Treatment With Gilead's Vesatolimod Is Evaluated for Safety and Virologic and Immunologic Response Versus Placebo in Phase 1B HIV Functional Cure Study

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-- Results Presented at CROI 2020 Support Further Evaluation of Vesatolimod as Part of Investigational Curative Regimens Aimed at Achieving ART-Free Control of HIV --

BOSTON--(BUSINESS WIRE)-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced results from a Phase 1b trial evaluating the company's investigational toll-like receptor 7 (TLR7) agonist vesatolimod as part of a human immunodeficiency virus (HIV) cure research program. These findings mark the first clinical data showing TLR7 stimulation by vesatolimod is associated with a modestly increased time to viral rebound compared to placebo, as well as enhanced immune function and decreased levels of intact HIV DNA. These results will be presented at the Conference on Retroviruses and Opportunistic Infections (CROI) 2020, along with additional preclinical studies evaluating the potential of combination regimens with vesatolimod to achieve viral remission in the absence of antiretroviral therapy (ART).

"This is the first study done in people that has shown with an immunotherapy that you can enhance immune function resulting in both a smaller viral reservoir and an increased time to viral rebound after treatment is interrupted. The effects are modest, and no one came close to any definition of a cure, but the data suggests real progress might be made when the drug is used in combination with other approaches," said principal investigator Steven Deeks, Professor of Medicine at the University of California, San Francisco (UCSF).

"While HIV treatment has advanced dramatically over the past three decades, people living with HIV still face a lifetime of therapy and potential complications," said Diana Brainard, MD, Senior Vice President, HIV and Emerging Viruses, Gilead Sciences. "Curing HIV remains the ultimate long-term goal for Gilead's HIV research and development efforts. The breadth of our research presented at CROI 2020 furthers the collective scientific knowledge on potential pathways to achieve a 'functional cure', or long-term viral suppression in the absence of ART, for people living with HIV."

Abstracts on cure research strategies presented at CROI 2020 include:

Oral 3982: Safety and Analytic Treatment Interruption Outcomes of Vesatolimod in HIV Controllers

This randomized, double-blind, placebo-controlled study evaluated 25 people living with HIV who had demonstrated partial viral suppression (HIV RNA of 50 to 5,000 copies per mL) prior to starting ART, a group referred to as "HIV controllers". Participants received 10 biweekly doses of the investigational TLR7 agonist vesatolimod or placebo while continuing ART, followed by a treatment interruption in which they stopped therapy and were carefully monitored for viral rebound and safety.

The study found that vesatolimod was associated with a longer period of viral suppression following treatment interruption compared with placebo. The median time to viral rebound (>50 copies/mL) was 4.1 weeks for the vesatolimod group compared with 3.9 weeks for placebo (p=0.036). For rebound to >200 copies/mL, the median time was five weeks for vesatolimod compared with four weeks for placebo (p=0.024). Four individuals in the vesatolimod group had no virologic rebound (>50 c/mL) for six or more weeks.

Vesatolimod is an investigational agent and has not been approved anywhere globally; its safety and efficacy has not been established.

Oral 4545: Combined Active and Passive Immunization in SHIV-Infected Rhesus Monkeys

A separate study evaluated the potential of combining an investigational therapeutic vaccination, investigational broadly neutralizing antibodies (bNAbs), and Gilead's investigational TLR7 agonist vesatolimod as an HIV cure strategy to activate and eliminate the latent HIV reservoir. HIV bNAbs are a class of antiviral and immunotherapy agents that were originally derived from HIV-infected individuals with a strong anti-HIV antibody response that are being developed to target HIV.

In the study, 49 Simian-Human Immunodeficiency Virus (SHIV)-infected rhesus monkeys were given tenofovir disoproxil fumarate/emtricitabine /dolutegravir (TDF/FTC/DTG) as ART. After 24 weeks, animals were assigned into four groups to determine the effect of active and passive immunization: a group that received Ad26/MVA therapeutic vaccination (n=12), a group that received the broadly neutralizing antibody (bNAb) PGT121 (n=12), a group that received both Ad26/MVA and PGT121 (n=10), and sham controls (n=15). All groups except the sham controls additionally received 10 doses of vesatolimod. At week 86, ART was discontinued, and viral rebound was monitored for 140 days. In 6 out of 10 animals, vesatolimod combined with therapeutic vaccination and the PGT121 bNAb resulted in both delayed viral rebound and post-rebound virologic control following ART discontinuation, as compared to 0 out of 15 of the sham control animals. These results support further study of this multi-pronged approach.

Poster 4549: PGT121 and Vesatolimod in Chronically Treated SHIV-Infected Rhesus Monkeys

This study evaluated the efficacy of the investigational combination of broadly neutralizing antibodies (bNAbs) with vesatolimod in SHIV-infected rhesus monkeys who had been treated with continuous daily suppressive ART (TDF/FTC/DTG) for 30 months after one year of chronic infection. Twenty-four SHIV-infected rhesus monkeys were assigned into three groups: a group that received PGT121 and vesatolimod (n=8), a group that received an Fc-modified version of this antibody GS-9721 and vesatolimod (n=9), and a sham control (n=7). At week 42 following initial antibody dosing, which was 24 weeks after the final antibody and vesatolimod doses, ART was discontinued, and viral rebound was monitored for 140 days. Following ART discontinuation, 100 percent (7 of 7) of sham controls exhibited rapid viral rebound, with a median rebound time of 21 days, while the combination of vesatolimod and either PGT121 or GS-9721 prevented viral rebound in 41 percent of subjects. These results suggest the potential therapeutic efficacy of combining bNAbs with TLR7 stimulation in targeting the viral reservoir in rhesus monkeys that initiated ART during the chronic infection phase.

"These data help inform strategies aimed at a functional cure for HIV," said co-author Dan H. Barouch, MD, PhD, Professor of Medicine at Harvard

Medical School and Director of the Center for Virology and Vaccine Research at Beth Israel Deaconess Medical Center. “These findings help focus research efforts in support of the goal to help transform care for people living with HIV.”

Additional studies focused on HIV cure research presented at CROI 2020 include:

- Oral 3126: Safety & Pharmacokinetics of GS-9722 in HIV-Negative Participants & People with HIV
- Poster 1708: Impact of GS-986, PGT121 & N6-LS on CNS Immune Activation in SHIV-infected Macaques
- Poster 3797: NOD2 & TLR8 Agonists Enhance IL-15-Mediated Activation of HIV Expression

Vesatolimod, the bNAbs PGT121 and GS-9721, and the other experimental compounds noted are investigational and are not approved by the U.S. Food and Drug Administration or any other regulatory authority. Their safety and efficacy have not been established.

There is no cure for HIV infection or AIDS.

About Gilead Sciences

Gilead Sciences, Inc. is a research-based biopharmaceutical company that discovers, develops and commercializes innovative medicines in areas of unmet medical need. The company strives to transform and simplify care for people with life-threatening illnesses around the world. Gilead has operations in more than 35 countries worldwide, with headquarters in Foster City, California.

For more than 30 years, Gilead has been a leading innovator in the field of HIV, driving advances in treatment, prevention, testing and linkage to care, and cure research. Today, it’s estimated that more than 12 million people living with HIV globally receive antiretroviral therapy provided by Gilead or one of the company’s manufacturing partners.

Forward-Looking Statement

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 and additional clinical trials involving vesatolimod, GS-9722 and other investigational compounds, and the possibility that we are unable to complete one or more of such trials on the currently anticipated timelines or at all. In addition, it is possible that Gilead may make a strategic decision to discontinue development of these investigational compounds, and as a result, they may never be successfully commercialized. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead’s Annual Report on Form 10-K for the year ended December 31, 2019, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

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

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