Gilead Announces 144-Week Data Evaluating Safety and Efficacy of Genvoya® for Treatment of HIV-1 in Treatment-Naïve Adults

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– Through Three Years of Treatment, Genvoya Demonstrates Significantly Higher Rates of Virologic Suppression and Favorable Renal and Bone Laboratory Parameters Compared to Stribild® –

SEATTLE--(BUSINESS WIRE)--Feb. 14, 2017-- Gilead Sciences, Inc. (NASDAQ: GILD) today announced 144-week data from two Phase 3 studies (Studies 104 and 111) evaluating the safety and efficacy of Genvoya® (elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg and tenofovir alafenamide 10 mg) for the treatment of HIV-1 infection in treatment-naïve adults. Through Week 144, Genvoya demonstrated significantly higher rates of virologic suppression compared to Gilead's Stribild® (elvitegravir 150 mg, cobicistat 150 mg, emtricitabine 200 mg and tenofovir disoproxil fumarate 300 mg), based on the percentage of patients with HIV-1 RNA levels less than 50 copies/mL. Patients receiving Genvoya also demonstrated favorable renal and bone laboratory parameters compared to those treated with Stribild. The data were presented in a poster session (Poster 0393) at the 2017 Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle.

Genvoya is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA levels less than 50 copies/mL) on a stable antiretroviral regimen for at least six months with no history of treatment failure and no known resistance to the components of Genvoya. Genvoya has a boxed warning in its product label regarding the risks of lactic acidosis/severe hepatomegaly with steatosis, and post treatment acute exacerbation of hepatitis B. See below for important safety information.

"As people grow older with HIV, physicians are increasingly looking for highly effective medications that may help address the evolving needs of their patients who face a lifetime of antiretroviral therapy," said Jose Arribas, MD, Associated Professor of Medicine, Hospital La Paz, IdiPAZ, Madrid, Spain and the lead study investigator. "These study results further demonstrate that Genvoya provides durable viral suppression and has a demonstrated safety profile for long-term use by a range of appropriate HIV patients."

In the combined analysis of Studies 104 and 111, a total of 1,733 treatment-naïve adults with HIV were randomized to receive either Genvoya or Stribild. At Week 144, 84.2 percent (n=729/866) of patients taking Genvoya and 80 percent (n=694/867; 95 percent CI: 0.6 percent to 7.8 percent, p=.021) of patients taking Stribild achieved HIV-1 RNA levels less than 50 copies/mL. Additionally, at Week 144, 81.1 percent (n=702/866) of patients taking Genvoya and 75.8 percent (n=657/867; 95 percent CI: 1.5 to 9.2 percent, p=.006) of patients taking Stribild achieved HIV-1 RNA levels less than 20 copies/mL, a secondary endpoint. At Week 144, virologic failure was similar between groups (Genvoya, 4.6 percent; Stribild, 3.9 percent); the difference in overall results was driven by fewer discontinuations on Genvoya due to adverse events or other reasons not related to efficacy (Genvoya, 11.2 percent; Stribild, 16.0 percent). There were statistically significant fewer adverse events leading to discontinuation in the Genvoya arm compared to the Stribild arm (Genvoya, 1.3 percent; Stribild, 3.3 percent, p=0.01). The most common drug-related adverse events in both groups were nausea, diarrhea and headache.

A separate analysis investigated the effect of the two regimens on laboratory parameters of kidney, bone and plasma lipid levels. To examine kidney function, specific protein markers of glomerular and tubular function were examined, all of which favored Genvoya. This included a statistically significant difference in the median change in estimated glomerular filtration rate (eGFR) from baseline to Week 144 (Genvoya, -1.6 mL/min; Stribild, -7.7 mL/min, p<0.001). There were no cases of renal tubulopathy in the Genvoya arm and four cases in the Stribild arm. No participants on Genvoya had renal-related discontinuations compared to 12 participants in the Stribild arm (p<0.001). The analysis also found that decreases in bone mineral density (BMD) were significantly less in the Genvoya group versus the Stribild group for both lumbar

spine and total hip (spine: Genvoya, -0.92 percent; Stribild, -2.95 percent, p<0.001; hip: Genvoya, -0.75 percent; Stribild, -3.36 percent, p<0.001). The long-term clinical significance of changes in eGFR and BMD is not known. Finally, patients on Genvoya had statistically higher increases in total, LDL and HDL cholesterol from baseline to Week 144 compared to patients on Stribild. There was no significant difference in the total cholesterol-to-HDL ratio at Week 144, nor any difference in the rate of initiation of lipid-modifying agents.

About Studies 104 and 111

Studies 104 and 111, originally planned for 96 weeks and extended to 144 weeks, were randomized, double-blind, controlled Phase 3 trials conducted among 1,733 treatment-naïve adults living with HIV. The primary endpoint of the study was at Week 48, in which Genvoya was non-inferior to Stribild. Genvoya was also non-inferior at the secondary endpoint of efficacy at Week 96. At study enrollment, 15 percent of subjects were women, 25 percent identified themselves as Black or of African descent and 23 percent had viral loads ≥100,000 copies/mL. Patients were randomized 1:1 to receive a single tablet regimen of Genvoya or Stribild; randomization included stratification for CD4 count (< 50 cells/µL, 50 to 199 cells/µL, or ≥ 200 cells/µL) and region (United States or ex-United States) at screening.

Additional information about the studies can be found at www.clinicaltrials.gov.

Important U.S. Safety Information for Genvoya

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs in combination with other antiretrovirals.**
- **Genvoya is not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of Genvoya have not been established in patients coinfected with HIV-1 and HBV. Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of Genvoya. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue Genvoya. If appropriate, initiation of anti-hepatitis B therapy may be warranted.**

Contraindications

- **Coadministration:** Do not use with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events. Do not use with drugs that strongly induce CYP3A as this may lead to loss of efficacy and possible resistance to Genvoya. Do not use with alfuzosin, carbamazepine, phenobarbital, phenytoin, rifampin, lurasidone, pimozide, dihydroergotamine, ergotamine, methylergonovine, cisapride, lovastatin, simvastatin, sildenafil for pulmonary arterial hypertension, triazolam, oral midazolam, or St. John's wort.

Warnings and precautions

- **Drug interactions:** See Contraindications and Drug Interactions sections. Consider the potential for drug interactions prior to and during Genvoya therapy and monitor for adverse reactions.
- **Fat redistribution** or accumulation has been observed in patients receiving antiretroviral therapy.
- **Immune reconstitution syndrome,** including the occurrence of autoimmune disorders with variable time to onset, has been reported.
- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir prodrugs. In clinical trials of Genvoya, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate Genvoya in patients with estimated creatinine

clearance (CrCl) <30 mL/min. Patients with impaired renal function and/or taking nephrotoxic agents (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue Genvoya in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome.

Renal monitoring: In all patients, monitor serum creatinine, serum phosphorus, CrCl, urine glucose, and urine protein prior to initiating and during therapy as clinically appropriate. If serum creatinine increases >0.4 mg/dL from baseline, closely monitor for renal safety.

Adverse reactions

- **Common adverse reactions** (incidence ≥5%; all grades) in clinical studies were nausea (10%), diarrhea (7%), headache (6%), and fatigue (5%).

Drug interactions

- **Prescribing information:** Consult the full prescribing information for Genvoya for more information on Contraindications, Warnings, and potentially significant drug interactions, including clinical comments.
- **Metabolism:** Genvoya can increase the concentration of drugs metabolized by CYP3A, CYP2D6, P-gp, BCRP, OATP1B1, or OATP1B3. Drugs that inhibit CYP3A, P-gp, or BCRP can increase the concentrations of components of Genvoya. Drugs that induce CYP3A or P-gp can decrease the concentrations of components of Genvoya.
- **Drugs affecting renal function:** Coadministration of Genvoya with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of emtricitabine and tenofovir and the risk of adverse reactions.

Dosage and administration

- **Dosage:** Patients 12 years and older (≥35 kg): 1 tablet taken orally once daily with food.
- **Renal impairment:** Not recommended in patients with CrCl <30 mL/min.
- **Hepatic impairment:** Not recommended in patients with severe hepatic impairment.
    - **Testing prior to initiation:** Test patients for HBV infection.
    - **Testing prior to initiation and during treatment**: Assess serum creatinine, serum phosphorus, CrCl, urine glucose and urine protein as clinically appropriate.

Pregnancy and Lactation

- **Pregnancy:** There are insufficient data on the use of Genvoya during pregnancy. In animal studies, no adverse developmental effects were observed with the components of Genvoya. An Antiretroviral Pregnancy Registry has been established.
- **Lactation:** Women infected with HIV-1 should be instructed not to breastfeed, due to the potential for HIV-1 transmission.

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

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 risk that physicians may not see the benefits of prescribing Genvoya for the treatment of HIV. 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, 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.

*U.S. full prescribing information for Genvoya and Stribild, including **BOXED WARNINGS**, is available at www.gilead.com.*

GENVOYA and STRIBILD are trademarks of Gilead Sciences, Inc., or its related companies.

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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