CRISPR Therapeutics Highlights Strategic Priorities and Anticipated 2025 Milestones

-Ongoing launch of CASGEVY® continues to gain momentum-

-2025 is poised to be a catalyst-rich year with key updates across several programs-

-Starting 2025 with a strong balance sheet with approximately $1.9 billion in cash, cash equivalents, and marketable securities-

ZUG, Switzerland and BOSTON, Jan. 13, 2025 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (Nasdaq: CRSP), a biopharmaceutical company focused on creating transformative gene-based medicines for serious diseases, today highlighted its strategic priorities and anticipated 2025 milestones.

"As we look ahead to 2025, we are in a privileged position with an approved commercial product, a rich pipeline, a strong balance sheet and an organizational foundation to drive our pipeline forward," said Samarth Kulkarni, Ph.D., Chairman and Chief Executive Officer of CRISPR Therapeutics. "Building on the success of CASGEVY's launch, we continue to broaden our portfolio across oncology, autoimmune and cardiometabolic indications. 2025 promises to be a milestone-rich year, with clinical data updates across several programs spanning a range of indications. In parallel, we are continuously innovating on our platform with next-generation gene editing and delivery technologies, which have the potential to broaden our ability to address additional diseases with curative treatments."

Strategic Priorities and Recent Advancements
2025 is an important inflection year for CRISPR Therapeutics as we establish CASGEVY® and advance our pipeline candidates to human proof-of-concept and beyond.

Key Priorities:

- Ongoing launch of CASGEVY, driven by strong patient demand and robust payer and system support.
- Continue advancing our pipeline candidates, with several key updates in 2025, including CTX112™ in oncology and autoimmune diseases, as well as CTX310™ and CTX320™ in cardiovascular indications, alongside the potential for further updates across our pipeline.
- Continue advancing our next-generation gene editing and lipid nanoparticle (LNP) delivery platform for the liver, hematopoietic stem cells (HSCs), and other target organs.

Hemoglobinopathies and CASGEVY® (exagamglogene autotemcel [exa-cel]):
2024 served as a foundational year for the launch of CASGEVY. In its first year, CASGEVY has seen strong global patient demand, and our partner, Vertex, has made significant progress in activating authorized treatment centers (ATCs) and securing payer access.

- Rapid pace of global approvals underscores high unmet need and transformative potential of CASGEVY. On December 31, 2024, CASGEVY received regulatory approval in the United Arab Emirates (UAE) for the treatment of both sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT).
- Progress in cell collections has been strong, with high demand across all regions and indications. As of the end of 2024, more than 50 patients have initiated cell collection.
- Significant progress has been made in activating ATCs, with more than 50 ATCs globally.
- Strong payer support has been established in regions where CASGEVY is approved, through major payer contracts and early access programs. In the U.S., Vertex recently negotiated a first-of-its-kind, voluntary agreement with the Centers for Medicare & Medicaid Services (CMS), which will provide a single outcomes-based arrangement for CASGEVY, available to all state Medicaid programs to ensure broad and equitable access for patients.
- Additionally, CRISPR Therapeutics continues to advance its internally developed targeted conditioning program as well as *in vivo* approaches utilizing LNP-mediated delivery through preclinical studies. Both initiatives could significantly expand the addressable patient populations for SCD and TDT.

Immuno-Oncology and Autoimmune Disease (AID):
CRISPR Therapeutics is developing CTX112 for both hematologic malignancies and autoimmune indications, with an emerging

best-in-class profile.

- CRISPR presented positive data from its ongoing Phase 1/2 trial of CTX112 in relapsed or refractory CD19+ B-cell malignancies at the 2024 American Society of Hematology Annual meeting, demonstrating strong efficacy comparable to autologous therapies, a tolerable safety profile and robust cell expansion.
- CTX112 was awarded regenerative medicine advanced therapy (RMAT) designation by the FDA based on these strong preliminary data.
- The most recent data with CTX112 demonstrate responses in patients who have received prior T-cell engager-based therapies (TCEs), with responses observed in all 6 patients, including 3 large B-cell lymphoma (LBCL) patients, who either relapsed post-TCE treatment or were refractory to TCEs.
- CRISPR Therapeutics plans to engage with regulatory authorities to align on the path forward for CTX112 in B-cell malignancies, with an update expected in mid-2025.
- Preliminary safety, pharmacokinetic, and pharmacodynamic data in oncology highlight the potential of CTX112 in autoimmune indications. Based on favorable oncology data, CRISPR Therapeutics is expanding the trial for CTX112 in system lupus erythematosus to include patients with systemic sclerosis and inflammatory myositis patients in a basket study, with updates expected in mid-2025.
- Clinical trials are on-going for CTX131™ in both solid tumors and hematologic malignancies, with updates expected in 2025. Additionally, we are advancing an autologous, gene-edited CAR T therapy targeting glypican-3 (GPC3) for the potential treatment of solid tumors and expect to initiate a clinical trial in the first half of 2025.

***In Vivo* Cardiovascular:**
CRISPR Therapeutics continues to make significant progress in advancing its proprietary LNP delivery technologies for gene editing in the liver, with ongoing development in both clinical and preclinical stages.

- Dose escalation for 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)]), is ongoing, with updates expected in the first half of 2025.
- CTX310 is being developed for patients with homozygous or heterozygous familial hypercholesterolemia, severe hypertriglyceridemia, or mixed dyslipidemias, and has the potential for approval based on validated biomarkers, pending regulatory discussions.
- CTX320 is being developed for patients with high Lp(a), a genetically determined cardiovascular risk factor affecting millions worldwide.
- Rapid preclinical progress is being made with CTX340™, targeting angiotensinogen (*AGT*) for refractory hypertension, as well as CTX450™, targeting 5'-aminolevulinate synthase 1 (*ALAS1*) for acute hepatic porphyria.

Regenerative Medicine:
Progress continues in regenerative medicine, with ongoing efforts to develop innovative therapies, including the clinical trial for CTX211™ in Type 1 diabetes (T1D) and subsequent next generation programs.

- These programs focus on allogeneic, gene-edited, stem cell-derived beta islet cell precursors for the treatment of T1D, which have the potential to render patients insulin-independent without the need for chronic immunosuppression. The Company anticipates providing an update in 2025.

Anticipated Key Milestones
CRISPR Therapeutics anticipates several key milestones in 2025 across its development portfolio.

- Quarterly updates on CASGEVY launch progress.
- Updates for CTX310 and CTX320 in the first half of 2025.
- A broad update with CTX112 in oncology and autoimmune disease in mid-2025.
- Update for CTX131 in 2025.
- Update in regenerative medicine in 2025.

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 recurrent vaso-occlusive crises (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 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. 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 the safety and efficacy of the product candidate in adult patients with systemic lupus erythematosus, systemic sclerosis, and inflammatory myositis.

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 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 evolved from a research-stage company advancing gene editing programs into a leader that celebrated the historic approval of the first-ever CRISPR-based therapy. The Company has a diverse portfolio of product candidates across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine, cardiovascular, autoimmune, and rare diseases. In 2018, CRISPR Therapeutics advanced the first-ever CRISPR/Cas9 gene-edited therapy into the clinic to investigate the treatment of sickle cell disease and transfusion-dependent beta thalassemia. Beginning in late 2023, CASGEVY® (exagamglogene autotemcel [exa-cel]) was approved in several countries to treat eligible patients with either of these conditions. The Nobel Prize-winning CRISPR technology 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 formed strategic partnerships with leading companies including 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. To learn more, visit www.crisprtx.com.

CRISPR Special Note Regarding Forward-Looking Statements

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 made by Dr. Kulkarni in this press release, as well as 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; (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) CRISPR Therapeutics strategy, goals, anticipated financial performance and the sufficiency of its cash resources; (iv) plans and expectations for the commercialization of, and anticipated benefits of, CASGEVY, including anticipated patient access to CASGEVY; (v) regulatory submissions and authorizations, including timelines for and expectations regarding additional regulatory agency decisions; (vi) the expected benefits of its collaborations; and (vii) the therapeutic value, development, and commercial potential of gene editing and delivery 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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Source: CRISPR Therapeutics AG