New Phase 3 Data Support the Sustained, Long-Acting Efficacy of Lenacapavir, Gilead's Investigational HIV-1 Capsid Inhibitor

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– Week 26 Data From the CAPELLA Trial Show Lenacapavir Leads to High Rates of Virologic Suppression in Heavily Treatment-Experienced People Living With Multi-Drug Resistant HIV –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Jul. 17, 2021-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced new results from the ongoing Phase 2/3 CAPELLA trial evaluating lenacapavir, the company's investigational, long-acting HIV-1 capsid inhibitor, in heavily treatment-experienced people living with multi-drug resistant HIV. The findings demonstrate that lenacapavir, administered subcutaneously every six months in combination with other antiretrovirals, achieved high rates of virologic suppression at Week 26 in people living with HIV whose virus was no longer effectively responding to therapy. In this patient population of high unmet medical need, 81% (n=29/36) of participants receiving lenacapavir in addition to an optimized background regimen achieved an undetectable viral load (<50 copies/mL) at Week 26. The data were presented at the 11th International AIDS Society (IAS) Conference on HIV Science.

These data support the ongoing evaluation of lenacapavir for the treatment of HIV-1 infection and form the basis of the New Drug Application (NDA) that the company recently submitted seeking U.S. Food & Drug Administration (FDA) approval for the treatment of HIV-1 infection in heavily treatment-experienced people with multi-drug resistant HIV-1 infection in combination with other antiretrovirals. If approved, lenacapavir would be the first capsid inhibitor and the only HIV-1 treatment option administered every six months.

“Despite the advances in treating HIV infection, there remains an unmet need for treatment options for people who struggle with multi-drug resistance. As a physician, it’s frustrating to have limited options for these patients who are at greater risk of progressing to AIDS,” said Jean-Michel Molina, MD, University of Paris, Professor of Infectious Diseases and Head of the Infectious Diseases Department at the Saint-Louis and Lariboisière Hospitals. “The CAPELLA results are exciting as they demonstrate that an undetectable viral load is achievable in a patient population that has typically had challenges with viral suppression over the course of their journey living with HIV. New, long-acting options in development, like lenacapavir, are critical to changing the clinical landscape, and I’m encouraged that lenacapavir can potentially help improve clinical outcomes.”

Lenacapavir is being developed in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing at least 35 kg with multi-drug resistant HIV-1 infection who are currently on a failing antiretroviral treatment regimen due to resistance, intolerance or safety considerations. Lenacapavir is a potentially first-in-class capsid inhibitor without overlapping resistance with any currently approved antiretroviral therapy (ART). Lenacapavir is designed to inhibit HIV replication by interfering with multiple, essential steps of the viral lifecycle, including capsid-mediated uptake of HIV-1 proviral DNA, virus assembly and release, and capsid core formation. In May 2019, the FDA granted Breakthrough Therapy Designation for the development of lenacapavir for the treatment of HIV-1 infection in heavily treatment-experienced patients with multi-drug resistance in combination with other antiretroviral drugs.

“Lenacapavir is a breakthrough innovation in HIV research. If approved, it has the potential to become a cornerstone of future long-acting HIV regimens,” said Frank Duff, Senior Vice President, Virology Therapeutic Area Head, Gilead Sciences. “Scientific advances are a key to helping end the HIV epidemic. Our researchers are committed to addressing the unmet needs of people living with HIV, including the exploration of different dosing intervals that may coincide with regularly scheduled visits with healthcare providers.”

In addition to 81% of CAPELLA participants achieving an undetectable viral load at Week 26, participants achieved a mean increase in CD4 count of 81 cells/µL. In the data presented at the *virtual* 28th Conference on Retroviruses and Opportunistic Infections (*virtual* CROI 2021), the CAPELLA trial achieved its primary endpoint by demonstrating that a significantly higher proportion of participants randomly allocated to receive lenacapavir (n=24) achieved a clinically meaningful viral load reduction of at least 0.5 $\log_{10}$ copies/mL from baseline compared with those randomly allocated to receive placebo (n=12) during the 14-day functional monotherapy period (88% vs. 17%, p<0.0001). Those who received lenacapavir achieved a statistically significantly greater mean decrease in viral load than those who received placebo during the functional monotherapy period (-1.93 $\log_{10}$ copies/mL vs. -0.29 $\log_{10}$ copies/mL, p<0.0001).

Lenacapavir was generally well tolerated, with no adverse events (AEs) leading to study drug discontinuation and no serious adverse events related to lenacapavir. The most common adverse events observed to date in the CAPELLA study were injection site reactions, which were mostly mild in severity. The most common injection site reactions were injection site swelling (26%) and erythema (24%). Four participants experienced treatment-emergent lenacapavir resistance and three of these four participants later re-suppressed while continuing lenacapavir in addition to their optimized background regimen. One participant did not re-suppress.

Gilead presented additional lenacapavir clinical development program data at the conference. Phase 2 data from CALIBRATE, an ongoing, open-label, active-controlled trial in treatment-naïve people with HIV-1 infection showed lenacapavir, given subcutaneously or orally, in combination with oral daily emtricitabine/tenofovir alafenamide (F/TAF) led to high rates of viral suppression by Week 28 (94%; n=147/157). Specifically, in the pooled subcutaneous lenacapavir + F/TAF arms, 93% (n=98/105) achieved an undetectable viral load (<50 copies/mL). In the oral lenacapavir + F/TAF arm, 94% (n=49/52) achieved an undetectable viral load (<50 copies/mL). These results support the ongoing evaluation and further development of lenacapavir in combination with other long-acting partner agents for the treatment of HIV-1 infection and will support Gilead’s long-acting oral and injectable development program.

Lenacapavir was generally well tolerated. The most common AEs observed to date in the CALIBRATE study among those who received subcutaneous lenacapavir were injection site reactions, which were generally mild in severity. The most common injection site reactions were injection site swelling (18%) and erythema (17%). Importantly, there were no serious AEs related to study drug. Two participants discontinued due to AEs (both due to mild injection site induration). One participant had treatment-emergent resistance to study drugs.

Lenacapavir is an investigational compound and is not approved by any regulatory authority for any use and its safety and efficacy are not established.

There is no cure for HIV or AIDS.

About CAPELLA (NCT04150068)

CAPELLA is a Phase 2/3, double-blinded, placebo-controlled global multicenter study designed to evaluate the antiviral activity of Gilead's investigational, long-acting HIV-1 capsid inhibitor lenacapavir administered every six months as a subcutaneous injection in heavily treatment-experienced people with multi-drug resistant HIV-1 infection. CAPELLA includes men and women living with HIV-1 and is being conducted at research centers in North America, Europe and Asia.

In CAPELLA, 36 participants with multi-class HIV-1 drug resistance and a detectable viral load while on a failing regimen were randomly allocated to receive oral lenacapavir or placebo in a 2:1 ratio for 14 days, in addition to continuing their failing regimen (functional monotherapy). An additional 36 participants were enrolled in a separate treatment cohort. Both cohorts are part of the ongoing maintenance period of the study evaluating the safety and efficacy of subcutaneous lenacapavir administered every six months in combination with an optimized background regimen. The primary endpoint was the proportion of participants randomly allocated to receive lenacapavir or placebo for 14 days, in addition to continuing their failing regimen, achieving ≥0.5 $\log_{10}$ copies/mL reduction from baseline in HIV-1 RNA at the end of the functional monotherapy period.

Following the 14-day functional monotherapy period, participants randomly allocated to receive lenacapavir or placebo, in addition to continuing their failing regimen, started open-label lenacapavir and an optimized background regimen, while those enrolled in a separate treatment cohort received open-label lenacapavir and an optimized background regimen on Day 1. This ongoing maintenance period of the study is evaluating the additional trial endpoints of safety and efficacy of subcutaneous lenacapavir administered every six months in combination with an optimized background regimen.

For further information, please see https://clinicaltrials.gov/ct2/show/NCT04150068.

About CALIBRATE (NCT04143594)

CALIBRATE is an ongoing, phase 2, open-label, active-controlled study in treatment-naïve people with HIV-1 infection designed to evaluate the efficacy and safety profile of lenacapavir-containing regimens. CALIBRATE includes men and women living with HIV-1 and is being conducted at research centers in North America, Puerto Rico and the Dominican Republic.

In CALIBRATE, 182 participants were randomly allocated (2:2:2:1) into one of the four treatment groups. The first and second groups received subcutaneous lenacapavir every 26 weeks following an oral lead-in period together with oral daily emtricitabine/tenofovir alafenamide (F/TAF); at Week 28, those achieving HIV-1 RNA viral load <50 copies/mL switched their F/TAF to oral daily TAF or bictegravir, while continuing lenacapavir. The third group received oral daily lenacapavir with F/TAF. The fourth group received oral daily bictegravir/F/TAF (B/F/TAF). The primary endpoint of the study is the proportion of participants achieving a viral load of <50 c/mL at Week 54. Lenacapavir was generally well tolerated, with no study drug-related serious AEs. The most common AEs observed were injection site reactions, which were generally mild in severity.

For further information, please see https://clinicaltrials.gov/ct2/show/NCT04143594.

About Lenacapavir

Lenacapavir is a potential first-in-class, long-acting HIV-1 capsid inhibitor in development for the treatment and prevention of HIV-1 infection. Lenacapavir's multi-stage mechanism of action is distinguishable from currently approved classes of antiviral agents and is designed to provide a new avenue for the development of long-acting therapy options for people living with or at risk for HIV-1. While most antivirals act on just one stage of viral replication, lenacapavir is designed to inhibit HIV-1 at multiple stages of its lifecycle and has no known cross resistance to other existing drug classes.

The safety and efficacy of lenacapavir are being evaluated in multiple ongoing clinical studies. Data presented at AIDS 2020 from a Phase 1 study support further evaluation of lenacapavir administered subcutaneously every six months for both HIV-1 treatment and prevention. During June 2021, the company initiated the first of its two planned prevention trials evaluating the use of lenacapavir as an injectable PrEP option administered every six months among cisgender men, gender non-binary individuals and persons of trans experience who have sex with men. The prevention trial among cisgender adolescent girls and young women is projected to commence later this summer.

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.

For more than 30 years, Gilead has been a leading innovator in the field of HIV, driving advances in treatment, prevention and cure research. Gilead researchers have developed 11 HIV medications, including the first single tablet regimen to treat HIV and the first once-daily oral antiretroviral tablet for pre-exposure prophylaxis (PrEP) to reduce the risk of acquiring HIV infection. These advances in medical research have helped to transform HIV into a preventable, chronic condition for millions of people.

Gilead is committed to continued scientific innovation to provide solutions for the evolving needs of people affected by HIV around the world. Through partnerships and collaborations, the company also aims to improve education, expand access and address barriers to care, with the goal of ending the HIV epidemic for everyone, everywhere.

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 Gilead's ability to initiate, progress or complete clinical trials or studies involving lenacapavir within currently anticipated timelines or at all; the possibility of unfavorable results from ongoing or additional clinical trials or studies involving lenacapavir; Gilead's ability to receive regulatory approvals in a timely manner or at all, including FDA approval of lenacapavir for the treatment of HIV-1 infection in HTE people with MDR HIV-1 infection, and the risk that any such approvals may be subject to significant limitations on use; the possibility that Gilead may make a strategic decision to discontinue development of lenacapavir and that, as a result, lenacapavir may never be successfully

commercialized; 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 March 31, 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 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.

For more information about Gilead, please visit the company's website at www.gilead.com, follow Gilead on Twitter (@Gilead Sciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

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