CRISPR Therapeutics Provides Business Update and Reports First Quarter 2023 Financial Results

-Regulatory submissions complete for exagamglogene autotemcel (exa-cel), formerly known as CTX001™, in the U.S. for transfusion-dependent beta thalassemia (TDT) and severe sickle cell disease (SCD)-

-EU and U.K. submissions validated by European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA); exa-cel has been granted an Innovation Passport under the Innovative Licensing and Access Pathway (ILAP) from the MHRA-

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

-Initiated clinical trials for next generation CAR T candidates, 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)-

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

ZUG, Switzerland and BOSTON, May 08, 2023 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today reported financial results for the first quarter ended March 31, 2023.

"In the first quarter of 2023, we continued strong momentum across our portfolio. We and our partner Vertex have now completed regulatory submissions for exa-cel in the United States, European Union and United Kingdom, positioning exa-cel to potentially become the first approved CRISPR-based therapy in the world, a remarkable pace of progress considering the discovery of the CRISPR platform took place a little more than a decade ago," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "In parallel, we continue to drive our portfolio programs, including the initiation of clinical trials for our next-generation CAR T candidates, CTX112 and CTX131. In addition, we expect to advance CTX310, our lead *in vivo* program targeting ANGPTL3, into clinical trials later this year. We are well-positioned to drive towards our mission of bringing transformative and potentially curative therapies to patients in need."

Recent Highlights and Outlook

- **Hemoglobinopathies**
  - In April, CRISPR Therapeutics and Vertex Pharmaceuticals announced the completion of the rolling submissions of their biologics licensing applications (BLAs) to the U.S. Food and Drug Administration (FDA) for the investigational treatment exagamglogene autotemcel (exa-cel), formerly known as CTX001™, for severe sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT). The BLAs include requests for Priority Review, which, if granted, would shorten the FDA's review of the application to eight months from the time of submission versus a standard review timeline of 12 months. In the U.S., exa-cel has been granted Fast Track, Regenerative Medicine Advanced Therapy (RMAT), Orphan Drug (ODD) and Rare Pediatric Disease designations.
  - In December 2022, CRISPR Therapeutics and Vertex Pharmaceuticals completed regulatory submissions for exa-cel 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 Applications (MAAs), indicating acceptance of the marketing applications and initiation of the review. Exa-cel has been granted Priority Medicines (PRIME) and ODD in the EU. In the U.K., exa-cel has been granted an Innovation Passport under the Innovative Licensing and Access Pathway (ILAP) from the MHRA.
  - 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**
  - CRISPR Therapeutics continues to enroll and dose patients in a Phase 2 single-arm potentially registrational clinical trial of CTX110®, its wholly-owned allogeneic chimeric antigen receptor T cell (CAR T) investigational therapy targeting CD19+ B-cell malignancies.
  - CRISPR Therapeutics continues to enroll and dose patients in 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 preliminary 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.
  - CRISPR Therapeutics has begun enrolling patients in the CTX112™ clinical trial, its next generation CAR T candidate targeting CD19+ B-cell malignancies, following the previously-announced clearance of its Investigational New Drug (IND) application by the 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. CRISPR Therapeutics also has initiated a clinical trial for CTX131™, its next generation CAR T cell candidate targeting CD70, 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.
  - In April, CRISPR Therapeutics presented an oral presentation of preclinical data at the New Drugs on the Horizon Session (Part 1) in the American Association for Cancer Research (AACR) 2023 Annual Meeting for CTX112 and CTX131, entitled CTX112 and CTX131: Next-generation CRISPR/Cas9-engineered allogeneic CAR T cells incorporating novel edits that increase potency and efficacy in the treatment of lymphoid and solid tumors.
- **Regenerative Medicine and *In Vivo***
  - In March, CRISPR Therapeutics and Vertex and CRISPR Therapeutics and ViaCyte, Inc., which was acquired by Vertex in 2022, entered into agreements relating to the research, development, manufacturing and commercialization of therapeutic products in the diabetes field, including a new non-exclusive licensing agreement for the use of CRISPR Therapeutics' CRISPR/Cas9 gene editing technology to accelerate the development of Vertex's hypoimmune cell therapies for type 1 diabetes (T1D). In connection with entering into the agreements with Vertex and ViaCyte, CRISPR Therapeutics received $100 million up-front from Vertex. CRISPR Therapeutics will be eligible for up to an additional $230 million in research and development milestones and receive royalties on any future products resulting from the non-exclusive licensing agreement. CRISPR Therapeutics and ViaCyte continue to collaborate on their existing gene-edited allogeneic stem cell therapies, using ViaCyte cells, for the treatment of diabetes under the terms of their collaboration.
  - Based upon ongoing progress with its *in vivo* approaches for liver gene editing, CRISPR Therapeutics expects to move multiple programs utilizing *in vivo* approaches into the clinic within the next 12 months. The Company continues to advance its lead *in vivo* program, CTX310™, targeting angiopoietin-related protein 3 (ANGPTL3) into clinical trials this year.
- **Other Corporate Matters**
  - In March, CRISPR Therapeutics announced the appointment of Raju Prasad, Ph.D., as Chief Financial Officer. He joined CRISPR Therapeutics from William Blair & Company, where he served as a Partner and Senior Equity Research Analyst covering cell therapy, gene therapy, and gene editing companies.
  - In March, CRISPR Therapeutics announced the departure of Brad Bolzon, Ph.D., Chairman and Managing Director of Versant Ventures, from the Board of Directors after nearly a decade of service.

First Quarter 2023 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $1,889.5 million as of March 31, 2023, compared to $1,868.4 million as of December 31, 2022. The increase in cash of $21.1 million was primarily driven by the upfront payment received from Vertex in connection with a non-exclusive license agreement and a benefit from changes in net-working capital, offset by operating expenses.
- **Revenue:** Total collaboration revenue was $100.0 million for the quarter ended March 31, 2023. Collaboration revenue for the first quarter of 2022 was not material. Collaboration revenue recognized in the first quarter of 2023 was primarily attributable to revenue recognized in connection with the upfront payment from Vertex.
- **R&D Expenses:** R&D expenses were $99.9 million for the first quarter of 2023, compared to $118.2 million for the first quarter of 2022. The decrease in R&D expense was primarily driven by reduced variable external research and manufacturing costs.
- **G&A Expenses:** General and administrative expenses were $22.4 million for the first quarter of 2023, compared to $28.0 million for the first quarter of 2022. The decrease in G&A expense was primarily driven by a decrease in external professional costs.
- **Collaboration Expense:** Collaboration expense, net, was $42.2 million for the first quarter of 2023, compared to $30.6

million for the first quarter of 2022. The increase in collaboration expense, net, was primarily driven by an increase in manufacturing and pre-commercial costs associated with the exa-cel program.

- **Net Loss:** Net loss was $53.1 million for the first quarter of 2023, compared to a net loss of $179.2 million for the first quarter of 2022.

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 vaso-occlusive crises (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. In the U.K., exa-cel has been granted an Innovation Passport under the Innovative Licensing and Access Pathway (ILAP) from the MHRA.

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 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 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 investigated for the treatment of relapsed or refractory T-cell hematologic malignancies in the COBALT-LYM trial and for renal cell carcinoma in the COBALT-RCC 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.

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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 preclinical studies, clinical trials and pipeline products and programs, including, without limitation, the status of such studies and trials, regulatory filings for exa-cel and timing of data releases and regulatory submissions; (ii) potential benefits of exa-cel and the FDA's review of the BLAs and impact of Priority Review on such timing; (iii) benefits of Dr. Prasad's employment; (iv) the sufficiency of its cash resources; (v) benefits of its collaborations, including potential milestone payments and royalties on future products under the non-exclusive license agreement; and (vi) 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.

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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 March 31,	
	2023	2022
Revenue:		
Collaboration revenue	$ 100,000	$ 178
Grant revenue	—	762
Total revenue	$ 100,000	$ 940
Operating expenses:		
Research and development	99,935	118,245
General and administrative	22,360	28,021
Collaboration expense, net	42,192	30,646
Total operating expenses	164,487	176,912
Total operating expenses	(64,487)	(175,972)
Total other income, net	12,742	363
Net loss before income taxes	(51,745)	(175,609)
Provision for income taxes	(1,320)	(3,608)
Net loss before income taxes	(53,065)	(179,217)
Foreign currency translation adjustment	32	(27)
Unrealized gain (loss) on marketable securities	6,227	(11,799)
Comprehensive loss	$ (46,806)	$ (191,043)
Net loss per common share — basic	$ (0.67)	$ (2.32)
Basic weighted-average common shares outstanding	78,676,986	77,098,319
Net loss per common share — diluted	$ (0.67)	$ (2.32)
Diluted weighted-average common shares outstanding	78,676,986	77,098,319

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

	As of	
	March 31, 2023	December 31, 2022
Cash and cash equivalents	$ 344,407	$ 211,885
Marketable securities	1,538,763	1,603,433
Marketable securities, non-current	6,320	53,130
Working capital	1,761,172	1,731,919
Total assets	2,244,364	2,243,057
Total shareholders' equity	1,854,896	1,875,479



Source: CRISPR Therapeutics AG