Vertex Presents Positive Long-Term Data On CASGEVY™ (exagamglogene autotemcel) at the 2024 Annual European Hematology Association (EHA) Congress

June 14, 2024

- Results from CLIMB-111, -121 and -131 accepted for oral presentation -

- Data from these trials, with the longest follow-up of more than five years, demonstrate transformative, consistent and durable benefit of CASGEVY™ -

- Safety profile consistent with busulfan conditioning and autologous hematopoietic stem cell transplant -

BOSTON--(BUSINESS WIRE)--Jun. 14, 2024-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced longer-term data for CASGEVY™ (exagamglogene autotemcel [exa-cel]) from global clinical trials in people with severe sickle cell disease (SCD) or transfusion-dependent beta thalassemia (TDT). The results, presented at the annual European Hematology Association (EHA) Congress, confirm the transformative, consistent and durable clinical benefits of CASGEVY over time. CASGEVY is the first and only approved CRISPR-based gene-editing therapy.

The data being presented are from more than 100 patients (46 SCD; 56 TDT) treated with exa-cel in clinical trials, with the longest follow-up now extending more than 5 years. The efficacy results are consistent with the previously reported primary and key secondary endpoints analyses from these exa-cel studies and continue to demonstrate transformative clinical benefit with durable and stable levels of fetal hemoglobin (HbF) and allelic editing.

“The transformative benefit seen in patients with sickle cell disease in the trial is impressive given the significant and cumulative burden of disease faced by people living with this blood disorder,” said Haydar Frangoul, M.D., M.S., Medical Director of Pediatric Hematology and Oncology at Sarah Cannon Research Institute and HCA Healthcare’s TriStar Centennial Children’s Hospital. “I am eager to offer this therapy and the opportunity of a potential functional cure to my eligible patients.”

“The comprehensive data set presented today for adult and adolescent TDT patients adds to the growing body of evidence for CASGEVY, and it is important to now ensure the availability of this innovative treatment to patients in the real world as soon as possible,” said Franco Locatelli, M.D., Ph.D., Professor of Pediatrics at the Catholic University of the Sacred Heart of Rome, Director of the Department of Pediatric Hematology and Oncology at Bambino Gesù Children’s Hospital. “With the longest follow up now more than five years, alongside stable editing and sustained fetal hemoglobin levels, I have conviction in the durable benefit to the patients treated with CASGEVY.”

New data presented from CASGEVY pivotal trials

- In SCD 36/39 (92.3%) evaluable patients (those with at least 16 months of follow-up) were free from vaso-occlusive crises (VOCs) for at least 12 consecutive months (VF12), consistent with the previously reported primary endpoint data. Mean duration of VOC-free was 27.9 months, with a maximum of 54.8 months.
    - 38/39 (97.4%) patients with at least 16 months of follow-up were free from hospitalizations related to VOCs for at least 12 consecutive months (HF12), consistent with the previously reported key secondary endpoint data.
- In TDT 49/52 (94.2%) evaluable patients (those with at least 16 months of follow-up) were transfusion-independent for at least 12 consecutive months with a mean weighted hemoglobin of at least 9 g/dL (TI12), consistent with the previously reported primary endpoint data. Mean duration of transfusion independence was 31.0 months, with a maximum of 59.4 months.
- All TDT patients dosed with at least 16 months of follow up are transfusion free.
    - Two of the three patients who did not achieve TI12 in CLIMB-111 achieved TI12 in the long-term follow-up study, CLIMB-131, and have been transfusion independent for over one year. The third has been transfusion free for 3.4 months.
- Both SCD and TDT patients reported sustained and clinically meaningful improvements in their quality of life, including physical, emotional, social/family and functional well-being, and overall health status.

In both SCD and TDT patients, edited levels of *BCL11A* alleles were stable over time in bone marrow and peripheral blood indicating successful editing in the long-term hematopoietic stem cells. All patients engrafted neutrophils and platelets after exa-cel infusion. The safety profile of exa-cel was generally consistent with myeloablative conditioning with busulfan and autologous hematopoietic stem cell transplant.

These longer-term data for CASGEVY from the CLIMB clinical trials will be shared as outlined below:

- Abstracts S273 and S274 will be oral presentations entitled “Exagamglogene Autotemcel For Severe Sickle Cell Disease,” and “Exagamglogene Autotemcel For Transfusion-Dependent Beta-Thalassemia,” on Sunday, June 16 at 12:15 CEST and 12:30 CEST, respectively.
- Abstracts P1493 and P1525 will be poster presentations entitled “Health-Related Quality Of Life Improvements After Exagamglogene Autotemcel In Patients With Severe Sickle Cell Disease,” and “Health-Related Quality Of Life Improvements After Exagamglogene Autotemcel In Patients With Transfusion-Dependent Beta-Thalassemia,” on Friday,

June 14 at 18:00 CEST.

- These presentations will include updated pivotal trial data from patients treated with CASGEVY in CLIMB-111 and CLIMB-121 and followed in CLIMB-131.

Vertex will also share five health economics abstracts at the EHA Congress.

1. Abstract P1483 is entitled “Adherence, Treatment Use, and Clinical Outcomes in Patients With Sickle Cell Disease With Recurrent Vaso-Occlusive Crises Treated With L-Glutamine, Voxelotor, or Crizanlizumab in the United States.”
2. Abstract P1506 is entitled “Mortality and Clinical Complications Among Patients with Sickle Cell Disease With Recurrent VOCs in Canada.”
3. Abstract P1507 is entitled “Treatment Utilization and Clinical Complications in Patients with Sickle Cell Disease Receiving Frequent Red Blood Cell Transfusions in the United States.”
4. Abstract P2191 is entitled “Clinical Complications and Treatment Use Among Patients With Sickle Cell Disease With Recurrent Vaso-Occlusive Crises in the Netherlands.”
5. Abstract PB3248 is entitled “Clinical Complications Among Patients With Transfusion-Dependent Beta-Thalassemia in the Netherlands.”

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 potentially 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 potentially 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 transfusion requirements for patients with TDT.

CASGEVY is approved for certain indications in multiple jurisdictions for eligible patients.

About the CLIMB Studies

The ongoing Phase 1/2/3 open-label trials, CLIMB-111 and CLIMB-121, are designed to assess the safety and efficacy of a single dose of CASGEVY in patients ages 12 to 35 years with TDT or with SCD, characterized by recurrent VOCs, respectively. The trials are now closed for enrollment. Patients will be followed for approximately two years after CASGEVY infusion. Each patient will be asked to participate in the ongoing long-term, open-label trial, CLIMB-131. CLIMB-131 is designed to evaluate the safety and efficacy of CASGEVY in patients who received CASGEVY in other CLIMB studies. The trial is designed to follow patients for up to 15 years after CASGEVY infusion.

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
- beta thalassemia (β-thalassemia) who need regular blood transfusions

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 sickle cell disease and eliminate the need for regular blood transfusions in people with beta thalassemia.

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 for 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 mobilization medicine(s). 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 acute and neuropathic pain, APOL1-mediated kidney disease, IgA nephropathy, autosomal dominant polycystic kidney disease, type 1 diabetes, myotonic dystrophy type 1 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, Latin America and the Middle East. 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, 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, the statements by Haydar Frangoul, M.D., M.S., and Franco Locatelli, M.D., Ph.D., in this press release, and statements regarding our expectations for and the anticipated benefits of CASGEVY, our plans to share longer-term data for CASGEVY from the CLIMB clinical trials and to share health economics abstracts at the EHA Congress, and our plans for and design of the CLIMB studies. While we believe 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, 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, or the scientific data presented. Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

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Vertex Pharmaceuticals Incorporated

Investors:
InvestorInfo@vrtx.com

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

Source: Vertex Pharmaceuticals Incorporated