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

-FDA accepted Biologics License Applications (BLAs) for exagamglogene autotemcel (exa-cel) for severe Sickle Cell Disease (SCD) and Transfusion-Dependent Beta Thalassemia (TDT); Priority Review for SCD and Standard Review for TDT-

-PDUFA target action date of December 8, 2023, for SCD and March 30, 2024, for TDT-

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

-Enrollment ongoing and dosing initiated 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 the clinic this year-

ZUG, Switzerland and BOSTON, Aug. 07, 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 second quarter ended June 30, 2023.

"The second quarter of 2023 was a period of continued substantial progress toward our goal of delivering innovative gene edited therapies to patients, including the FDA's acceptance of the exa-cel BLAs for SCD and TDT and the presentation of updated interim exa-cel trial data at EHA, which demonstrated transformative, consistent and durable benefit to patients," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "In parallel, we continue to advance our various clinical programs rapidly, including our next-generation CAR T candidates. In addition, we plan to initiate a clinical trial for CTX310, our lead *in vivo* program targeting ANGPTL3, this year. All together, we are well-positioned to realize our mission of bringing transformative and potentially curative therapies to patients in need and look forward to continued momentum in the months ahead."

Recent Highlights and Outlook

- **Hemoglobinopathies**
    - In June, CRISPR Therapeutics and Vertex Pharmaceuticals announced that the U.S. Food and Drug Administration (FDA) accepted the Biologics License Applications (BLAs) for the investigational treatment exagamglogene autotemcel (exa-cel) for severe sickle cell disease (SCD) and transfusion-dependent beta thalassemia (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. The FDA has indicated that it plans to hold an advisory committee meeting for exa-cel. In the U.S., exa-cel has been granted Fast Track, Regenerative Medicine Advanced Therapy (RMAT), Orphan Drug and Rare Pediatric Disease designations.
    - Additionally, in the fourth quarter of 2022, CRISPR Therapeutics and Vertex completed regulatory submissions for exa-cel in the EU and the United Kingdom, and the European Medicines Agency (EMA), and the Medicines and Healthcare products Regulatory Agency (MHRA), are reviewing the regulatory submissions for exa-cel in SCD and TDT. In the EU, exa-cel has been granted Orphan Drug Designation from the European Commission, as well as PRIME designation from the EMA for the treatment of both TDT and SCD. In the United Kingdom, exa-cel has been granted an Innovation Passport under the Innovative Licensing and Access Pathway from the MHRA.
    - In June, CRISPR Therapeutics and Vertex Pharmaceuticals presented positive interim results from the pivotal trials of exa-cel in SCD and TDT at the 2023 Annual European Hematology Association (EHA) Congress. Both trials met the primary and key secondary endpoints at pre-specified interim analyses, and the data continue to demonstrate transformative, consistent and durable benefit. The data presented at EHA were the basis of the EMA and MHRA regulatory filings for exa-cel. CRISPR Therapeutics and Vertex expect to present updated clinical data that served as the basis of the FDA filing at a future medical congress.

- 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 continue to enroll and dose 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 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. Based on encouraging preliminary data, CTX110 was granted RMAT designation by the FDA.
  - CRISPR Therapeutics continues to enroll and dose patients in the 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 encouraging preliminary data, CTX130 was granted RMAT designation by the FDA.
  - CRISPR Therapeutics continues to enroll and has initiated dosing in a Phase 1 clinical trial of CTX112™, its next generation CAR T candidate targeting CD19+ B-cell malignancies. CTX112 incorporates the edits in CTX110 plus additional edits to the genes encoding Regnase-1 and transforming growth factor-beta (TGF-β) receptor type 2 (TGFBR2), which have been shown to increase CAR T potency and reduce CAR T exhaustion in pre-clinical studies. In addition, CRISPR Therapeutics continues to enroll patients and has initiated dosing patients in a Phase 1 clinical trial of 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 TGFBR2.

- **Regenerative Medicine**
  - 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 and 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. As part of the licensing agreement, a research milestone was achieved in the second quarter of 2023, triggering a payment of $70 million to be received by CRISPR Therapeutics in the third quarter of 2023.
  - 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. Enrollment and dosing are ongoing in a Phase 1/2 clinical trial of VCTX211™ for the treatment of T1D.

- ***In Vivo***
  - CRISPR Therapeutics continues to build out its *in vivo* platform, focused on lipid nanoparticle (LNP)-based delivery to the liver and extrahepatic tissues. The Company is advancing multiple *in vivo* programs directed towards cardiovascular indications and beyond.
  - CRISPR Therapeutics remains on track to advance its lead *in vivo* program, CTX310™, targeting angiopoietin-related protein 3 (ANGPTL3) into the clinic this year. Natural history studies showing 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 validate targeting ANGPTL3 for the treatment of atherosclerotic cardiovascular disease (ASCVD).
  - Additionally, CRISPR Therapeutics is advancing an investigational program targeting lipoprotein (a) (Lp(a)) and expects 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.
  - Beyond CTX310 and CTX320, CRISPR Therapeutics is advancing additional programs utilizing *in vivo* delivery to address both rare and common diseases.

Second Quarter 2023 Financial Results

- **Cash & Accounts Receivable:** Cash, cash equivalents, marketable securities and accounts receivables were $1,843.0 million as of June 30, 2023, compared to $1,868.4 million as of December 31, 2022. The decrease in cash and accounts receivable of $25.4 million was primarily driven by operating expenses, offset by the $100.0 million upfront payment received from Vertex in connection with a non-exclusive license agreement in the first quarter of 2023 and $70.0 million receivable resulting from a research milestone achieved during the current quarter.
- **Revenue:** Total collaboration revenue was $70.0 million for the quarter ended June 30, 2023. Collaboration revenue for the second quarter of 2022 was not material. Collaboration revenue recognized in the second quarter of 2023 was primarily attributable to a research milestone achieved during the current quarter in connection with a non-exclusive license agreement with Vertex.
- **R&D Expenses:** R&D expenses were $101.6 million for the second quarter of 2023, compared to $123.2 million for the second 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 $19.0 million for the second quarter of 2023, compared to $26.3 million for the second 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 $44.6 million for the second quarter of 2023, compared to $33.9 million for the second 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 $77.7 million for the second quarter of 2023, compared to a net loss of $185.8 million for the second 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 incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion.

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 incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion.

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, expected timing of data releases, timing of regulatory submissions and the regulatory filings for exa-cel; (ii) the sufficiency of its cash resources; (iii) the expected benefits of its collaborations; and (iv) the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene editing technologies and therapies. Without limiting the foregoing, the words "believes," "anticipates," "plans," "expects" and similar expressions are intended to identify forward-looking statements. You are cautioned that forward-looking statements are inherently uncertain. Although CRISPR Therapeutics believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: the potential for preliminary data from any clinical trial not to be indicative of final trial results; the potential that clinical trial results may not be favorable; that one or more of its internal or external product candidate programs will not proceed as planned for technical, scientific or commercial reasons; that future competitive or other market factors may adversely affect the commercial potential for its product candidates; uncertainties inherent in the initiation and completion of preclinical studies for its product candidates and whether results from such studies will be predictive of future results of future studies or clinical trials; uncertainties about regulatory approvals to conduct trials or to market products; it may not realize the potential benefits of its collaborations; uncertainties regarding the intellectual property protection for its technology and intellectual property belonging to third parties, and the outcome of proceedings (such as an interference, an opposition or a similar proceeding) involving all or any portion of such intellectual property; and those risks and uncertainties described under the heading "Risk

Factors" in CRISPR Therapeutics' most recent annual report on Form 10-K, quarterly report on Form 10-Q and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. CRISPR Therapeutics disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this press release, other than to the extent required by law.

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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,	
	2023	2022	2023	2022
Revenue:				
Collaboration revenue	$ 70,000	$ 158	$ 170,000	$ 336
Grant revenue	—	—	—	762
Total revenue	$ 70,000	$ 158	$ 170,000	$ 1,098
Operating expenses:				
Research and development	101,555	123,223	201,490	241,468
General and administrative	19,032	26,273	41,392	54,294
Collaboration expense, net	44,636	33,922	86,828	64,568
Total operating expenses	165,223	183,418	329,710	360,330
Loss from operations	(95,223)	(183,260)	(159,710)	(359,232)
Total other income, net	18,406	3,544	31,148	3,907
Net loss before income taxes	(76,817)	(179,716)	(128,562)	(355,325)
Provision for income taxes	(923)	(6,118)	(2,243)	(9,726)
Net loss	(77,740)	(185,834)	(130,805)	(365,051)
Foreign currency translation adjustment	28	(69)	60	(95)
Unrealized gain (loss) on marketable securities	452	(3,380)	6,679	(15,180)
Comprehensive loss	$ (77,260)	$ (189,283)	$ (124,066)	$ (380,326)
Net loss per common share — basic	$ (0.98)	$ (2.40)	$ (1.66)	$ (4.72)
Basic weighted-average common shares outstanding	79,091,061	77,513,327	78,885,168	77,306,970
Net loss per common share — diluted	$ (0.98)	$ (2.40)	$ (1.66)	$ (4.72)
Diluted weighted-average common shares outstanding	79,091,061	77,513,327	78,885,168	77,306,970

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

	As of	
	June 30, 2023	December 31, 2022
Cash and cash equivalents	$ 444,796	$ 211,885
Marketable securities	1,323,307	1,603,433

Marketable securities, non-current	4,901	53,130
Working capital	1,726,735	1,731,919
Total assets	2,197,014	2,243,057
Total shareholders' equity	1,816,028	1,875,479

Source: CRISPR Therapeutics AG