



## CRISPR Therapeutics and Vertex Announce Positive Safety and Efficacy Data From First Two Patients Treated With Investigational CRISPR/Cas9 Gene-Editing Therapy CTX001® for Severe Hemoglobinopathies

November 19, 2019

*-Two patients treated with CTX001 successfully engrafted and demonstrated an initial safety profile consistent with myeloablative busulfan conditioning and autologous hematopoietic stem cell transplant-*

*-Beta thalassemia: Patient is transfusion independent with total hemoglobin level of 11.9 g/dL and 10.1 g/dL fetal hemoglobin at nine months after CTX001 infusion-*

*-Sickle cell disease: Patient is free of vaso-occlusive crises with total hemoglobin level of 11.3 g/dL and 46.6% fetal hemoglobin at four months after CTX001 infusion-*

*-CRISPR Therapeutics will host a conference call today at 8:00 a.m. ET to review these data-*

ZUG, Switzerland and CAMBRIDGE, Mass. and BOSTON, Nov. 19, 2019 (GLOBE NEWSWIRE) -- [CRISPR Therapeutics](#) (NASDAQ: CRSP) and [Vertex Pharmaceuticals Incorporated](#) (NASDAQ: VRTX) today announced positive, interim data from the first two patients with severe hemoglobinopathies treated with the investigational CRISPR/Cas9 gene-editing therapy CTX001 in ongoing Phase 1/2 clinical trials. One patient with transfusion-dependent beta thalassemia (TDT) received CTX001 in the first quarter of 2019 and data for this patient reflect nine months of safety and efficacy follow-up. One patient with severe sickle cell disease (SCD) received CTX001 in mid-2019 and data for this patient reflect four months of safety and efficacy follow-up. These studies are ongoing and patients will be followed for approximately two years following infusion. Several additional patients have been enrolled and have had drug product manufactured across the two studies.

### Transfusion-Dependent Beta Thalassemia

The patient with TDT has the  $\beta^0/IVS-I-110$  genotype and required 16.5 transfusions per year (annualized rate during the two years prior to consenting for the study) before enrolling in the clinical study. The patient achieved neutrophil engraftment 33 days after CTX001 infusion and platelet engraftment 37 days after infusion. Two serious adverse events (SAEs) occurred, neither of which the principal investigator (PI) considered related to CTX001: pneumonia in the presence of neutropenia and veno-occlusive liver disease attributed to busulfan conditioning; both subsequently resolved. At nine months after CTX001 infusion, the patient was transfusion independent and had total hemoglobin levels of 11.9 g/dL, 10.1 g/dL fetal hemoglobin, and 99.8% F-cells (erythrocytes expressing fetal hemoglobin).

### Sickle Cell Disease

The patient with SCD experienced seven vaso-occlusive crises (VOCs) per year (annualized rate during the two years prior to consenting for the study) before enrolling in the clinical study. The patient achieved neutrophil and platelet engraftment 30 days after CTX001 infusion. Three SAEs occurred, none of which the PI considered related to CTX001: sepsis in the presence of neutropenia, cholelithiasis, and abdominal pain, all of which resolved. At four months after CTX001 infusion, the patient was free of VOCs and had total hemoglobin levels of 11.3 g/dL, 46.6% fetal hemoglobin, and 94.7% F-cells (erythrocytes expressing fetal hemoglobin).

"We are very encouraged by these preliminary data, the first such data to be reported for patients with beta thalassemia and sickle cell disease treated with our CRISPR/Cas9 edited autologous hematopoietic stem cell candidate, CTX001," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "These data support our belief in the potential of our therapies to have meaningful benefit for patients following a one-time intervention. We continue to enroll these studies as we drive forward to develop CRISPR/Cas9 therapies as a new class of transformative medicines to treat serious diseases."

"The data we announced today are remarkable and demonstrate that CTX001 has the potential to be a curative CRISPR/Cas9-based gene-editing therapy for people with sickle cell disease and beta thalassemia," said Jeffrey Leiden, M.D., Ph.D., Chairman, President and Chief Executive Officer of Vertex. "While the data are exciting, we are still in the early phase of this clinical program. We look forward to continuing to work with physicians, patients, caregivers and families over the coming months and years to bring forward the best possible therapy for these two serious diseases and to continue to accelerate our gene-editing programs for other serious diseases such as Duchenne muscular dystrophy and myotonic dystrophy type 1."

### About the Phase 1/2 Study in Transfusion-Dependent Beta Thalassemia

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 18 to 35 with TDT. The study 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 study. Enrollment is ongoing at six clinical trial sites in the United States, Canada and Europe.

### About the Phase 1/2 Study in Sickle Cell Disease

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 18 to 35 with severe SCD. The study 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 study. Enrollment is ongoing at 12 clinical trial sites in the United States, Canada and Europe.

### About the Gene-Editing Process in These Trials

Patients who enroll in these studies will have 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.

### **CRISPR Therapeutics Conference Call and Webcast**

CRISPR Therapeutics will host a conference call and webcast today at 8:00 a.m. ET. The webcast and presentation will be made available on the CRISPR Therapeutics website at <https://crisprtx.qcs-web.com/events> in the Investors section under Events and Presentations. Following the live audio webcast, a replay will be available on the Company's website for approximately 30 days.

### **Dial-In Information**

Live (U.S. / Canada): (800) 895-3361

Live (International): (785) 424-1062

Conference ID: 87198237

### **About CTX001**

CTX001 is an investigational *ex vivo* CRISPR gene-edited therapy that is being evaluated for patients suffering from TDT or severe SCD in which a patient's hematopoietic stem cells are engineered 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 and is then replaced by the adult form of hemoglobin. The elevation of HbF by CTX001 has the potential to alleviate transfusion requirements for TDT patients and painful and debilitating sickle crises for SCD patients.

CTX001 is being developed under a co-development and co-commercialization agreement between CRISPR Therapeutics and Vertex.

### **About the CRISPR-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. CTX001 represents the first treatment to emerge from the joint research program. CRISPR Therapeutics and Vertex will jointly develop and commercialize CTX001 and equally share all research and development costs and profits worldwide.

### **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 AG, 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 London, United Kingdom. For more information, please visit [www.crisprtx.com](http://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 regarding CRISPR Therapeutics' expectations about any or all of the following: (i) the safety, efficacy and clinical progress of CRISPR Therapeutics' CTX001 clinical program; (ii) the status and scope of ongoing and potential future clinical trials (including, without limitation, the timing of filing of clinical trial applications and INDs, any approvals thereof and the timing of commencement of clinical trials), development timelines and discussions with regulatory authorities related to product candidates under development by CRISPR Therapeutics and its collaborators; (iii) the number of patients that will be evaluated, the anticipated date by which enrollment will be completed and 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; v(iv) the intellectual property coverage and positions of CRISPR Therapeutics, its licensors and third parties; (v) the sufficiency of CRISPR Therapeutics' cash resources; 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 potential for initial and preliminary data from any clinical trial (including CTX001) not to be indicative of final trial results; the risk that the initial data from a limited number of patients (as is the case with CTX001 at this time) may not be indicative of results from the full planned study population; the outcomes for each CRISPR Therapeutics' planned clinical trials and studies may not be favorable; that one or more of CRISPR Therapeutics' 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 CRISPR Therapeutics' product candidates; uncertainties inherent in the initiation and completion of preclinical studies for CRISPR Therapeutics' product candidates; availability and timing of results from preclinical studies; whether results from a preclinical trial will be predictive of future results of the future trials; uncertainties about regulatory approvals to conduct trials or to market products; uncertainties regarding the intellectual property protection for CRISPR Therapeutics' 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, 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](http://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.*

### **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 four 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 disease. In addition, Vertex has a rapidly expanding pipeline of genetic and cell 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, UK. 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 10 consecutive years on Science magazine's Top Employers list and top five on the 2019 Best Employers for Diversity list by Forbes. For company updates and to learn more about Vertex's history of innovation, visit [www.vrtx.com](http://www.vrtx.com) or follow us on Facebook, Twitter, LinkedIn, YouTube and Instagram.

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**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, the information provided regarding the status of, and expectations with respect to, the CTX001 clinical development program. 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 factors that could cause actual events or results to differ materially from those indicated by such forward-looking statements. Those risks and uncertainties include that the development of CTX001 may not proceed due to safety, efficacy or other reasons, and other risks listed under Risk Factors in Vertex's annual report and quarterly reports filed with the Securities and Exchange Commission and available through the company's website at [www.vrtx.com](http://www.vrtx.com). Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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