Vertex and CRISPR Therapeutics Announce US FDA Approval of CASGEVY™ (exagamglogene autotemcel) for the Treatment of Sickle Cell Disease

– First-ever approval of a CRISPR-based gene-editing therapy in the U.S. –

– Approximately 16,000 patients 12 years of age and older with severe sickle cell disease may now be eligible for this one-time treatment –

– Multiple authorized treatment centers activated –

BOSTON & ZUG, Switzerland--(BUSINESS WIRE)--Dec. 8, 2023-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) and CRISPR Therapeutics (Nasdaq: CRSP) announced today that the U.S. Food and Drug Administration (FDA) has approved CASGEVY™ (exagamglogene autotemcel [exa-cel]), a CRISPR/Cas9 genome-edited cell therapy, for the treatment of sickle cell disease (SCD) in patients 12 years and older with recurrent vaso-occlusive crises (VOCs). This approval means that for the first time, approximately 16,000 patients with SCD may be eligible for a durable one-time therapy that offers the potential of a functional cure for their disease by eliminating severe VOCs and hospitalizations caused by severe VOCs.

"CASGEVY's approval by the FDA is momentous: it is the first CRISPR-based gene-editing therapy to be approved in the U.S. As importantly, CASGEVY is a first-in-class treatment that offers the potential of a one-time transformative therapy for eligible patients with sickle cell disease," said Reshma Kewalramani, M.D., Chief Executive Officer and President of Vertex. "I want to convey my deepest gratitude to the patients and investigators whose trust in this program paved the way for this landmark approval."

"When our company was founded, we had a vision to translate CRISPR technology into multiple breakthrough therapies. So, this U.S. approval of the first-ever medicine using CRISPR gene editing is breathtaking, and a truly humbling moment for me personally and for the whole organization," said Samarth Kulkarni, Ph.D., Chairman and Chief Executive Officer of CRISPR Therapeutics.

"It has been remarkable to be part of this groundbreaking program," said Stephan Grupp, M.D., Ph.D., Section Chief of the Cellular Therapy and Transplant Section and Director of the Kelly Center for Cancer Immunotherapy at the Children's Hospital of Philadelphia, and Steering Committee Chair for the CLIMB-121 clinical program. "CASGEVY has the potential to be a transformative treatment for patients, and I look forward to continuing the work to ensure eligible patients can access this therapy across the country."

The administration of CASGEVY requires specialized experience in stem cell transplantation; therefore, Vertex is engaging with experienced hospitals to establish a network of independently operated, authorized treatment centers (ATCs) throughout the U.S. to offer CASGEVY to patients. The following ATCs are already activated:

- Boston Medical Center in Boston, Mass.
- Children's National Hospital in Washington, D.C.
- City of Hope Children's Cancer Center in Los Angeles, Calif.
- Medical City Children's Hospital in Dallas, Texas
- Methodist Children's Hospital in San Antonio, Texas
- Nationwide Children's Hospital in Columbus, Ohio
- The Children's Hospital at TriStar Centennial in Nashville, Tenn.
- The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute in Columbus, Ohio
- University of Chicago/Comer Children's Hospital in Chicago, Ill.

Additional ATCs will be activated in the coming weeks and a complete list of ATCs, including updates following approval, can be accessed at CASGEVY.com.

About CASGEVY™ (exagamglogene autotemcel [exa-cel])
CASGEVY is a genome-edited cellular therapy consisting of autologous CD34+ hematopoietic stem cells (HSCs) edited by CRISPR/Cas9 technology at the erythroid-specific enhancer region of the *BCL11A* gene. CASGEVY is intended for one time administration via a hematopoietic stem cell transplant procedure where the patient's own CD34+ cells are modified to reduce

BCL11A expression in erythroid lineage cells, leading to increased fetal hemoglobin (HbF) production. 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 vaso-occlusive crises for patients with SCD.

CASGEVY was granted a conditional marketing authorization in Great Britain by the U.K. Medicines and Healthcare products Regulatory Agency and by the National Health Regulatory Authority in Bahrain for patients 12 years of age and older with SCD characterized by recurrent vaso-occlusive crises or transfusion-dependent beta thalassemia (TDT), for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related hematopoietic stem cell donor is not available. CASGEVY is currently under review by the European Medicines Agency and the Saudi Food and Drug Agency for both SCD and TDT.

The use of CASGEVY for the treatment of TDT in the U.S. remains investigational. Vertex has submitted a BLA to the U.S. FDA for the potential use of CASGEVY for patients 12 years and older with TDT and has been assigned a Prescription Drug User Fee Act (PDUFA) target action date of March 30, 2024.

About the Vertex/CRISPR Collaboration Financial Reporting
Vertex leads global development, manufacturing and commercialization of CASGEVY with support from CRISPR Therapeutics. In conjunction with the FDA approval of CASGEVY, Vertex will make a $200 million milestone payment to CRISPR, which will be capitalized and amortized to cost of sales. Additionally, Vertex will record 100 percent of CASGEVY revenues; costs of sales; and selling, general and administrative expenses and will record CRISPR's 40 percent share in the net profits or losses from CASGEVY within its cost of sales. Lastly, Vertex will record 60 percent of research and development expenses, net of CRISPR's 40 percent share.

About Sickle Cell Disease
Sickle cell disease (SCD) is a debilitating, progressive and life-shortening disease. SCD patients report health-related quality of life scores well below the general population, and the lifetime health care costs in the U.S. of managing SCD for patients with recurrent VOCs is estimated between $4 and $6 million. 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" red blood cells. The clinical hallmark of SCD is VOCs, which are caused by blockages of blood vessels by sickled red blood cells and result in severe and debilitating pain that can happen anywhere in the body at any time. SCD requires a lifetime of treatment and results in a reduced life expectancy. In the U.S., the median age of death for patients living with SCD is approximately 45 years. A cure for SCD today is a stem cell transplant from a matched donor, but this option is only available to a small fraction of patients living with SCD because of the lack of available donors.

Helping Patients on the CASGEVY Journey
Vertex Connects™ is a program for eligible patients in theU.S. who have been prescribed CASGEVY. Through Vertex Connects, Care Managers are available to provide educational resources, communications and support to navigate the treatment journey, and additional assistance is available for eligible patients.

For more information on ATCs, the CASGEVY treatment journey, and Vertex Connects, call 1-833-VERTEX-5 (1-833-837-8395) — and learn more about our patient support program at VertexConnects.com.

U.S. INDICATIONS AND IMPORTANT SAFETY INFORMATION FOR CASGEVY (exagamglogene autotemcel)

CASGEVY is a one-time therapy used to treat people aged 12 years and older with sickle cell disease (SCD) who have frequent vaso-occlusive crises or VOCs.

CASGEVY is made specifically for each patient, using the patient's own edited blood stem cells, and increases the production of a special type of hemoglobin called hemoglobin F (fetal hemoglobin or HbF). Having more HbF increases overall hemoglobin levels and has been shown to improve the production and function of red blood cells. This can eliminate VOCs in people with SCD.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about CASGEVY?
After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections). Your doctor will monitor this and give you treatment as required. The doctor will tell you when blood cell levels return to safe levels.

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of platelet cells:
    - severe headache
    - abnormal bruising

    - prolonged bleeding
    - bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of white blood cells:
    - fever
    - chills
    - infections

You may experience side effects associated with other medicines administered as part of the treatment regimen with CASGEVY. Talk to your physician regarding those possible side effects. Your healthcare provider may give you other medicines to treat your side effects.

How will I receive CASGEVY?
Your healthcare provider will give you other medicines, including a conditioning medicine, as part of your treatment with CASGEVY. It's important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

After receiving the conditioning medicine, it may not be possible for you to become pregnant or father a child. You should discuss options for fertility preservation with your healthcare provider before treatment.

STEP 1: Before CASGEVY treatment, a doctor will give you a mobilization medicine. This medicine moves blood stem cells from your bone marrow into the blood stream. The blood stem cells are then collected in a machine that separates the different blood cells (this is called apheresis). This entire process may happen more than once. Each time, it can take up to one week.

During this step, rescue cells are also collected and stored at the hospital. These are your existing blood stem cells and are kept untreated just in case there is a problem in the treatment process. If CASGEVY cannot be given after the conditioning medicine, or if the modified blood stem cells do not take hold (engraft) in the body, these rescue cells will be given back to you. If you are given rescue cells, you will not have any treatment benefit from CASGEVY.

STEP 2: After they are collected, your blood stem cells will be sent to the manufacturing site where they are used to make CASGEVY. It may take up to 6 months from the time your cells are collected to manufacture and test CASGEVY before it is sent back to your healthcare provider.

STEP 3: Shortly before your stem cell transplant, your healthcare provider will give you a conditioning medicine for a few days in hospital. This will prepare you for treatment by clearing cells from the bone marrow, so they can be replaced with the modified cells in CASGEVY. After you are given this medicine, your blood cell levels will fall to very low levels. You will stay in the hospital for this step and remain in the hospital until after the infusion with CASGEVY.

STEP 4: One or more vials of CASGEVY will be given into a vein (intravenous infusion) over a short period of time.

After the CASGEVY infusion, you will stay in hospital so that your healthcare provider can closely monitor your recovery. This can take 4-6 weeks, but times can vary. Your healthcare provider will decide when you can go home.

What should I avoid after receiving CASGEVY?

- Do not donate blood, organs, tissues, or cells at any time in the future

What are the possible or reasonably likely side effects of CASGEVY?
The most common side effects of CASGEVY include:

- Low levels of platelet cells, which may reduce the ability of blood to clot and may cause bleeding
- Low levels of white blood cells, which may make you more susceptible to infection

Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells). Tell your healthcare provider right away if you get any of the following symptoms:

- fever
- chills
- infections
- severe headache
- abnormal bruising
- prolonged bleeding

- bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CASGEVY
Talk to your healthcare provider about any health concerns.

Please see full Prescribing Information including Patient Information for CASGEVY.

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.

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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 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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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 Stephan Grupp, M.D., Ph.D., and statements regarding the anticipated patient population eligible for CASGEVY in the U.S., expectations for the potential benefits of CASGEVY, expectations that additional ATCs will be activated in the coming weeks, Vertex's plan to make milestone payments to CRISPR, and Vertex's anticipated accounting treatment for milestone payments, anticipated revenue, the cost of sales, expenses, and net profits or losses related to CASGEVY. 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 or other reasons, that obtaining approval for and commercializing CASGEVY in Europe and the Kingdom of Saudi Arabia may not occur on the anticipated timeline, or at all, and other risks listed under the heading "Risk Factors" in Vertex's most recent annual report and subsequent filings 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.

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 Reshma Kewalramani, M.D., Samarth Kulkarni, Ph.D., and Stephan Grupp, M.D., Ph.D., in this press release, as well as statements regarding CRISPR Therapeutics': (i) plans and expectations for the commercialization of, and anticipated benefits of, CASGEVY, including the anticipated patient population eligible for CASGEVY in the United States and patient access to CASGEVY; (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) receipt of the milestone payment from 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 approval or renewal of conditional authorization; regulatory approval in other jurisdictions may not occur on anticipated timelines or at all; adequate pricing or reimbursement may not be secured to support continued development or commercialization of exa-cel following regulatory approval; 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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Source: Vertex Pharmaceuticals Incorporated