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

-CASGEVY™ approved for the treatment of patients 12 years of age and older with sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT) in Switzerland and Canada-

-45 authorized treatment centers (ATCs) activated globally for CASGEVY and approximately 40 patients have had cells collected across all regions as of mid-October-

-Two clinical trials are ongoing for next generation CAR T product candidate, CTX112™ targeting CD19, in B-cell malignancies and systemic lupus erythematosus-

-Two clinical trials are ongoing for next generation CAR T product candidate, CTX131™, targeting CD70, in solid tumors and hematological malignancies-

-Company plans to provide an update on the Phase 1 dose escalation study of CTX112 in B cell malignancies at the American Society of Hematology (ASH) 2024 Annual Meeting-

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

-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 $1.9 billion in cash, cash equivalents, and marketable securities as of September 30, 2024-

ZUG, Switzerland and BOSTON, Nov. 05, 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 third quarter ended September 30, 2024.

"We continue to make significant progress across our pipeline of *in vivo* and *ex vivo* CRISPR-based therapies," said Samarth Kulkarni, Ph.D., Chief Executive Officer and Chairman of CRISPR Therapeutics. "In addition to the continued momentum of CASGEVY's launch, we are pleased to share that CASGEVY has received regulatory approvals for the treatment of patients 12 years of age and older with SCD or TDT in Switzerland and Canada. In parallel, we remain focused on advancing our portfolio of clinical trials across oncology, autoimmune, diabetes and cardiovascular indications in a capital efficient manner. We look forward to a number of important data catalysts over the next 9-12 months as we advance our portfolio."

Recent Highlights and Outlook

- **Hemoglobinopathies and CASGEVY™ (exagamglogene autotemcel [exa-cel])**
    - CASGEVY has received regulatory approvals for the treatment of patients 12 years of age and older with sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT) in Switzerland and Canada. CASGEVY is also 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 SCD and TDT, and launches are ongoing. CASGEVY is a collaboration product between CRISPR Therapeutics and Vertex Pharmaceuticals, and 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-October, 45 authorized treatment centers (ATCs) have been activated globally, including centers in all regions where CASGEVY is approved, and approximately 40 patients have already had at least one cell collection across all regions.
    - Vertex announced a reimbursement agreement with NHS England for eligible TDT patients to access CASGEVY.

They have also entered into commercial discussions with NHS England to secure access to CASGEVY for eligible patients with SCD.

- The Italian Medicines Agency (IMA) approved the request for the implementation of an early access program (EAP), for the use of CASGEVY for the treatment of TDT and SCD.
- Enrollment has been completed in two global Phase 3 studies of CASGEVY in children 5 to 11 years of age with SCD or TDT and the trials are ongoing.
- CRISPR Therapeutics has two next generation approaches with the potential to significantly expand the addressable population with SCD and TDT. The Company 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.
  - CRISPR Therapeutics announced that it will present a poster from the Company's ongoing Phase 1 dose escalation study evaluating the safety and efficacy of CTX112, a next-generation CD19 allogeneic CAR T cell therapy, in relapsed or refractory (r/r) CD19-positive B-cell malignancies at the American Society of Hematology (ASH) 2024 Annual Meeting. The ASH abstract includes preliminary data on nine high-risk/heavily pretreated lymphoma patients showing an overall response rate (ORR) of 67% across multiple histologies and a complete response rate (CRR) of 44%, with four patients having achieved responses lasting for more than 6 months, including one patient treated at DL1 who remains in complete remission over a year after CTX112 infusion. Concordant with efficacy, pharmacokinetic (PK) data showed rapid cell expansion for CTX112 with many fold improvements in PK compared to the previous generation CTX110® CAR T. No dose limiting toxicities (DLTs) or adverse events (AEs) of graft versus host disease, hemophagocytic lymphohistiocytosis, or grade (Gr) ≥3 infections were observed, in addition to no Gr ≥3 cytokine release syndrome (CRS), or Gr ≥2 immune effector cell associated neurotoxicity syndrome (ICANS). Compared with first generation allogeneic CAR T therapies like CTX110, CTX112 results in better efficacy at lower doses, higher response rates, and improved PK. These data provide the first clinical evidence that disruptions in the genes encoding Regnase-1 and transforming growth factor beta receptor 2 can lead to increased expansion and functional persistence of CAR T cells. The poster presentation will include additional results from the trial.
  - CTX112 is also in a Phase 1 clinical trial in systemic lupus erythematosus (SLE), with the potential to expand into additional autoimmune indications in the future. Early clinical studies conducted by third parties 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 is currently in ongoing clinical trials in solid tumors and hematologic malignancies including T cell lymphomas (TCL). The Company plans to announce an update from the Phase 1 solid tumor trial in 2025. In certain hematologic malignancies such as TCL, allogeneic CAR T approaches may have greater potential to meet the unmet need in this patient population given the patients' own T cells are not suitable for autologous manufacturing.

- ***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.
- CTX310 is currently in an ongoing Phase 1 clinical trial targeting ANGPTL3 in patients with homozygous familial hypercholesterolemia (HoFH), severe hypertriglyceridemia (SHTG), heterozygous familial hypercholesterolemia (HeFH), or mixed dyslipidemias. Natural loss-of-function mutations in ANGPTL3 are associated with reduced low-density lipoprotein (LDL-C), triglycerides (TG) and atherosclerotic cardiovascular disease (ASCVD) risk without any negative impact on overall health. CRISPR Therapeutics expects to provide an update from this program in 2025.
- CTX320 is currently in an ongoing Phase 1 clinical trial targeting LPA in patients with elevated lipoprotein(a) [Lp(a)], which has shown to have an independent association with major adverse cardiovascular events (MACE). Up to 20% of the global population has elevated Lp(a) levels. CRISPR Therapeutics expects to provide an update from this program in 2025.
- The Company continues to advance two additional preclinical programs, CTX340™ targeting angiotensinogen (AGT) for the treatment of refractory hypertension and CTX450™ targeting 5' aminolevulinic acid synthase 1 (ALAS1) for the treatment of acute hepatic porphyrias (AHP). CRISPR Therapeutics is conducting IND/CTA-enabling studies and expects to initiate both clinical trials in the second half of 2025.

- **Regenerative Medicine**

  - CTX211™, an allogeneic, gene-edited, stem cell-derived beta islet cell precursor, is currently in an ongoing Phase 1 clinical trial 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.

- **Third Quarter 2024 Financial Results**

  - **Cash Position:** Cash, cash equivalents, and marketable securities were $1,935.6 million as of September 30, 2024, compared to $1,695.7 million as of December 31, 2023. The increase in cash was primarily driven by proceeds from the $280.0 million February 2024 registered direct offering, a $200.0 million milestone payment received from Vertex Pharmaceuticals 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 $82.2 million for the third quarter of 2024, compared to $90.7 million for the third 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 $17.4 million for the third quarter of 2024, compared to $18.3 million for the third quarter of 2023.
  - **Collaboration Expense:** Collaboration expense, net, was $11.2 million for the third quarter of 2024, compared to $23.4 million for the third quarter of 2023. The decrease in collaboration expense, net, was primarily attributable to the time of reaching the deferral limit on costs related to the CASGEVY program.
  - **Net Loss:** Net loss was $85.9 million for the third quarter of 2024, compared to a net loss of $112.2 million for the third 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 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 being developed for both oncology and autoimmune indications. CTX112 is a next-generation, wholly-owned, allogeneic CAR T product candidate targeting Cluster of Differentiation 19, or CD19, which incorporates edits designed to evade the immune system, 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. In addition, CTX112 is being investigated in an ongoing clinical trial designed to assess safety and efficacy of the product candidate in adult patients with system lupus erythematosus.

About CTX131
CTX131 is being developed for both solid tumors and hematologic malignancies, including T cell lymphomas (TCL). 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 edits designed to evade the immune system, prevent fratricide, enhance CAR T potency and reduce CAR T exhaustion. CTX131 is being investigated in ongoing clinical trials designed to assess the safety and efficacy of the product candidate in adult patients with relapsed or refractory solid tumors and hematologic malignancies, including TCL.

About *In Vivo* Programs
CRISPR Therapeutics has established a proprietary lipid nanoparticle (LNP) platform for the delivery of CRISPR/Cas9 to the liver. The Company's *in vivo* portfolio includes its lead investigational programs, CTX310 (directed towards angiopoietin-related protein 3 (ANGPTL3)) and CTX320 (directed towards LPA, the gene encoding apolipoprotein(a) (apo(a)), a major component of lipoprotein(a) [Lp(a)]). Both are targeting validated therapeutic targets for cardiovascular disease. CTX310 and CTX320 are in ongoing clinical trials in patients with heterozygous familial hypercholesterolemia, homozygous familial hypercholesterolemia, mixed dyslipidemias, or severe hypertriglyceridemia, and in patients with elevated lipoprotein(a), respectively. 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 type 1 diabetes (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. A Phase 1 clinical trial for CTX211 for the treatment of T1D is ongoing.

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 [exa-cel]) 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

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding any or all of the following: (i) CRISPR Therapeutics 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, safety and efficacy generally; as well as its plans to and the clinical data being presented at the 2024 ASH Annual Meeting; (ii) its strategy, goals, anticipated financial performance and the sufficiency of its cash resources; (iii) regulatory submissions and authorizations, including timelines for and expectations regarding additional regulatory agency decisions; (iv) the expected benefits of its collaborations; and (v) the therapeutic value, development, and commercial potential of gene editing technologies and therapies, including CRISPR/Cas9. Risks that contribute to the uncertain nature of the forward-looking statements include, without limitation, the risks and uncertainties discussed under the heading "Risk Factors" in its most recent annual report on Form 10-K and in any other subsequent filings made by CRISPR Therapeutics with the U.S. Securities and Exchange Commission. 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. We disclaim 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.

This press release discusses CRISPR/Cas9 gene editing investigational therapies and is not intended to convey conclusions about efficacy or safety as to those investigational therapies or uses of such investigational therapies. There is no guarantee that any investigational therapy will successfully complete clinical development or gain approval from applicable regulatory authorities.

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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,	
	2024	2023	2024	2023
Revenue:				
Collaboration revenue	$ —	$ —	$ —	$ 170,000
Grant revenue	602	—	1,623	—
Total revenue	$ 602	$ —	$ 1,623	$ 170,000
Operating expenses:				
Research and development	82,160	90,698	238,498	292,188
General and administrative	17,419	18,291	54,853	59,683
Collaboration expense, net	11,153	23,422	110,250	110,250
Total operating expenses	110,732	132,411	403,601	462,121
Loss from operations	(110,130)	(132,411)	(401,978)	(292,121)
Total other income, net	25,064	20,671	75,924	51,819
Net loss before income taxes	(85,066)	(111,740)	(326,054)	(240,302)
Provision for income taxes	(876)	(412)	(2,887)	(2,655)
Net loss	(85,942)	(112,152)	(328,941)	(242,957)

Foreign currency translation adjustment	76	(49)	66	12
Unrealized gain on marketable securities	13,368	2,160	8,586	8,838
Comprehensive loss	$ (72,498)	$ (110,041)	$ (320,289)	$ (234,107)
Net loss per common share — basic	$ (1.01)	$ (1.41)	$ (3.92)	$ (3.07)
Basic weighted-average common shares outstanding	85,234,926	79,414,098	83,988,063	79,063,415
Net loss per common share — diluted	$ (1.01)	$ (1.41)	$ (3.92)	$ (3.07)
Diluted weighted-average common shares outstanding	85,234,926	79,414,098	83,988,063	79,063,415

CRISPR Therapeutics AG

Condensed Consolidated Balance Sheets Data
(Unaudited, in thousands)

	As of	
	September 30, 2024	December 31, 2023
Cash and cash equivalents	$ 225,670	$ 389,477
Marketable securities	1,709,975	1,304,215
Marketable securities, non-current	—	1,973
Working capital	1,854,081	1,799,287
Total assets	2,256,130	2,229,571
Total shareholders' equity	1,939,658	1,882,803

Source: CRISPR Therapeutics AG