Vertex and CRISPR Therapeutics Present New Data in 22 Patients With Greater Than 3 Months Follow-Up Post-Treatment With Investigational CRISPR/Cas9 Gene-Editing Therapy, CTX001™ at European Hematology Association Annual Meeting

June 11, 2021

- Beta thalassemia: All 15 patients were transfusion independent after CTX001 infusion -
- Sickle cell disease: All seven patients were free of vaso-occlusive crises after CTX001 infusion -

BOSTON & ZUG, Switzerland & CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 11, 2021-- Vertex Pharmaceuticals Incorporated (Nasdaq:VRTX) and CRISPR Therapeutics (Nasdaq:CRSP) today announced new data on 22 patients, with follow-up of at least 3 months, and ranging from 4 months to 26 months, treated with the investigational CRISPR/Cas9-based gene-editing therapy, CTX001, that show a consistent and sustained response to treatment. CTX001 is being investigated in two ongoing Phase 1/2 clinical trials as a potential one-time therapy for patients suffering from transfusion-dependent beta thalassemia (TDT) and severe sickle cell disease (SCD). In total, more than 40 patients have been dosed across both studies to date.

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All 15 patients with TDT, including six who have the beta zero/beta zero or other severe genotypes, were transfusion-free at last follow-up, and all seven patients with severe SCD were free of vaso-occlusive crises (VOCs) from CTX001 infusion through last follow-up. Five patients with TDT and two patients with SCD now have follow-up of greater than one year, demonstrating a stable and durable response to treatment. These data are available as e-posters beginning on June 11, 2021, at 09:00 CEST, and a partial presentation of these data were presented during the Joint EHA-ASH Symposium on June 10, 2021 from 17:30-18:30 CEST. A summary of the results from the CLIMB-111 and CLIMB-121 Phase 1/2 clinical trials is provided below.

“The data presented today in 22 patients are impressive in both the consistency and durability of effect. These results add to the growing body of evidence that CTX001 may hold the promise for a one-time functional cure for sickle cell disease and beta thalassemia. We are working with urgency to complete enrollment and look forward to finalizing regulatory discussions and moving towards filing,” said Reshma Kewalramani, M.D., Chief Executive Officer and President at Vertex.

“The continued progress and momentum of CTX001 validate the role that CRISPR gene-editing technology could have in the future of therapeutics,” added Samarth Kulkarni, Ph.D., Chief Executive Officer at CRISPR Therapeutics. “We are excited about these results and look forward to additional longer-term data and to moving this investigational medicine forward for a larger population of patients with these two devastating diseases.”

“As a physician caring for patients suffering from beta thalassemia, I have a high sense of urgency for novel and efficacious treatments,” said Dr. Franco Locatelli, Professor of Pediatrics at the Sapienza University of Rome, Director of the Department of Pediatric Hematology and Oncology at Bambino Gesù Children’s Hospital. “These results suggest the potential for a durable benefit for patients with transfusion-dependent beta thalassemia.”

“It is thrilling to work on a groundbreaking program like CTX001,” said Dr. Stephan Grupp, Section Chief, Cellular Therapy and Transplant, Division of Oncology, Children's Hospital of Philadelphia. “This approach uses CRISPR/Cas9 gene editing to enable the patient’s own cells to produce fetal hemoglobin, and to see results that demonstrate the potential for a treatment that may transform the lives of many patients is an exciting time for me and the team.”

CLIMB-111 Trial in TDT: Updated Results
The 15 patients with TDT reported at EHA are patients who had reached at least three months of follow-up after CTX001 dosing and therefore could be assessed for initial safety and efficacy. All 15 patients showed a similar pattern of response, with rapid and sustained increases in total hemoglobin, fetal hemoglobin and transfusion independence.

All 15 patients were transfusion independent with follow-up ranging from 4 to 26 months after CTX001 infusion and had clinically meaningful improvements in total hemoglobin from 8.9 to 16.9 g/dL and fetal hemoglobin from 67.3% to 99.6% at last visit.

Bone marrow allelic editing data collected from 10 patients with at least 6 months of follow-up, of which five patients had at least 12 months of follow-up and one patient had at least 24 months of follow-up, demonstrated a durable effect.

The safety data from all 15 patients were generally consistent with an autologous stem cell transplant and myeloablative conditioning. As previously reported, there were four serious adverse events (SAEs) considered related or possibly related to CTX001 reported in one patient: headache, hemophagocytic lymphohistiocytosis (HLH), acute respiratory distress syndrome and idiopathic pneumonia syndrome. All four SAEs occurred in the context of HLH and have resolved. The majority of non-serious adverse events were considered mild to moderate.

The presentations at EHA and the data summarized in this press release cover all TDT patients dosed with CTX001 with three or more months of follow-up as of the data cut on March 30, 2021. In addition to the data presented above, a TDT patient, with less than three months of follow-up and therefore not included in the data cut, experienced an SAE; this SAE of cerebellar hemorrhage, which was considered related to busulfan conditioning, has resolved.

Enrollment and dosing are ongoing.

CLIMB-121 Trial in Severe SCD: Updated Results
The seven patients reported at EHA are patients who had reached at least three months of follow-up after CTX001 dosing and therefore could be

assessed for initial safety and efficacy. All seven patients showed a similar pattern of response, with rapid and sustained increases in total hemoglobin and fetal hemoglobin, as well as elimination of VOCs.

All seven patients remained VOC-free with follow-up ranging from five to 22 months after CTX001 infusion and had clinically meaningful improvements in total hemoglobin from 11 to 15.9 g/dL and fetal hemoglobin levels from 39.6% to 49.6% at last visit.

Bone marrow allelic editing data collected from four patients who have at least six months of follow-up, of which two had 12 months of follow-up, demonstrated a durable effect.

The safety data from all seven patients were generally consistent with an autologous stem cell transplant and myeloablative conditioning. There were no SAEs considered related to CTX001, and the majority of non-serious adverse events were considered mild to moderate.

Enrollment and dosing are ongoing.

About CTX001
CTX001 is an investigational, autologous, *ex vivo* CRISPR/Cas9 gene-edited therapy that is being evaluated for patients suffering from TDT or severe SCD, in which a patient's hematopoietic stem cells are edited to produce high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. HbF is a form of the oxygen-carrying hemoglobin that is naturally present at birth, which then switches to the adult form of hemoglobin. The elevation of HbF by CTX001 has the potential to alleviate or eliminate transfusion requirements for patients with TDT and reduce or eliminate painful and debilitating sickle crises for patients with SCD. Earlier results from these ongoing trials were published as a Brief Report in *The New England Journal of Medicine* in January of 2021.

Based on progress in this program to date, CTX001 has been granted Regenerative Medicine Advanced Therapy (RMAT), Fast Track, Orphan Drug, and Rare Pediatric Disease designations from the U.S. Food and Drug Administration (FDA) for both TDT and SCD. CTX001 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.

Among gene-editing approaches being investigated/evaluated for TDT and SCD, CTX001 is the furthest advanced in clinical development.

About CLIMB-111
The ongoing Phase 1/2 open-label trial, CLIMB-Thal-111, is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 12 to 35 with TDT. The trial will enroll up to 45 patients and follow patients for approximately two years after infusion. Each patient will be asked to participate in a long-term follow-up trial.

About CLIMB-121
The ongoing Phase 1/2 open-label trial, CLIMB-SCD-121, is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 12 to 35 with severe SCD. The trial will enroll up to 45 patients and follow patients for approximately two years after infusion. Each patient will be asked to participate in a long-term follow-up trial.

About CLIMB-131
This is a long-term, open-label trial to evaluate the safety and efficacy of CTX001 in patients who received CTX001 in CLIMB-111 or CLIMB-121. The trial is designed to follow participants for up to 15 years after CTX001 infusion.

About the Gene-Editing Process in These Trials
Patients who enroll in these trials will have their own hematopoietic stem and progenitor cells collected from peripheral blood. The patient's cells will be edited using the CRISPR/Cas9 technology. The edited cells, CTX001, will then be infused back into the patient as part of a stem cell transplant, a process which involves, among other things, a patient being treated with myeloablative busulfan conditioning. Patients undergoing stem cell transplants may also encounter side effects (ranging from mild to severe) that are unrelated to the administration of CTX001. Patients will initially be monitored to determine when the edited cells begin to produce mature blood cells, a process known as engraftment. After engraftment, patients will continue to be monitored to track the impact of CTX001 on multiple measures of disease and for safety.

About the Vertex-CRISPR Collaboration
Vertex and CRISPR Therapeutics 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. CTX001 represents the first potential treatment to emerge from the joint research program. Under a recently amended collaboration agreement, Vertex will lead global development, manufacturing and commercialization of CTX001 and split program costs and profits worldwide 60/40 with CRISPR Therapeutics.

About Vertex
Vertex is a global biotechnology company that invests in scientific innovation to create transformative medicines for people with serious diseases. The company has multiple approved medicines that treat the underlying cause of cystic fibrosis (CF) — a rare, life-threatening genetic disease — and has several ongoing clinical and research programs in CF. Beyond CF, Vertex has a robust pipeline of investigational small molecule medicines in other serious diseases where it has deep insight into causal human biology, including pain, alpha-1 antitrypsin deficiency and APOL1-mediated kidney diseases. In addition, Vertex has a rapidly expanding pipeline of cell and genetic therapies for diseases such as sickle cell disease, beta thalassemia, Duchenne muscular dystrophy and type 1 diabetes mellitus.

Founded in 1989 in Cambridge, Mass., Vertex's global headquarters is now located in Boston's Innovation District and its international headquarters is in London. Additionally, the company has research and development sites and commercial offices in North America, Europe, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including 11 consecutive years on Science magazine's Top Employers list and a best place to work for LGBTQ equality by the Human Rights Campaign. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

Vertex Special Note Regarding Forward-Looking Statements
This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, statements made by Dr. Reshma Kewalramani, Dr. Samarth Kulkarni, Dr. Franco Locatelli, and Dr. Stephan Grupp, and statements regarding expectations that data will be presented and available as e-posters beginning on June 11, 2021, the potential benefits of CTX001, the potential

benefits of our collaboration with CRISPR and CRISPR gene-editing technology, our plans and expectations for our clinical trials, including our expectations for the gene-editing process in these clinical trials, the status of our clinical trials of our product candidates under development by us and our collaborators, including activities at the clinical trial sites and patient enrollment, our expectations and plans regarding our regulatory discussions and future regulatory filings, and our expectations regarding the future activities of the parties pursuant to the amended collaboration agreement with CRISPR. While Vertex believes the forward-looking statements contained in this press release are accurate, these forward-looking statements represent the company's beliefs only as of the date of this press release and there are a number of risks and uncertainties that could cause actual events or results to differ materially from those expressed or implied by such forward-looking statements. Those risks and uncertainties include, among other things, that data from a limited number of patients may not be indicative of final clinical trial results, that data from the company's development programs, including its programs with its collaborators, may not support registration or further development of its compounds due to safety and/or efficacy, or other reasons, that the COVID-19 pandemic may impact the status or progress of our clinical trials and clinical trial sites and the clinical trials and clinical trial sites of our collaborators, including patient enrollment, or other reasons, and other risks listed under the heading “Risk Factors” in Vertex's most recent annual report and subsequent quarterly reports filed with the Securities and Exchange Commission at www.sec.gov and available through the company's website at www.vrtx.com. You should not place undue reliance on these statements or the scientific data presented. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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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 rare diseases. To accelerate and expand its efforts, CRISPR Therapeutics has established strategic collaborations 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 Cambridge, Massachusetts, and business offices in San Francisco, California and 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. Reshma Kewalramani, Dr. Samarth Kulkarni, Dr. Franco Locatelli, and Dr. Stephan Grupp in this press release, as well as statements regarding CRISPR Therapeutics’ expectations about any or all of the following: (i) the safety, efficacy and clinical progress of CRISPR Therapeutics’ various clinical programs, including CTX001, including expectations regarding the data presented and available as e-posters beginning on June 11, 2021 and a partial presentation of such data during the Joint EHA-ASH Symposium on June 10, 2021; (ii) the potential and expected benefits of CRISPR Therapeutics’ collaboration with Vertex; and (iii) 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, existing and prospective investors are cautioned that forward-looking statements are inherently uncertain, are neither promises nor guarantees and not to place undue reliance on such statements, which speak only as of the date they are made. 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 initial and preliminary data from any clinical trial and initial data from a limited number of patients (as is the case with CTX001 at this time) not to be indicative of final or future trial results; the potential that CTX001 clinical trial results may not be favorable or may not support registration or further development; the potential that future competitive or other market factors may adversely affect the commercial potential for CTX001; CRISPR Therapeutics may not realize the potential benefits of the collaboration with Vertex; potential impacts due to the coronavirus pandemic, such as to the timing and progress of clinical trials; uncertainties regarding the intellectual property protection for CRISPR Therapeutics’ technology and intellectual property belonging to third parties; 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. 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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