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

-Advisory Committee meeting for exagamglogene autotemcel (exa-cel) for the treatment of severe sickle cell disease (SCD) completed October 31, 2023; exa-cel assigned Prescription Drug User Fee Act (PDUFA) target action date of December 8, 2023 for SCD-

-Exa-cel assigned PDUFA target action date of March 30, 2024 for transfusion-dependent beta thalassemia (TDT)-

-Clinical trials ongoing for our CAR T product candidates, CTX110® and CTX112™, targeting CD19 in B-cell malignancies-

-Clinical trials ongoing for our CAR T product candidates, CTX130™ and CTX131™, targeting CD70 in T cell malignancies and solid tumors-

-Clinical trial ongoing for VCTX211™, an allogeneic, gene-edited, stem cell derived product candidate for the treatment of Type 1 Diabetes (T1D)-

-Clinical trial initiated for CTX310™, targeting angiopoietin-related protein 3 (ANGPTL3)-

ZUG, Switzerland and BOSTON, Nov. 06, 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 third quarter ended September 30, 2023.

"The third quarter marked significant progress across our broad clinical pipeline of potentially curative gene edited therapies," said Samarth Kulkarni, Ph.D., Chief Executive Officer and Chairman of the Board of CRISPR Therapeutics. "We are excited about the upcoming PDUFA date for exa-cel, which could potentially bring a transformative therapy to patients living with sickle cell disease. If approved, exa-cel would be the first CRISPR-based medicine available to patients in the U.S., highlighting the groundbreaking opportunity of this technology to treat people with serious diseases. Additionally, we are excited to initiate clinical trials for our *in vivo* programs, adding a new pillar to our clinical portfolio. We remain well positioned and well capitalized to bring several transformative medicines for patients suffering from serious diseases."

Recent Highlights and Outlook

- **Hemoglobinopathies**
  - In October, the U.S. Food and Drug Administration's (FDA) Cellular, Tissue, and Gene Therapies Advisory Committee completed their meeting for exagamglogene autotemcel (exa-cel) for the treatment of sickle cell disease (SCD) in people ages 12 and older with recurrent vaso-occlusive crises (VOCs). Exa-cel is the first potential therapy to emerge from a strategic partnership between CRISPR Therapeutics and Vertex Pharmaceuticals.
  - In November, it was announced that two abstracts (details below) on exa-cel clinical data have been accepted for oral presentations at the 2023 American Society of Hematology (ASH) Annual Meeting and Exposition. The updated clinical data will include additional patients with longer follow-up duration from pivotal Phase 3 trials demonstrating exa-cel's potential as a one-time functional cure for SCD and transfusion-dependent beta thalassemia (TDT). The accepted abstracts are available online on the ASH website.
    - Abstract #1052 entitled "Exagamglogene Autotemcel for Severe Sickle Cell Disease" will be an oral presentation on Monday, December 11 at 4:45 pm PST.
    - Abstract #1053 entitled "Exagamglogene Autotemcel for Transfusion-Dependent Beta-Thalassemia" will be an oral presentation on Monday, December 11 at 5:00 pm PST.
  - CRISPR Therapeutics and Vertex Pharmaceuticals previously announced that the FDA accepted the Biologics License Applications (BLAs) for exa-cel for severe SCD and TDT. The FDA has granted Priority Review for SCD and Standard Review for TDT and assigned Prescription Drug User Fee Act (PDUFA) target action dates of December 8, 2023, and March 30, 2024, respectively. In the U.S., exa-cel has been granted Fast Track, Regenerative Medicine Advanced Therapy (RMAT), Orphan Drug and Rare Pediatric Disease designations.
  - A marketing authorization application for exa-cel has also been submitted to the Saudi Food and Drug Authority (SFDA). Exa-cel is the first investigational medicine to receive Breakthrough Designation from the SFDA, reflecting the high unmet need for patients with SCD and TDT in the Kingdom of Saudi Arabia.

- 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 global Phase 3 studies of exa-cel are ongoing for patients 5 to 11 years of age with TDT or SCD.
- CRISPR Therapeutics continues to advance its anti-CD117 (c-Kit) antibody-drug conjugate (ADC), its internal targeted conditioning program, in preclinical studies. This targeted conditioning agent has the potential to significantly expand the patient population that can benefit from exa-cel.

- **Immuno-Oncology**
  - Clinical trials are ongoing for CTX110® and CTX112™, CRISPR Therapeutics' first and next-generation allogeneic chimeric antigen receptor T cell CAR T) investigational therapies targeting CD19 in B-cell malignancies. Based on encouraging preliminary data, CTX110 was granted RMAT designation by the FDA.
  - Clinical trials are ongoing for CTX130™ and CTX131™, CRISPR Therapeutics' first and next-generation allogeneic CAR T investigational therapies targeting CD70 in T cell malignancies and solid tumors. Based on encouraging preliminary data, CTX130 was granted RMAT designation by the FDA.
  - Earlier this month, CRISPR Therapeutics presented new preclinical data at the Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting demonstrating the continued advancement of its immuno-oncology programs and platform.

- **Regenerative Medicine**

  - CRISPR Therapeutics and ViaCyte continue to collaborate on their existing gene-edited allogeneic stem cell therapies for the treatment of diabetes under the terms of their collaboration. The clinical trial for VCTX211 ™ for the treatment of T1D is ongoing.

- ***In Vivo***

  - CRISPR Therapeutics continues to progress its *in vivo* platform, focused on lipid nanoparticle (LNP)-based delivery to the liver and extrahepatic tissues. The Company continues to advance multiple *in vivo* programs directed towards cardiovascular indications and beyond.
  - CRISPR Therapeutics initiated a Phase 1 clinical trial for CTX310™, targeting angiopoietin-like 3 protein (ANGPTL3). Natural history studies have shown that individuals with natural loss-of-function variants of *ANGPTL3* have lower triglyceride levels, lower LDL-C levels, and a lower risk of coronary artery disease, validating targeting ANGPTL3 for the treatment of atherosclerotic cardiovascular disease (ASCVD).
  - Additionally, CRISPR Therapeutics continues to advance CTX320™, an investigational program targeting lipoprotein(a) (Lp(a)) and remains on track to enter the clinic in the first half of 2024. High levels of Lp(a) are an independent and causal risk factor for ASCVD. CTX310 and CTX320 have the potential to shift the treatment paradigm for ASCVD with a single-dose, potentially life-long durable editing approach.
  - In November, CRISPR Therapeutics announced preclinical data from the Company's investigational programs for the treatment of cardiovascular disease at the American Heart Association (AHA) Scientific Sessions 2023. The data will be presented on Saturday, November 11, 2023, in two oral sessions, entitled "CTX310: An Investigational *in vivo* CRISPR-Based Therapy Efficiently and Durably Reduces ANGPTL3 Protein and Triglyceride Levels in Non-Human Primates After a Single Dose" and "CTX320: An Investigational *in vivo* CRISPR-Based Therapy Efficiently and Durably Reduces Lipoprotein(a) Levels in Non-Human Primates After a Single Dose."
  - Beyond CTX310 and CTX320, CRISPR Therapeutics is advancing additional programs utilizing *in vivo* delivery to address both rare and common diseases.
  - In October, CRISPR Therapeutics received a new grant from the Bill & Melinda Gates Foundation to research *in vivo* gene editing of hematopoietic stem and progenitor cells (HSPCs). The grant builds upon CRISPR Therapeutics' proprietary gene editing technology and expertise in editing HSPCs and contributes to efforts to accelerate transformative medicines for global health.

- **Other Corporate Matters**
  - In October, CRISPR Therapeutics announced its proposal to elect Sandy Mahatme, LL.M. to its Board of Directors at the Company's upcoming annual general meeting to be held in 2024. Mr. Mahatme, LL.M., brings a considerable breadth of experience to CRISPR Therapeutics gained from his senior roles at industry-leading companies and has a strong track record of success in finance, business development and corporate strategy.

Third Quarter 2023 Financial Results

- **Cash Position:** Cash, cash equivalents, and marketable securities were $1,739.8 million as of September 30, 2023,

compared to $1,868.4 million as of December 31, 2022. The decrease in cash of $128.6 million was primarily driven by operating expenses, offset by payments received from Vertex in connection with a non-exclusive license agreement and related milestone, as well as interest income.

- **R&D Expenses:** R&D expenses were $90.7 million for the third quarter of 2023, compared to $116.6 million for the third 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 $18.3 million for the third quarter of 2023, compared to $27.0 million for the third 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 $23.4 million for the third quarter of 2023, compared to $38.9 million for the third quarter of 2022. The decrease of approximately $15.5 million in collaboration expense, net, was due to the fact that we reached the $110.3 million deferral limit on costs related to the exa-cel program in the third quarter of 2023, whereas the limit was not reached until the fourth quarter of 2022.
- **Net Loss:** Net loss was $112.2 million for the third quarter of 2023, compared to a net loss of $174.5 million for the third quarter of 2022.

About exagamglogene autotemcel (exa-cel)

Exa-cel is an investigational, autologous, *ex vivo* CRISPR/Cas9 gene-edited cell therapy that is being evaluated for patients with SCD or TDT, 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 reduce or eliminate painful and debilitating VOCs for patients with SCD and alleviate transfusion requirements for patients with TDT. Earlier results from these ongoing trials were published in *The New England Journal of Medicine* in January of 2021 and presented at the American Society of Hematology Annual Congress in 2022 and the European Hematology Association Annual Meeting in 2023.

Exa-cel has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, Orphan Drug, and Rare Pediatric Disease designations from the U.S. FDA for both TDT and SCD. The FDA has accepted the Biologics License Applications (BLAs) for exa-cel and assigned Prescription Drug User Fee Act (PDUFA) action dates of December 8, 2023, for SCD and March 30, 2024, for TDT.

In the EU, exa-cel has been granted Orphan Drug Designation from the European Commission, as well as Priority Medicines (PRIME) designation from the European Medicines Agency (EMA), for both SCD and TDT. In the U.K., exa-cel has also been granted an Innovation Passport under the Innovative Licensing and Access Pathway (ILAP) from the Medicines Healthcare products Regulatory Agency (MHRA). In Europe, the Marketing Authorization Applications (MAAs) for exa-cel were submitted in December 2022 and validated by the EMA and MHRA in January 2023.

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

The ongoing long-term, open-label trial, CLIMB-131, is designed to evaluate the safety and efficacy of exa-cel in patients who received exa-cel in CLIMB-111, CLIMB-121, CLIMB-141, CLIMB-151 or CLIMB-161. 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 with the plan to extend to ages 2 to less than 5 years at a later date. Each trial will enroll approximately 15 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 CLIMB-161

The ongoing Phase 3b trial, CLIMB-161, is to support expansion of our manufacturing footprint after initial potential approval and launch. This trial will enroll approximately 12 patients with either TDT or with SCD, characterized by recurrent VOCs, ages 12 to 35 years. Patients will be followed for approximately one year after infusion. Each patient will be asked to participate in CLIMB-131, a long-term follow-up trial.

About the CRISPR Collaboration and Vertex

CRISPR Therapeutics and Vertex entered into a strategic research collaboration in 2015 focused on the use of CRISPR/Cas9 to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. Exa-cel represents the first 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 CD19 Candidates

CTX110 is a wholly-owned, healthy donor-derived gene-edited allogeneic CAR T investigational therapy targeting cluster of differentiation 19, or CD19, and CTX112, a next-generation, wholly-owned, investigational, allogeneic CAR T product candidate targeting CD19, which incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion. Both CTX110 and CTX112 are being investigated in ongoing clinical trials designed to assess the safety and efficacy of the applicable product candidate 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.

About CD70 Candidates

CTX130 is a wholly-owned, 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, and CTX131, a next-generation, wholly-owned, investigational allogeneic CAR T product candidate targeting CD70 in a basket of solid tumors, which incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion. The safety and efficacy of CTX130 is being evaluated in two independent clinical trials, one for the treatment of relapsed or refractory T or B cell malignancies and on for the treatment of relapsed or refractory clear cell renal cell carcinoma. CTX131 is being investigated in a clinical trial designed to assess the safety and efficacy of the product candidate in adult patients with relapsed or refractory solid tumors. 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).

About VCTX211

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 cardiometabolic 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, data, expected timing of data releases, timing of regulatory submissions and the regulatory filings for exa-cel; (ii) the potential benefits of exa-cel for patients; (iii) plans to and the pre-clinical and clinical data that are being presented during oral presentations at the 2023 ASH Annual Meeting and Exposition and AHA Scientific Sessions 2023; (iv) Mr. Mahatme's election to the Board of Directors and the expected benefits thereof; (v) the sufficiency of its cash resources; (vi) the expected benefits of its collaborations; and (vii) the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and therapies. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects" and similar expressions are intended to identify forward-looking statements.

You are cautioned that forward-looking statements are inherently uncertain. Although CRISPR Therapeutics believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: the efficacy and safety results from ongoing

clinical trials, including of exa-cel, will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory submissions; the FDA or other regulatory authorities may not approve exa-cel on a timely basis or at all; adequate pricing or reimbursement may not be secured to support continued development or commercialization of exa-cel following regulatory approval; clinical trial results may not be favorable; one or more of its product candidate programs will not proceed as planned for technical, scientific or commercial reasons; future competitive or other market factors may adversely affect the commercial potential for its product candidates; initiation and completion of preclinical studies for its product candidates is uncertain and results from such studies may not be predictive of future results of future studies or clinical trials; regulatory approvals to conduct trials or to market products are uncertain; 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 September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue:				
Collaboration revenue	$ —	$ 94	$ 170,000	$ 430
Grant revenue	—	—	—	762
Total revenue	$ —	$ 94	$ 170,000	$ 1,192
Operating expenses:				
Research and development	90,698	116,622	292,188	358,090
General and administrative	18,291	27,001	59,683	81,295
Collaboration expense, net	23,422	38,859	110,250	103,427
Total operating expenses	132,411	182,482	462,121	542,812
Loss from operations	(132,411)	(182,388)	(292,121)	(541,620)
Total other income, net	20,671	7,264	51,819	11,171
Net loss before income taxes	(111,740)	(175,124)	(240,302)	(530,449)
(Provision) benefit for income taxes	(412)	575	(2,655)	(9,151)
Net loss	(112,152)	(174,549)	(242,957)	(539,600)
Foreign currency translation adjustment	(49)	(100)	12	(195)
Unrealized gain (loss) on marketable securities	2,160	(1,820)	8,838	(17,001)
Comprehensive loss	$ (110,041)	$ (176,469)	$ (234,107)	$ (556,796)
Net loss per common share — basic	$ (1.41)	$ (2.24)	$ (3.07)	$ (6.96)
Basic weighted-average common shares outstanding	79,414,098	78,021,520	79,063,415	77,547,771
Net loss per common share — diluted	$ (1.41)	$ (2.24)	$ (3.07)	$ (6.96)
Diluted weighted-average common shares outstanding	79,414,098	78,021,520	79,063,415	77,547,771

CRISPR Therapeutics AG

Condensed Consolidated Balance Sheets Data

(Unaudited, in thousands)

	As of	
	September 30, 2023	December 31, 2022
Cash and cash equivalents	$ 527,765	$ 211,885
Marketable securities	1,212,061	1,603,433
Marketable securities, non-current	—	53,130
Working capital	1,649,352	1,731,919
Total assets	2,086,830	2,243,057
Total shareholders' equity	1,727,794	1,875,479

Source: CRISPR Therapeutics AG