Phase 2/3 Interim Data Evaluating the Safety, Tolerability and Clinical Outcomes of Veklury® (Remdesivir) in Pediatric Patients With COVID-19 Presented at CROI 2022

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FOSTER CITY, Calif.--(BUSINESS WIRE)--Feb. 11, 2022--Gilead Sciences, Inc. (Nasdaq: GILD) today announced new data from an interim analysis of its ongoing, Phase 2/3 single arm, open-label study to evaluate the safety, tolerability and pharmacokinetics of Veklury® (remdesivir) in pediatric patients hospitalized with COVID-19 with ages ranging from 28 days to less than 18 years. This data will be presented at the 29th Conference on Retroviruses and Opportunistic Infections (virtual CROI 2022) taking place from February 12-16.

These latest data demonstrate that Veklury was generally well tolerated among pediatric patients hospitalized with COVID-19 with a high proportion of participants showing clinical improvement and recovery. Overall, no new safety findings for Veklury were noted, and 85% of patients showed clinical improvement based on the clinical ordinal scale and the recovery rate was 83% at last assessment (N=53).

“More children are being hospitalized with COVID-19 than ever before, and up to a third of them require admission to intensive care units. We need antiviral options that can help children recover faster and leave the hospital sooner,” said Amina Ahmed, MD, FAPP, epidemiologist and professor of infectious disease at Atrium Health’s Levine Children’s Hospital, North Carolina, U.S. “These interim findings from the CARAVAN study are encouraging, showing that remdesivir was generally well tolerated among children under the age of 18. Remdesivir can potentially provide meaningful clinical improvement, by reducing disease severity and returning children home to their families more quickly.”

The primary objective of this study was to evaluate the safety, tolerability, and pharmacokinetics of Veklury in pediatric patients, as assessed by the proportion of participants experiencing treatment-emergent adverse events; proportion of participants experiencing treatment-emergent graded laboratory abnormalities; and plasma concentrations of Veklury and metabolites, respectively. Safety was assessed by adverse events (AEs) and lab tests (hematology, chemistry, urine, inflammatory, coagulation). Clinical outcomes included improvement on a 7-point ordinal scale, time to discharge, and oxygenation modality. Virologic outcomes included days to confirmed negative SARS-CoV-2 PCR (defined as 2 consecutive negative results).

In this study of 53 pediatric patients across five cohorts grouped by age (median age 7 years [2,12]) with more than half (57%) being on high-flow oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) at baseline. Of the 53 pediatric patients enrolled in the study, no new safety signals were apparent for Veklury. Overall, 38 patients (72%) experienced AEs, with 11 patients (21%) experiencing serious adverse events (SAEs) that were determined not to be study-drug related, including 3 participant deaths which were consistent with the patients’ underlying medical conditions prior to study entry or with COVID-19 disease during hospitalization. Children weighing at least 40kg were in cohorts 1 and 8 and received 200mg on Day 1 followed by 100mg daily. Infants and children weighing 3kg to less than 40kg were in cohorts 2-4 and received weight-based dosing of 5mg/kg on Day 1 followed by 2.5mg/kg daily. In the analysis, the most common adverse event in patients taking Veklury was constipation (17%), followed by acute kidney injury (11%), hyperglycemia (9%) and pyrexia (9%). Additionally, 8% of participants had an increase in alanine transaminase (ALT).

“This interim data highlights the possible benefits of Veklury for children with COVID-19, showing that Veklury was generally well-tolerated, may help to prevent disease progression and has the potential to help children to recover faster,” said Anu Osinusi, Vice President, Clinical Research, Hepatitis, Respiratory and Emerging Viruses at Gilead Sciences. “Gilead remains committed to supporting the most vulnerable patients and continues to pursue multiple approaches to address the evolving unmet needs of patients with COVID-19.”

On January 21, 2022, the U.S. Food and Drug Administration (FDA) expanded the pediatric Emergency Use Authorization (EUA) of Veklury to include non-hospitalized pediatric patients weighing at least 3.5 kg who are younger than 12 years of age or weighing less than 40 kg who are at high risk of disease progression, in addition to those with COVID-19 requiring hospitalization. Gilead has submitted this interim data to the FDA, EMA and other regulatory agencies. The use of Veklury in pediatric patients younger than 12 years of age or weighing less than 40 kg is investigational and Veklury is not approved by the FDA for this use. Please see below for more information on the approved use of Veklury and the EUA for pediatric patients.

About the CARAVAN Study (GS-US-540-5823)

Study GS-US-540-5823 (CARAVAN) is a Phase 2/3 single arm, open-label study evaluating the safety, tolerability and pharmacokinetics of remdesivir in participants from birth to <18 years of age hospitalized with COVID-19. The primary study endpoints are the proportion of participants experiencing treatment-emergent adverse events; proportion of participants experiencing treatment-emergent graded laboratory abnormalities; and plasma concentrations of remdesivir and metabolites, respectively. The 10 secondary endpoints include: change from baseline in oxygenation use; change from baseline in the use of mechanical ventilation or extracorporeal membrane oxygenation (ECMO); assessment of clinical improvement based on scoring using the 7-point ordinal scale; and time (days) to discharge from hospital.

About Veklury

Veklury (remdesivir) is a nucleotide analog invented by Gilead, building on more than a decade of the company’s antiviral research. Veklury is the antiviral standard of care for the treatment of hospitalized patients with COVID-19 and is a recommended treatment for reducing disease progression in non-hospitalized patients at high risk of disease progression. At this time, more than half of patients hospitalized with COVID-19 in the United States are treated with Veklury. It can help reduce disease progression across a spectrum of disease severity and enable patients to recover faster, freeing up limited hospital resources and saving healthcare systems money.

Veklury was approved by the FDA on October 22, 2020 for adults and pediatric patients 12 years of age and older and weighing at least 40 kg for the treatment of COVID-19 requiring hospitalization. On January 21, 2022, the FDA approved a supplemental new drug application (sNDA) for Veklury to expand the indication to the treatment of non-hospitalized adult and adolescent patients who are at high risk of progression to severe COVID-19 including hospitalization or death. The expanded indication allows for Veklury to be administered in qualified outpatient settings that can administer daily intravenous (IV) infusions over three consecutive days. The FDA also expanded the pediatric Emergency Use Authorization (EUA) of Veklury to include non-hospitalized pediatric patients weighing at least 3.5 kg who are younger than 12 years of age or weighing less than 40 kg who are at high risk of disease progression based on the clinical ordinal scale and the recovery rate was 83% at last assessment (N=53).
risk of disease progression, in addition to those with COVID-19 requiring hospitalization. Veklury is contraindicated in patients who are allergic to Veklury or any of its components; please see below for additional Important Safety Information for Veklury.

Veklury directly inhibits viral replication inside of the cell by targeting the SARS-CoV-2 viral RNA polymerase. On entering the body Veklury is transformed into the active metabolite remdesivir triphosphate, which is then incorporated into the viral RNA and stops replication of the virus within the host cell. As new SARS-CoV-2 variants of concern emerge around the world, Gilead continuously evaluates the effectiveness of Veklury against viral variants. In vitro laboratory testing in multiple independent studies shows that Veklury retains activity against the Omicron variant. To date, no major genetic changes have been identified in any of the known variants of concern that would significantly alter the viral RNA polymerase targeted by Veklury. Gilead continues to experimentally evaluate the activity of Veklury against identified SARS-CoV-2 variants through in vitro antiviral testing. Veklury's antiviral activity has been confirmed in vitro against all major previously identified variants of SARS-CoV-2 including Alpha, Beta, Gamma, Delta, Epsilon, and Omicron.

Veklury is approved or authorized for temporary use in approximately 50 countries worldwide. To date, Veklury and generic remdesivir have been made available to more than 10 million patients around the world, including nearly 7 million people in 127 middle- and low-income countries through Gilead’s voluntary licensing program. These licenses currently remain royalty-free, reflecting Gilead’s existing commitment to enabling broad patient access to remdesivir.

U.S. Indication for Veklury

Veklury® (remdesivir 100 mg for injection) is indicated for the treatment of COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, who are:

- Hospitalized, or
- Not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.

Veklury should only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion or hypersensitivity reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary. Veklury must be administered by intravenous infusion. Veklury is contraindicated in patients who are allergic to Veklury or any of its components. For more information, please see the U.S. full Prescribing Information available at www.gilead.com.

U.S. Important Information for Veklury Emergency Use for Pediatric Patients

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of Veklury for the treatment of COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg with positive results of direct SARS-CoV-2 viral testing, who are:

- Hospitalized, or
- Not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.

Veklury has been authorized by FDA for these emergency uses. Veklury is not FDA-approved for these uses. Veklury is authorized for these uses only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of Veklury unless the authorization is terminated or revoked sooner.

The only authorized dosage form of Veklury for use in pediatric patients under the EUA is Veklury 100 mg for injection, supplied as a lyophilized powder. For information about the authorized use of Veklury, including dosage and administration instructions for pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg, please see the Fact Sheet for Healthcare Providers, available here.

U.S. Important Safety Information for Veklury

Contraindication

Veklury is contraindicated in patients with a history of clinically significant hypersensitivity reactions to Veklury or any of its components.

Warnings and precautions

- Hypersensitivity, including infusion-related and anaphylactic reactions: Hypersensitivity, including infusion-related and anaphylactic reactions, has been observed during and following administration of Veklury; most occurred within one hour. Monitor patients during infusion and observe for at least one hour after infusion is complete for signs and symptoms of hypersensitivity as clinically appropriate. Symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering. Slower infusion rates (maximum infusion time up to 120 minutes) can potentially prevent these reactions. If a severe infusion-related hypersensitivity reaction occurs, immediately discontinue Veklury and initiate appropriate treatment (see Contraindications).
- Increased risk of transaminase elevations: Transaminase elevations have been observed in healthy volunteers and in patients with COVID-19 who received Veklury; these elevations have also been reported as a clinical feature of COVID-19. Perform hepatic laboratory testing in all patients (see Dosage and administration). Consider discontinuing Veklury if ALT levels increase to >10x ULN. Discontinue Veklury if ALT elevation is accompanied by signs or symptoms of liver inflammation.
- Risk of reduced antiviral activity when coadministered with chloroquine or hydroxychloroquine: Coadministration of Veklury
with chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on data from cell culture experiments, demonstrating potential antagonism, which may lead to a decrease in antiviral activity of Veklury.

Adverse reactions

- The most common adverse reaction (≥5% all grades) was nausea.
- The most common lab abnormalities (≥5% all grades) were increases in ALT and AST.

Drug interactions

- Drug interaction trials of Veklury and other concomitant medications have not been conducted in humans.

Dosage and administration

- Dosage: For adults and pediatric patients ≥12 years old and weighing ≥40 kg: 200 mg on Day 1, followed by once-daily maintenance doses of 100 mg from Day 2 administered only via intravenous infusion. Veklury should be initiated as soon as possible after diagnosis of symptomatic COVID-19.
- Treatment duration:
  - For hospitalized patients requiring invasive mechanical ventilation and/or ECMO, the recommended total treatment duration is 10 days.
  - For hospitalized patients not requiring invasive mechanical ventilation and/or ECMO, the recommended treatment duration is 5 days. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days for a total treatment duration of up to 10 days.
  - For non-hospitalized patients diagnosed with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death, the recommended total treatment duration is 3 days.
- Testing prior to and during treatment: Perform eGFR, hepatic laboratory, and prothrombin time testing prior to initiating Veklury and during use as clinically appropriate.
- Renal impairment: Veklury is not recommended in individuals with eGFR <30 mL/min.
- Dose preparation and administration: See full Prescribing Information.

Pregnancy and lactation

- Pregnancy: A pregnancy registry has been established. There are insufficient human data on the use of Veklury during pregnancy. COVID-19 is associated with adverse maternal and fetal outcomes, including preeclampsia, eclampsia, preterm birth, premature rupture of membranes, venous thromboembolic disease, and fetal death.
- Lactation: It is not known whether Veklury can pass into breast milk. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Adverse Event Reporting

For use under the EUA, healthcare providers and/or their designee are responsible for mandatory FDA MedWatch reporting of all serious adverse events and medication errors potentially related to Veklury within 7 calendar days from the healthcare provider’s awareness of the event. Healthcare providers are additionally encouraged to report adverse events occurring under the approved use of Veklury. MedWatch adverse event reports can be submitted to FDA online at www.fda.gov/medwatch or by calling 1-800-FDA-1088.

About Gilead Sciences

Gilead Sciences, Inc. is a biopharmaceutical company that has pursued and achieved breakthroughs in medicine for more than three decades, with the goal of creating a healthier world for all people. The company is committed to advancing innovative medicines to prevent and treat life-threatening diseases, including HIV, viral hepatitis and cancer. Gilead operates in more than 35 countries worldwide, with headquarters in Foster City, California.

Forward-Looking Statements

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the possibility of unfavorable results from ongoing or additional clinical trials involving Veklury; Gilead’s ability to initiate, progress or complete clinical trials within currently anticipated timelines or at all, including those involving Veklury; Gilead’s ability to receive regulatory approvals in a timely manner or at all, including additional regulatory approvals of Veklury, and the risk that any such approvals, if granted, may be subject to significant limitations on use; and any assumptions underlying any of the foregoing. These and other risks, uncertainties and factors are described in detail in Gilead’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, as filed with the U.S. Securities and Exchange Commission. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. The reader is cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties and is cautioned not to place undue reliance on these forward-looking statements. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation and disclaims any intent to update any such forward-looking statements.

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