



## **CRISPR Therapeutics and Vertex Announce Progress in Clinical Development Programs for the Investigational CRISPR/Cas9 Gene-Editing Therapy CTX001**

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*-First patient infused with CTX001 in a Phase 1/2 clinical trial for patients with beta thalassemia-*

*-First patient enrolled in a Phase 1/2 clinical trial of CTX001 for patients with sickle cell disease-*

ZUG, Switzerland and CAMBRIDGE and BOSTON, Mass., Feb. 25, 2019 (GLOBE NEWSWIRE) -- CRISPR Therapeutics (NASDAQ:CRSP) and Vertex Pharmaceuticals Incorporated (NASDAQ:VRTX) today reviewed recent progress in the clinical development programs for CTX001, an investigational, autologous, CRISPR/Cas9 gene-edited hematopoietic stem cell therapy being evaluated for patients suffering from severe hemoglobinopathies. The companies announced that the first patient has been treated with CTX001 in a Phase 1/2 clinical study of patients with transfusion-dependent beta thalassemia (TDT), marking the first company-sponsored use of a CRISPR/Cas9 therapy in a clinical trial. In parallel, the companies are investigating CTX001 for the treatment of severe sickle cell disease (SCD) and also announced that the first patient has been enrolled in a Phase 1/2 clinical study of CTX001 in severe SCD in the U.S. and is expected to be infused with CTX001 in mid-2019.

"We have made tremendous progress with CTX001 and are pleased to announce that we've treated the first patient with beta thalassemia in this clinical study," said Samarth Kulkarni, Ph.D., Chief Executive Officer of CRISPR Therapeutics. "Treating the first patient in this study marks an important scientific and medical milestone and the beginning of our efforts to fully realize the promise of CRISPR/Cas9 therapies as a new class of potentially transformative medicines to treat serious diseases."

"Beta thalassemia and sickle cell disease are serious, life-threatening diseases, and we are evaluating ex vivo treatment with CTX001 with the goal of creating a one-time potential curative therapy," said David Altshuler M.D., Ph.D., Executive Vice President and Chief Scientific Officer at Vertex. "Our collaboration with CRISPR Therapeutics offers an exciting new potential therapeutic approach that complements our strategy of using scientific innovation to create transformative medicines for serious diseases."

### **About the Phase 1/2 Study in Beta Thalassemia**

The Phase 1/2 open-label trial is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 18 to 35 with TDT, non-beta zero/beta zero subtypes. The first two patients in the trial will be treated sequentially and, pending data from these initial two patients, the trial will open for broader concurrent enrollment. The companies plan to target presentations of data at scientific conferences once there is sufficient data on multiple patients.

The study is currently being conducted at multiple clinical trial sites in Canada and Europe. In addition, CRISPR Therapeutics and Vertex expanded the U.S. Investigational New Drug Application (IND) for CTX001 to include beta thalassemia and plan to begin enrollment of the Phase 1/2 study at clinical trial sites in the U.S. this year.

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

The Phase 1/2 open-label trial is designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 18 to 35 with severe SCD. Similar to the trial in beta thalassemia, the first two patients in the trial will be treated sequentially prior to broader concurrent enrollment. The companies plan to target presentations of data at scientific conferences once there is sufficient data on multiple patients.

The study is currently being conducted at clinical trial sites in the United States. CTX001 was granted Fast Track Designation by the U.S. Food and Drug Administration for the treatment of SCD in January of this year. In addition, CRISPR Therapeutics and Vertex have obtained approvals of Clinical Trial Applications (CTAs) for CTX001 for SCD in Canada and additional countries in Europe and plan to initiate the Phase 1/2 study at clinical trial sites outside the U.S. this year.

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

Patients who enroll in these studies will have hematopoietic stem 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. 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.

### **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 Beta Thalassemia and Sickle Cell Disease**

Beta thalassemia is an inherited blood disorder caused by mutations in the beta-globin gene that results in low or no beta-globin production, which is an important building block of hemoglobin. Patients with TDT, a severe form of beta thalassemia, suffer from anemia and are dependent on blood transfusions, which can lead to iron accumulation and complications that damage organs and shorten life span.

SCD is an inherited blood disorder caused by mutations in the beta-globin gene that lead to an abnormal hemoglobin, called sickle hemoglobin (HbS). Because of this abnormal hemoglobin, red blood cells can become rigid and block small blood vessels. Patients with severe SCD can suffer from

acute pain, acute chest syndrome, organ damage, as well as other potential complications, including shortened life span.

### **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) 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; (ii) 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; (iii) the scope and timing of ongoing and potential future clinical trials; (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 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 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 and life-threatening diseases. In addition to clinical development programs in CF, Vertex has more than a dozen ongoing research programs focused on the underlying mechanisms of other serious diseases.

Founded in 1989 in Cambridge, Mass., Vertex's headquarters is now located in Boston's Innovation District. Today, the company has research and development sites and commercial offices in the United States, Europe, Canada, Australia and Latin America. Vertex is consistently recognized as one of the industry's top places to work, including being named to Science magazine's Top Employers in the life sciences ranking for nine years in a row.

For additional information and the latest updates from the Company, please visit [www.vrtx.com](http://www.vrtx.com).

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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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