# Vertex Receives CHMP Positive Opinion for the First CRISPR/Cas9 Gene-Edited Therapy, CASGEVY™ (exagamglogene autotemcel), for the Treatment of Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia

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*- If approved by the European Commission, patients 12 years of age and older with severe sickle cell disease or transfusion-dependent beta thalassemia, for whom hematopoietic stem cell transplantation is appropriate and a human leukocyte antigen matched related donor is not available, would be eligible for treatment -*

*- Approval decision from the European Commission is expected in Q1 2024 -*

BOSTON--(BUSINESS WIRE)--Dec. 15, 2023-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today that the European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for the conditional approval of CASGEVY ™ (exagamglogene autotemcel [exa-cel]), a CRISPR/Cas9 gene-edited therapy, for the treatment of severe sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT).

If approved, exa-cel would be the only genetic therapy for patients in the European Union who are 12 years of age and older with either severe SCD with recurrent vaso-occlusive crises (VOCs) or TDT, for whom hematopoietic stem cell (HSC) transplantation is appropriate and a human leukocyte antigen matched related HSC donor is not available. An approval decision by the European Commission is expected in February 2024.

"This positive opinion is yet another important regulatory milestone underscoring the potentially transformative benefit of CASGEVY for eligible patients with sickle cell and transfusion-dependent beta thalassemia," said Nia Tatsis, Ph.D., Executive Vice President and Chief Regulatory and Quality Officer at Vertex.

"There is an urgent need for new potentially curative treatments in beta thalassemia and sickle cell disease, as people with these diseases still have a shorter life expectancy than the general population and an impaired quality of life," said Franco Locatelli, M.D., Ph.D., Principal investigator in the CLIMB-111 and CLIMB-121 studies, Professor of Pediatrics at the Catholic University of the Sacred Heart, Rome, and Director of the Department of Pediatric Hematology and Oncology at the Bambino Gesù Children's Hospital. "As an investigator, I have witnessed first-hand the transformative impact exa-cel can have on patients' lives and I eagerly await the approval in the European Union."

**About Sickle Cell Disease (SCD)**

SCD is a debilitating, progressive, life shortening genetic disease. SCD patients report health-related quality of life scores well below the general population and significant health care resource utilization. SCD 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 vaso-occlusive crises (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 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 Europe, the mean age of death for patients living with SCD is around 40 years. Stem cell transplant from a matched donor is a curative option but is only available to a small fraction of people living with SCD because of the lack of available donors.

**About Transfusion-Dependent Beta Thalassemia (TDT)**

TDT is a serious, life-threatening genetic disease. TDT patients report health-related quality of life scores below the general population and significant health care resource utilization. TDT requires frequent blood transfusions and iron chelation therapy throughout a person's life. Due to anemia, patients living with TDT may experience fatigue and shortness of breath, and infants may develop failure to thrive, jaundice and feeding problems. Complications of TDT can also include an enlarged spleen, liver and/or heart, misshapen bones and delayed puberty. TDT 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 Europe, the mean age of death for patients living with TDT is 50-55 years. Stem cell transplant from a matched donor is a curative option but is only available to a small fraction of people living with TDT because of the lack of available donors.

**About CASGEVY™ (exagamglogene autotemcel [exa-cel])**

CASGEVY™ is a non-viral,*ex vivo* CRISPR/Cas9 gene-edited cell therapy for eligible patients with SCD or TDT, in which a patient's own hematopoietic stem and progenitor cells are edited at the erythroid specific enhancer region of the *BCL11A* gene through a precise double-strand break. This edit results in the production of high levels of fetal hemoglobin (HbF; hemoglobin F) in red blood cells. 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 VOCs for patients with SCD and alleviate transfusion requirements for patients with TDT.

The use of CASGEVY in the European Union remains investigational.

CASGEVY is approved in the U.S. to treat people aged 12 years and older with SCD who have recurrent VOCs. CASGEVY was granted a conditional marketing authorization in Great Britain by the U.K. Medicines and Healthcare products Regulatory Agency for patients 12 years of age and older with SCD characterized by recurrent VOCs or 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 Saudi Food and Drug Authority for both SCD and TDT and the U.S. Food and Drug Administration for TDT.

**About Conditional Marketing Authorizations (CMAs)**

CMAs are for medicines that fulfil 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 the benefit of the medicine to address a significant unmet need outweighs the need for data that will become available in the future. CMAs are valid for one year and renewable annually with ongoing regulatory review of data.

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

**WHAT IS CASGEVY?**

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 cause of multiple chronic, life-shortening genetic diseases — cystic fibrosis, sickle cell disease and transfusion-dependent beta thalassemia — and continues to advance clinica 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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**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, statements made by Nia Tatsis, Ph.D., and Franco Locatelli, M.D., Ph.D., in this press release and statements regarding our expectations for regulatory approval for CASGEVY ™, including anticipated timing of approval, the anticipated population eligible for treatment, our expectation that, if approved, CASGEVY will be the only genetic therapy available for eligible patients in the European Union, and our beliefs regarding the benefits of our genetic therapy. 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 regulatory authorities may not approve CASGEVY on a timely basis or at all, and other risks listed under the heading “Risk Factors” in Vertex's annual report and in subsequent filings filed with the Securities and Exchange Commission and available through the company's website at www.vrtx.com and www.sec.gov. 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.

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