with general and administration expenses of $28.8 million for the second quarter of 2021.

- **Collaboration Expense:** Collaboration expense, net, was $33.9 million for the second quarter of 2022, compared to $26.9 million for the second quarter of 2021. The increase in collaboration expense, net, was primarily driven by increased pre-commercial and manufacturing scale-up costs associated with our hemoglobinopathies programs under our collaboration with Vertex.

- **Net Loss:** Net loss was $185.8 million for the second quarter of 2022, compared to net income of $759.2 million for the second quarter of 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 CARBON Trial

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, a 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. CTX110 has been granted Regenerative Medicine Advanced Therapy designation from the FDA.

About CTX130 and COBALT Trials

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 (COBALT™-RCC), and T-cell and B-cell hematologic malignancies (COBALT™-LYM). 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. CTX130 has been granted Orphan Drug designation for the treatment of T-cell lymphoma from the FDA.

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 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 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) its plans for and its preclinical studies, clinical trials and pipeline products and programs; (ii) the safety, efficacy and progress of its various clinical and preclinical programs, including the actual or potential benefits of regulatory designations; (iii) the status of preclinical studies and clinical trials (including, without limitation, the expected timing of data releases, announcement of additional programs, and discussions with regulatory authorities, including the timing of regulatory submissions and the anticipated regulatory filings for exa-cel), as well as expectations regarding the data that is being presented; (iv) its intellectual property coverage and positions of its, its licensors and third parties, as well as the status and potential outcome of proceedings involving any such intellectual property; (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 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 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; potential impacts due to the coronavirus pandemic such as manufacturing and supply chain interruptions and the timing and progress of clinical trials; 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 THERAPEUTICS® standard character mark and design logo, COBALT™, CTX001™, CTX110®, CTX112™, CTX130™, CTX131™, CTX310™, VCTX210™, VCTX211™, and VCTX212™ are trademarks and registered trademarks of CRISPR Therapeutics AG. All other trademarks and registered trademarks are the property of their respective owners.

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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 June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Revenue:				
Collaboration revenue	$ 158	$ 900,202	$ 336	$ 900,404
Grant revenue	—	499	762	836
Total revenue	$ 158	$ 900,701	$ 1,098	$ 901,240
Operating expenses:				
Research and development	123,223	82,332	241,468	153,971
General and administrative	26,273	28,806	54,294	52,303
Collaboration expense, net	33,922	26,945	64,568	46,891
Total operating expenses	183,418	138,083	360,330	253,165
Total operating expenses	(183,260)	762,618	(359,232)	648,075
Total other income, net	3,544	750	3,907	2,705
Net loss before income taxes	(179,716)	763,368	(355,325)	650,780
Provision for income taxes	(6,118)	(4,143)	(9,726)	(4,718)
Net loss	(185,834)	759,225	(365,051)	646,062
Foreign currency translation adjustment	(69)	5	(95)	10
Unrealized loss on marketable securities	(3,380)	(173)	(15,180)	(556)
Comprehensive loss	$ (189,283)	$ 759,057	$ (380,326)	$ 645,516
Net loss per common share — basic	$ (2.40)	$ 10.01	$ (4.72)	$ 8.57
Basic weighted-average common shares outstanding	77,513,327	75,826,594	77,306,970	75,418,160
Net loss per common share — diluted	$ (2.40)	$ 9.44	$ (4.72)	$ 8.03
Diluted weighted-average common shares outstanding	77,513,327	80,449,956	77,306,970	80,458,855

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

	As of	
	June 30, 2022	December 31, 2021
Cash	$ 496,893	$ 923,031
Marketable securities	1,568,446	1,456,098
Marketable securities, non-current	8,392	—
Working capital	1,987,099	2,297,630
Total assets	2,463,363	2,751,877
Total shareholders' equity	2,090,831	2,399,460