Vertex and CRISPR Therapeutics Announce Authorization of the First CRISPR/Cas9 Gene-Edited Therapy, CASGEVY™ (exagamglogene autotemcel), by the United Kingdom MHRA for the Treatment of Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia

November 16, 2023

- First regulatory authorization of a CRISPR-based gene-editing therapy in the world –

- CASGEVY is indicated for the treatment of sickle cell disease in patients 12 years of age and older with recurrent vaso-occlusive crises who have the βS/βS, βS/β+ or βS/β0 genotype, for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related hematopoietic stem cell donor is not available -

- CASGEVY is indicated for the treatment of transfusion-dependent beta thalassemia in patients 12 years of age and older for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related hematopoietic stem cell donor is not available -

BOSTON & ZUG, Switzerland--(BUSINESS WIRE)--Nov. 16, 2023-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) and CRISPR Therapeutics (Nasdaq: CRSP) announced today that the United Kingdom (U.K.) Medicines and Healthcare products Regulatory Agency (MHRA) has granted conditional marketing authorization for CASGEVY™ (exagamglogene autotemcel [exa-cel]), a CRISPR/Cas9 gene-edited therapy, for the treatment of sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT).

CASGEVY has been authorized for the treatment of eligible patients 12 years of age and older with SCD with recurrent vaso-occlusive crises (VOCs) or TDT, for whom a human leukocyte antigen (HLA) matched related hematopoietic stem cell donor is not available. There are an estimated 2,000 patients eligible for CASGEVY in the U.K.

“Today is a historic day in science and medicine: this authorization of CASGEVY in Great Britain is the first regulatory authorization of a CRISPR-based therapy in the world,” said Reshma Kewalramani, M.D., Chief Executive Officer and President of Vertex.

“I hope this represents the first of many applications of this Nobel Prize winning technology to benefit eligible patients with serious diseases,” said Samarth Kulkarni, Ph.D., Chairman and Chief Executive Officer of CRISPR Therapeutics.”

In two global clinical trials of CASGEVY in SCD and TDT, the trials met their respective primary outcome of becoming free from severe VOCs or transfusion independent for at least 12 consecutive months. Once achieved, these benefits are potentially expected to be life-long. The safety profile of 97 SCD and TDT patients treated to date with CASGEVY in these ongoing studies is generally consistent with myeloablative conditioning with busulfan and hematopoietic stem cell transplant.

“This authorization offers a new option for eligible patients who are waiting for innovative therapies, and I look forward to patients having access to this therapy as quickly as possible,” said Professor Josu de la Fuente, Principal Investigator in the CLIMB-111 and CLIMB-121 studies, Professor of Practice (Cellular & Gene Therapy) at Imperial College London, and Consultant Haematologist at Imperial College Healthcare NHS Trust.

In the U.K., exa-cel was granted an Innovation Passport under the Innovative Licensing and Access Pathway (ILAP) from the MHRA, and Vertex is already working closely with national health authorities to secure access for eligible patients as quickly as possible.

About Sickle Cell Disease
Sickle cell disease (SCD) is an inherited blood disorder that affects the red blood cells, which are essential for carrying oxygen to all organs and tissues of the body. SCD causes severe pain, organ damage and shortened life span due to misshapen or “sickled” blood cells. People with SCD can experience painful blood vessel blockages, also known as vaso-occlusive crises (VOCs), that can lead to acute chest syndrome, stroke, jaundice and symptoms of heart failure. Individuals may also experience anemia, which can result in end-organ damage and premature death. VOCs are the hallmark of SCD, often resulting in severe and debilitating pain. Current standard treatment options for SCD are largely symptomatic treatments and do not adequately address the burden of disease or alleviate the need for chronic care. Most often, treatment is focused on relieving pain, minimizing organ damage, maintaining hydration and addressing fevers, requiring medication and sometimes monthly blood transfusions and frequent hospital visits. The only cure for SCD today is a stem cell transplant from a matched donor, but this option is only available to a

small fraction of people living with SCD. SCD requires lifelong treatment and significant use of health care resources, and ultimately results in reduced life expectancy and reduced lifetime earnings and productivity. In the U.K., the mean age of death for people living with SCD is around 40.

About Beta Thalassemia
Beta thalassemia is an inherited blood disorder that affects the red blood cells, which are essential for carrying oxygen to all organs and tissues of the body. A lack of red blood cells, also known as anemia, is the primary manifestation of beta thalassemia. Because of this anemia, people living with beta thalassemia may experience fatigue and shortness of breath, and infants may develop failure to thrive, jaundice and feeding problems. Complications of beta thalassemia can also include an enlarged spleen, liver and/or heart; misshapen bones; and delayed puberty. Treatment for beta thalassemia is personalized and depends on the severity of disease that each person experiences. Many people have to get regular blood transfusions to deliver healthy donated blood to their body. This requires many hospital visits and can also lead to an unhealthy buildup of iron. Today, stem cell transplant from a matched donor is a curative option but is only available to a small fraction of people living with beta thalassemia. Beta thalassemia requires lifelong treatment and significant use of health care resources, and ultimately results in reduced life expectancy, decreased quality of life and reduced lifetime earnings and productivity. In the U.K., the mean age of death for people living with TDT is around 55.

About CASGEVY™ (exagamglogene autotemcel [exa-cel])
CASGEVY™ is a genetically modified autologous CD34+ cell enriched population that contains human hematopoietic stem and progenitor cells edited *ex vivo* by CRISPR/Cas9 at the erythroid-specific enhancer region of the *BCL11A* gene.

The latest data from the ongoing pivotal trials was presented at the European Hematology Association Congress in June 2023.

Exa-cel is also under review by the European Medicines Agency, the Saudi Food and Drug Authority, and the U.S. Food and Drug Administration (FDA). The FDA has granted Priority Review for SCD and Standard Review for TDT and assigned Prescription Drug User Fee Act (PDUFA) target action dates of December 8, 2023, and March 30, 2024, respectively.

About Conditional Marketing Authorizations
Conditional marketing authorizations (CMAs) are for medicines that fulfill a significant unmet medical need such as being for serious and life-threatening diseases, where no satisfactory treatment methods are available or where the medicine offers a major therapeutic advantage. A CMA is granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon. CMAs are valid for one year and renewable annually with ongoing regulatory review of data.

About the Vertex and 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. Exa-cel represents the first treatment to emerge from the joint research program. Under an amended collaboration agreement, Vertex now leads global development, manufacturing and commercialization of exa-cel and splits 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 approved medicines that treat the underlying causes of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell disease and transfusion-dependent beta thalassemia — and continues to advance clinical and research programs in these diseases. Vertex also has a robust clinical pipeline of investigational therapies across a range of modalities in other serious diseases where it has deep insight into causal human biology, including APOL1-mediated kidney disease, acute and neuropathic pain, type 1 diabetes and alpha-1 antitrypsin deficiency.

Vertex was founded in 1989 and has its global headquarters in Boston, with international headquarters 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 14 consecutive years on Science magazine's Top Employers list and one of Fortune’s 100 Best Companies to Work For. For company updates and to learn more about Vertex's history of innovation, visit www.vrtx.com or follow us on LinkedIn, Facebook, Instagram, YouTube and Twitter/X.

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 Boston, Massachusetts and San Francisco, California, and business offices in London, United Kingdom. For more information, please visit www.crisprtx.com.

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(VRTX-GEN)

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, as amended, including, without limitation, the statements by Reshma Kewalramani, M.D., Samarth Kulkarni, Ph.D., and Professor Josu de la Fuente in this press release, and statements regarding our expectations for and the anticipated benefits of CASGEVY, including the expectation for certain life-long benefits of CASGEVY for patients, the estimated eligible patient population in the U.K., Vertex's efforts to secure access for eligible patients as quickly as possible, and Vertex's plans and expectations for the ongoing clinical trials evaluating exa-cel. 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 the company's development programs may not support registration or further development of its compounds due to safety, efficacy, and other reasons, that obtaining authorization and commercializing exa-cel in Europe, the Kingdom of Saudi Arabia, and the U.S. may not occur on the anticipated timeline, or at all, that adequate pricing and reimbursement for CASGEVY may not be achieved on the anticipated timeline, or at all, that the MHRA's conditional marketing authorization may not be renewed annually, or at all, 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. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

(CRSP-GEN)

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 by Reshma Kewalramani, M.D., Samarth Kulkarni, Ph.D., and Professor Josu de la Fuente in this press release, as well as statements regarding: (i) plans and expectations for the commercialization of, and anticipated benefits of, CASGEVY, including the longevity of such benefits for patients, the estimated eligible patient population in the U.K., and the speed by which access for eligible patients may be secured; (ii) expectations regarding the ongoing exa-cel clinical trials, including potential implications of clinical data for patients; (iii) timelines for and expectations regarding additional regulatory agency decisions; (iv) expectations for the benefits of CRISPR Therapeutics' collaboration with Vertex; and (v) expectations regarding 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, that: the clinical data from ongoing clinical trials of exa-cel will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory authorization or renewal of conditional authorization; adequate pricing or reimbursement may not be secured to support continued development or commercialization of exa-cel following regulatory authorization; future competitive or other market factors may adversely affect the commercial potential for CASGEVY; CRISPR Therapeutics may not realize the potential benefits of its collaboration with Vertex; there are 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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Vertex Pharmaceuticals Incorporated
Investors:
InvestorInfo@vrtx.com
or
Manisha Pai, +1 617-961-1899

Media:
mediainfo@vrtx.com
or
International: +44 20 3204 5275
or
U.S.: 617-341-6992
or
Heather Nichols: +1 617-839-3607

CRISPR Therapeutics
Investors:
Susan Kim
+1-617-315-4600
susan.kim@crisprtx.com

Media:
Rachel Eides
+1-617-315-4493
rachel.eides@crisprtx.com

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