CRISPR Therapeutics Provides Business Update and Reports First Quarter 2024 Financial Results

-More than 25 authorized treatment centers (ATCs) activated globally for CASGEVY™ and multiple patients have already had cells collected-

-Clinical trials ongoing for next generation CAR T product candidates, CTX112™ and CTX131™ targeting CD19 and CD70 respectively, across multiple indications-

-Clinical trials ongoing for in vivo *gene editing product candidates, CTX310™ and CTX320™ targeting ANGPTL3 and Lp(a) respectively-*

-Expands pipeline with new preclinical programs utilizing lipid nanoparticle (LNP) mediated delivery to the liver for refractory hypertension targeting angiotensinogen (AGT) and acute hepatic porphyria (AHP) targeting 5'-aminolevulinate synthase 1 (ALAS1)-

-Clinical trial ongoing for CTX211™, an allogeneic, hypoimmune, gene-edited, stem cell derived product candidate for the treatment of Type 1 Diabetes (T1D)-

-Strong balance sheet with approximately $2.1 billion in cash, cash equivalents, and marketable securities as of March 31, 2024-

ZUG, Switzerland and BOSTON, May 08, 2024 (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, 2024.

"This quarter, in addition the robust launch of CASGEVY, we are pleased to have nominated additional *in vivo* programs targeting both rare and common diseases to our portfolio based on promising preclinical data," said Samarth Kulkarni, Ph.D., Chief Executive Officer and Chairman of CRISPR Therapeutics. "Additionally, we continue to advance our portfolio of clinical trials across oncology, autoimmune, diabetes and cardiovascular indications in a capital efficient manner. With multiple data read-outs in the next 12-18 months, we are poised to broaden the number of patients that could potentially benefit from transformative gene-editing based therapies."

Recent Highlights and Outlook

- **Hemoglobinopathies and CASGEVY™ (exagamglogene autotemcel [exa-cel])**
    - CASGEVY is approved in the U.S., Great Britain, the European Union (EU), the Kingdom of Saudi Arabia (KSA), and the Kingdom of Bahrain (Bahrain) for the treatment of both sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT). Regulatory submissions for CASGEVY have been completed in both SCD and TDT in Switzerland and Canada; the submission in Canada was granted priority review. CASGEVY is the first therapy to emerge from a strategic partnership between CRISPR Therapeutics and Vertex Pharmaceuticals established in 2015. As part of an amendment to the collaboration agreement in 2021, Vertex now leads global development, manufacturing, regulatory and commercialization of CASGEVY with support from CRISPR Therapeutics.
    - As of mid-April, more than 25 authorized treatment centers (ATCs) have been activated globally, including centers in all regions where CASGEVY is approved, and multiple patients have already had cells collected.
    - Vertex has signed multiple agreements with both commercial and government health insurance providers in the U.S. to provide access to CASGEVY. Vertex has also secured reimbursed access for eligible people with SCD or TDT in KSA and Bahrain, as well as for people with TDT in France through an early access program.
    - CRISPR Therapeutics has two next-generation approaches with the potential to significantly expand the addressable population with SCD and TDT. CRISPR Therapeutics continues to advance its internally developed targeted conditioning program, an anti-CD117 (c-Kit) antibody-drug conjugate (ADC), through preclinical studies.

Additionally, the Company has ongoing research efforts to enable *in vivo* editing of hematopoietic stem cells. This work could obviate the need for conditioning altogether, expand geographic reach, and enable the treatment of multiple additional other diseases beyond SCD and TDT.

- **Immuno-Oncology and Autoimmune Diseases**

  - CRISPR Therapeutics' next-generation allogeneic CAR T candidates reflect the Company's mission of innovating continuously to bring potentially transformative medicines to patients as quickly as possible. Clinical trials are ongoing for the Company's next-generation CAR T product candidates, CTX112™ and CTX131™, targeting CD19 and CD70, respectively, across multiple indications. CTX112 and CTX131 both contain novel potency edits which can lead to significantly higher CAR T cell expansion and cytotoxicity, potentially representing best-in-class allogeneic CAR T products for these targets.

  - CTX112 is being developed for both oncology and autoimmune indications. In oncology settings, CTX112 is in a Phase 1/2 trial for CD19 positive relapsed or refractory B-cell malignancies, and the Company expects to report preliminary clinical data this year.

  - The Company remains on track to initiate a clinical trial for CTX112 in systemic lupus erythematosus (SLE) in the first half of this year, with the potential to expand into additional autoimmune indications in the future. Early clinical studies have shown that CD19-directed autologous CAR T therapy can produce long-lasting remissions in multiple autoimmune indications by deeply depleting B cells. The Company's first generation allogeneic CD19-directed CAR T program has demonstrated effective depletion of B cells in oncology settings, which supports the potential for CTX112 in autoimmune diseases.

  - CTX131, CRISPR Therapeutics' next generation CAR T targeting CD70, is currently in an ongoing clinical trial in solid tumors. The Company remains on track to initiate a clinical trial for CTX131 in hematologic malignancies in the first half of this year.

- ***In Vivo***

  - CRISPR Therapeutics has established a proprietary lipid nanoparticle (LNP) platform for the delivery of CRISPR/Cas9 to the liver. The first two *in vivo* programs utilizing this proprietary platform, CTX310™ and CTX320™, are directed towards validated therapeutic targets associated with cardiovascular disease, and are in ongoing clinical trials. Earlier today, the Company announced the addition of two additional preclinical programs, CTX340™ and CTX450™, utilizing this LNP delivery system, demonstrating the modularity and scalability of the platform.

  - Refractory hypertension is a serious unmet medical need affecting approximately 1.5 million patients in the U.S. alone. CTX340 is designed to inhibit production of hepatic angiotensinogen (AGT), a validated target to modulate the renin-angiotensin-aldosterone system (RAAS) and normalize blood pressure durably with a one-time treatment. In preclinical studies, CTX340 showed ~60% liver editing and ~90% AGT protein reduction, resulting in sustained ~30 mmHg blood pressure (BP) reduction out to 3 months in the spontaneously hypertensive rat (SHR) model.

  - Acute hepatic porphyria (AHP) is a group of rare genetic diseases of heme biosynthesis. Symptomatic patients have acute attacks, characterized by debilitating neurovascular symptoms, as well as multiple chronic symptoms, such as pain. There are approximately 5,000 patients diagnosed with AHP in the U.S., although the disease remains underdiagnosed. CTX450 is specifically designed to inhibit production of ALAS1 in the liver, preventing accumulation of neurotoxic aminolevulinic acid (ALA) and porphobilinogen (PBG). In preclinical studies, CTX450 showed ~70% liver editing and ~97% ALAS1 protein reduction, resulting in reduction of ALA and PBG disease biomarkers to normal levels in an AHP mouse model.

  - CRISPR Therapeutics has initiated IND/CTA-enabling studies for CTX340 and CTX450 and expects to initiate both clinical trials in the second half of 2025.

  - In addition to the pipeline updates expanding the liver-targeted *in vivo* pipeline, CRISPR Therapeutics reported initial data at the American Society of Gene and Cell Therapy Annual Meeting demonstrating its proprietary capabilities to deliver to and edit genes in the eye, opening a potential new focus area.

- **Regenerative Medicine**

    - CRISPR Therapeutics continues to advance a Phase 1 clinical trial for CTX211™ for the treatment of Type 1 Diabetes (T1D). CRISPR Therapeutics remains committed to its goal of developing a beta-cell replacement product that does not require chronic immunosuppression.

    - Vertex has non-exclusive rights to certain CRISPR Therapeutics' CRISPR/Cas9 technology to accelerate development of potentially curative cell therapies for T1D. CRISPR Therapeutics remains eligible for development milestones and would receive royalties on any future products resulting from this agreement.

- **Other Corporate Matters**

    - In March, CRISPR Therapeutics announced its proposal to elect Christian Rommel, Ph.D., to its Board of Directors at the Company's annual general meeting to be held this year. Dr Rommel brings in-depth experience in successfully accelerating innovation and advancing drug candidates across a breadth of modalities and disease areas.

    - In February, CRISPR Therapeutics announced that it had entered into an investment agreement for the sale of approximately $280 million of its common shares to a select group of institutional investors in a registered direct offering.

- **First Quarter 2024 Financial Results**

    - **Cash Position:** Cash, cash equivalents, and marketable securities were $2,108.1 million as of March 31, 2024, compared to $1,695.7 million as of December 31, 2023. The increase in cash was primarily driven by proceeds from the February 2024 registered direct offering, a $200.0 million milestone payment received from Vertex in connection with the approval of CASGEVY, proceeds from employee option exercises as well as interest income, offset by operating expenses.

    - **R&D Expenses:** R&D expenses were $76.2 million for the first quarter of 2024, compared to $99.9 million for the first quarter of 2023. 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 $18.0 million for the first quarter of 2024, compared to $22.4 million for the first quarter of 2023. The decrease in G&A expense was primarily driven by a decrease in employee related and stock-based compensation expense.

    - **Collaboration Expense:** Collaboration expense, net, was $47.0 million for the first quarter of 2024, compared to $42.2 million for the first quarter of 2023. The increase in collaboration expense, net, was primarily attributable to commercial and manufacturing costs.

    - **Net Loss:** Net loss was $116.6 million for the first quarter of 2024, compared to a net loss of $53.1 million for the first quarter of 2023.

About CASGEVY™ (exagamglogene autotemcel [exa-cel])

CASGEVY™ is a non-viral,*ex vivo* CRISPR/Cas9 gene-edited cell therapy for eligible patients with SCD or TDT, in which a patient's own hematopoietic stem and progenitor cells are edited at the erythroid specific enhancer region of the *BCL11A* gene. This edit results in the production of 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. CASGEVY has been shown to reduce or eliminate VOCs for patients with SCD and transfusion requirements for patients with TDT.

CASGEVY is approved for certain indications in multiple jurisdictions for eligible patients.

About the CRISPR Therapeutics-Vertex Collaboration
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. CASGEVY (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 CASGEVY and splits program costs and profits worldwide 60/40 with CRISPR Therapeutics. Vertex is the manufacturer and exclusive license holder of CASGEVY™.

About CTX112
CTX112 is a next-generation, wholly-owned, allogeneic CAR T product candidate targeting Cluster of Differentiation 19, or CD19, which incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion. CTX112 is being investigated in an ongoing clinical trial designed to assess safety and efficacy of the product candidate in adult patients with relapsed or refractory CD19-positive B-cell malignancies who have received at least two prior lines of therapy.

About CTX131
CTX131 is a next-generation, wholly-owned, allogeneic CAR T product candidate targeting Cluster of Differentiation 70, or CD70, an antigen expressed on various solid tumors and hematologic malignancies. CTX131 incorporates additional edits designed to enhance CAR T potency and reduce CAR T exhaustion. 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.

About *In Vivo* Programs
CRISPR Therapeutics has established a proprietary LNP platform for the delivery of CRISPR/Cas9 to the liver. The Company's *in vivo* portfolio includes its lead investigational *in vivo* programs, CTX310 (directed towards angiopoietin-related protein 3 (ANGPTL3)) and CTX320 (directed towards lipoprotein(a) (Lp(a)), two validated therapeutic targets for cardiovascular disease, are in ongoing clinical trials. In addition, the Company's research and preclinical development candidates include CTX340 and CTX450, targeting angiotensinogen (AGT) for refractory hypertension and 5'-aminolevulinate synthase 1 (ALAS1) for acute hepatic porphyria (AHP), respectively.

About CTX211
CTX211 is an allogeneic, gene-edited, stem cell-derived investigational therapy for the treatment of T1D, which incorporates gene edits that aim to make cells hypoimmune and 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
Since its inception over a decade ago, CRISPR Therapeutics has transformed from a research-stage company advancing programs in the field of gene editing, to a company that recently celebrated the historic approval of the first-ever CRISPR-based therapy and has a diverse portfolio of product candidates across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine, cardiovascular, autoimmune, and rare diseases. CRISPR Therapeutics advanced the first-ever CRISPR/Cas9 gene-edited therapy into the clinic in 2018 to investigate the treatment of sickle cell disease or transfusion-dependent beta thalassemia, and beginning in late 2023, CASGEVY™ (exagamglogene autotemcel) was approved in some countries to treat eligible patients with either of those conditions. The Nobel Prize-winning CRISPR science has revolutionized biomedical research and represents a powerful, clinically validated approach with the potential to create a new class of potentially transformative medicines. To accelerate and expand its efforts, CRISPR Therapeutics has established strategic partnerships with leading companies including Bayer and Vertex Pharmaceuticals. 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. To learn more, 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, including, without limitation, manufacturing capabilities, status of such studies and trials, potential expansion into new indications and expectations regarding data generally; (ii) the data that will be generated by ongoing and planned clinical trials, and the ability to use that data for the design and initiation of further clinical trials; (iii) plans and expectations for the commercialization of, and anticipated benefits of, CASGEVY, including the anticipated patient populations eligible for CASGEVY in jurisdictions where it has been or may be approved; (iv) the sufficiency of its cash resources; (v) the expected benefits of its collaborations; 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 efficacy and safety results from ongoing clinical trials will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory submissions; 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; uncertainties inherent in the operation of a manufacturing facility; 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,	
	2024	2023
Revenue:		
Collaboration revenue	$ —	$ 100,000
Grant revenue	504	—
Total revenue	504	$ 100,000
Operating expenses:		
Research and development	76,172	99,935
General and administrative	17,953	22,360
Collaboration expense, net	46,966	42,192
Total operating expenses	141,091	164,487
Loss from operations	(140,587)	(64,487)
Total other income, net	24,720	12,742
Net loss before income taxes	(115,867)	(51,745)
Provision for income taxes	(724)	(1,320)
Net loss	(116,591)	(53,065)
Foreign currency translation adjustment	(11)	32
Unrealized (loss) gain on marketable securities	(3,454)	6,227
Comprehensive loss	$ (120,056)	$ (46,806)
Net loss per common share — basic	$ (1.43)	$ (0.67)
Basic weighted-average common shares outstanding	81,794,630	78,676,986
Net loss per common share — diluted	$ (1.43)	$ (0.67)
Diluted weighted-average common shares outstanding	81,794,630	78,676,986

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

	As of	
	March 31, 2024	December 31, 2023
Cash and cash equivalents	$ 707,427	$ 389,477
Marketable securities	1,400,698	1,304,215
Marketable securities, non-current	—	1,973
Working capital	2,000,634	1,799,287
Total assets	2,439,017	2,229,571
Total shareholders' equity	2,083,936	1,882,803

Source: CRISPR Therapeutics AG