Gilead Presents Results from Phase 3 Studies Evaluating Switching to Descovy® (FTC/TAF)-Based Regimens from Truvada® (FTC/TDF)-Based Regimens

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– Descovy (FTC/TAF)-based Regimens Demonstrate Comparable Efficacy and Improved Renal and Bone Laboratory Parameters Compared to Truvada (FTC/TDF)-based Regimens –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Oct. 24, 2016-- Gilead Sciences, Inc. (Nasdaq:GILD) today announced two-year (96-week) data from a Phase 3 study and 48-week data from two Phase 3b studies evaluating the safety and efficacy of switching virologically suppressed HIV-1 infected patients from regimens containing Truvada® (emtricitabine and tenofovir disoproxil fumarate 200mg/300mg; FTC/TDF) to regimens containing Descovy® (emtricitabine and tenofovir alafenamide 200mg/25mg; FTC/TAF). Results demonstrated regimens containing Descovy to be statistically non-inferior to regimens containing Truvada, with improvements in certain renal and bone laboratory parameters among patients receiving Descovy (FTC/TAF)-based regimens. The data were presented in an oral session (Treatment Strategies) at the 2016 HIV Glasgow conference in Glasgow, Scotland, UK.

Descovy is indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in patients 12 years of age and older. Descovy should not be used as pre-exposure prophylaxis (PrEP) to reduce the risk of acquiring HIV-1 infection. Descovy 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 are living longer with HIV, several studies show that patients who switch from regimens containing Truvada to regimens containing Descovy are able to maintain viral suppression while improving renal and bone laboratory markers, which may help address long-term health needs,” said Dr. Chloe Orkin, Consultant, Barts Health NHS Trust, London. “Along with its favorable safety profile, Descovy offers patients and physicians a versatile treatment backbone that can be paired with a range of third agents.”

In Study 1089, 663 virologically suppressed, HIV infected adults were randomized to switch to regimens containing Descovy or continue on regimens containing Truvada, while remaining on the same third agents. At Week 96, virologic suppression (HIV-1 RNA <50 c/mL) was maintained in 89 percent of participants in both groups (difference in percentages: -0.5 percent; 95 percent CI: -5.3 percent to 4.4 percent). Drug-related serious adverse events were rare (Descovy (FTC/TAF)-based regimens, 0 percent; Truvada (FTC/TDF)-based regimens, 0.3 percent) and drug discontinuation due to adverse events was low for both treatment groups (Descovy (FTC/TAF)-based regimens, 2.4 percent; Truvada (FTC/TDF)-based regimens, 1.2 percent). The most commonly reported adverse events included upper respiratory tract infection, diarrhea and nasopharyngitis.

In the same study, the effect of the two regimens on laboratory parameters of kidney and bone health was investigated. Statistically significant differences were observed in mean changes from baseline to Week 96 in bone mineral density (BMD) between patients receiving Descovy (FTC/TAF)-based regimens compared to patients receiving Truvada (FTC/TDF)-based regimens (spine: 2.15 percent vs. -0.17 percent; hip: 1.85 percent vs. -0.33 percent; $p<0.05$ for both). Additionally, more patients receiving Descovy (FTC/TAF)-based regimens experienced a greater than three percent improvement in BMD from baseline to Week 96, compared with those receiving Truvada (FTC/TDF)-based regimens (spine: 40 percent vs. 18 percent; hip: 29 percent vs. 11 percent; $p<0.05$ for both).

Differences favoring regimens containing Descovy were also observed in multiple tests of renal laboratory parameters which included median changes from baseline to Week 96 in estimated glomerular filtration rate (eGFR; +10.00 mL/min vs. +4.00 mL/min; $p<0.05$) and median percent changes in: urine protein-to-creatinine ratio (-26.0 percent vs. +2.7 percent; $p<0.05$); urine albumin-to-creatinine ratio (+3.4 percent vs. +27.0 percent; $p<0.05$); urine retinol binding protein-to-creatinine ratio; (-4.1 percent vs. +42.6 percent; $p<0.05$); and urine beta-2 microglobulin-to-creatinine ratio (-29.7

percent vs. +46.8 percent; p<0.05). There were no cases of Fanconi syndrome. Additionally, there were no cases of proximal renal tubulopathy in the Descovy (FTC/TAF)-based regimens group, and one case in the Truvada (FTC/TDF)-based regimens group through Week 96.

Odefsey® (rilpivirine 25mg/emtricitabine 200mg/tenofovir alafenamide 25mg tablets; RPV/FTC/TAF) is a FTC/TAF-based single tablet regimen indicated as a complete regimen for the treatment of HIV-1 infection in patients 12 years of age and older who have no antiretroviral treatment history and HIV-1 RNA levels ≤100,000 c/mL. Odefsey is also indicated to replace a stable antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA <50 c/mL) for at least six months with no history of treatment failure and no known resistance to the individual components of Odefsey. Odefsey also 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.

In Study 1216, 630 virologically suppressed, HIV infected adults were randomized to switch to Odefsey or to continue on Complera® (rilpivirine 25mg/emtricitabine 200mg/tenofovir disoproxil fumarate 300mg tablets; RPV/FTC/TDF). At Week 48, similar rates of virologic suppression (HIV-1 RNA <50 c/mL) were maintained in both treatment groups (Odefsey, 94 percent; Complera, 94 percent; difference in percentages: −0.3 percent; 95 percent CI: −4.2 percent to +3.7 percent). Drug-related serious adverse events and drug discontinuation due to adverse events were low across both treatment groups (0.1 percent in both). The most commonly reported adverse events included upper respiratory tract infection, diarrhea and nasopharyngitis.

Statistically significant improvements favoring Odefsey were observed from baseline to Week 48 in mean BMD at the hip and spine compared to patients in the Complera group (spine: +1.61 percent vs. +0.08 percent; hip: +1.04 percent vs. -0.25 percent; p<0.001 for both). Additionally, improvements favoring Odefsey were observed in multiple tests of renal laboratory parameters, including median changes in eGFR from baseline to Week 48 (Odefsey, +4.5mL/min; Complera, +0.7 mL/min; p=0.002) and median percent changes in: urine protein-to-creatinine ratio (-18.0 percent vs. +21.5 percent; p<0.001); urine albumin-to-creatinine ratio (-7.8 percent vs. +16.8 percent; p<0.001); urine retinol binding protein-to-creatinine ratio; (-18.8 percent vs. +7.3 percent; p<0.001); and urine beta-2 microglobulin-to-creatinine ratio (-29.0 percent vs. +12.0 percent; p<0.001). No cases of Fanconi syndrome or proximal renal tubulopathy were reported through Week 48.

In Study 1160, 875 virologically suppressed, HIV infected adults were randomized to switch to Odefsey, or to continue on Atripla® (efavirenz 600mg/emtricitabine 200mg/tenofovir disoproxil fumarate 300mg tablets; EFV/FTC/TDF). At Week 48, high rates of virologic suppression (HIV-1 RNA <50 c/mL) were maintained in both treatment groups (Odefsey, 90 percent; Atripla, 92 percent; difference in percentages: -2.0 percent; 95 percent CI: -5.9% to +1.8%) and general safety was similar between the arms. The most commonly reported adverse events included upper respiratory tract infection, nasopharyngitis and cough.

Statistically significant improvements favoring Odefsey were observed from baseline to Week 48 in mean BMD at the hip and spine compared to patients in the Atripla group (spine: +1.65 percent vs. +0.05 percent; hip: +1.28 percent vs. -0.13 percent; p<0.001 for both). A larger percentage of patients receiving Odefsey showed improvements in their osteopenia or osteoporosis at either hip (p=0.004) or spine (p<0.001). Additionally, improvements favoring Odefsey were observed in multiple tests of renal laboratory parameters, demonstrated by changes in total and tubular proteinuria (p<0.001) and percent changes in: urine protein-to-creatinine ratio (-30.0 percent vs. -2.0 percent; p<0.001); urine albumin-to-creatinine ratio (-13.5 percent vs. +12.2 percent; p<0.001); urine retinol binding protein creatinine ratio (-27.6 percent vs. +29.1 percent; p<0.001); urine beta-2-microglobulin creatinine ratio (-41.0 percent vs. +17.1 percent; p<0.001). No cases of Fanconi syndrome or proximal renal tubulopathy were reported through Week 48.

“Results from the studies presented at HIV Glasgow further support the efficacy, as well as the renal and bone safety profile, of regimens containing Descovy as treatment options for appropriate virologically suppressed patients,” said Norbert W. Bischofberger, PhD, Gilead’s Executive Vice President, Research and Development and Chief Scientific Officer. “These data also demonstrate Gilead’s ongoing commitment to developing treatments that may improve health as people

grow older with HIV while we continue to search for a cure for the virus."

Odefsey combines Gilead's emtricitabine and tenofovir alafenamide with rilpivirine, marketed by Janssen Sciences Ireland UC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson. Gilead is responsible for the manufacturing, registration, distribution and commercialization of Odefsey in most countries, while Janssen will distribute it in approximately 18 markets and have co-detailing rights in several key markets, including the United States. The original agreement was established for the development and commercialization of Complera®, marketed as Eviplera® in the EU, and was expanded in 2014 to include Odefsey.

Additional Study Information

Study 1089 is a Phase 3, 96-week randomized, multi-center, double blind, active controlled study of 663 virologically suppressed HIV-1 infected adult patients receiving Truvada (FTC/TDF)-based regimens. The study was designed to evaluate the efficacy and safety of switching from Truvada to Descovy, versus continuing Truvada while remaining on the same third agent. The primary endpoint was virologic success (HIV-1 RNA <50 c/mL) at Week 48. The median age of participants was 49 years, and females comprised 15 percent of the study population. Inclusion criteria required an estimated glomerular filtration rate eGFR ≥ 50 mL/min, according to the Cockcroft-Gault formula for creatinine clearance. The median estimated eGFR at study initiation was 100 mL/min. Dosing of Descovy was dependent on the third agent: 200/10mg with ritonavir-boosted protease inhibitors (darunvair, atazanavir and lopinavir) and 200/25mg with unboosted third agents (raltegravir, dolutegravir, nevirapine, efavirenz, rilpivirine and maraviroc). In the United States, only one dose of Descovy (200/25mg) is approved for use with any third agent. Approximately 46 percent of patients enrolled were treated with a boosted protease inhibitor, 28 percent were treated with an integrase inhibitor and 25 percent were treated with a non-nucleoside reverse transcriptase inhibitor.

Study 1216 is a Phase 3b, 96-week randomized, double blind, multicenter study among 630 virologically suppressed adults (HIV-1 RNA levels <50 copies/mL) on a stable regimen of Complera for ≥ six months. The study was designed to evaluate the efficacy and safety of switching from Complera to Odefsey versus remaining on Complera. The primary endpoint was virologic success (HIV-1 RNA <50 c/mL) at Week 48. The median age of participants was 45 years, with 10 percent female and 19 percent black participants. Inclusion criteria required an eGFR ≥ 50 mL/min, according to the Cockcroft-Gault formula for creatinine clearance.

Study 1160 is a Phase 3b, 96-week randomized, double blind, multicenter study of 875 virologically suppressed adults (HIV-1 RNA levels <50 copies/mL) on a stable regimen of Atripla for ≥ six months. The study was designed to evaluate the efficacy and safety of switching from Atripla to Odefsey versus remaining on Atripla. The primary endpoint was virologic success (HIV-1 RNA <50 c/mL) at Week 48. The median age of participants was 49 years, and females comprised 13 percent of the study population. Inclusion criteria required an eGFR ≥ 50 mL/min, according to the Cockcroft-Gault formula for creatinine clearance.

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

Important U.S. Safety Information For Descovy And Odefsey

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.**
- **Descovy and Odefsey are not approved for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy 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 (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of Descovy or Odefsey. After discontinuation, 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. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

Contraindications

Contraindications for Descovy:

- **None**

Contraindications for Odefsey:

- **Coadministration.** Do not use with drugs that induce CYP3A or increase gastric pH as this may lead to loss of efficacy and possible resistance to Odefsey or the NNRTI class. Do not use with carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, proton pump inhibitors (e.g., dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole), systemic dexamethasone (>1 dose) and St. John's wort.

Warnings and precautions

Warnings and precautions for Descovy and Odefsey:

- **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 emtricitabine and tenofovir alafenamide (TAF) with elvitegravir and cobicistat, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate 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 in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Renal monitoring: In all patients, monitor CrCl, urine glucose, and urine protein prior to initiating and during therapy. In patients with chronic kidney disease, additionally monitor serum phosphorus.
- **Bone loss and mineralization defects:** Decreases in bone mineral density (BMD) have been reported with the use of tenofovir prodrugs. Consider monitoring BMD in patients with a history of pathologic fracture or risk factors for bone loss. Mineralization defects, including osteomalacia associated with PRT, have been reported with the use of TDF-containing products.

Additional warnings and precautions for Odefsey:

- **Skin and hypersensitivity reactions:** Severe skin and hypersensitivity reactions have been reported with the use of rilpivirine-containing regimens, including cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). In rilpivirine clinical trials, most rashes were Grades 1-2 and occurred in the first 4-6 weeks of treatment; Grades 2-4 rash occurred in 1% of subjects. Discontinue Odefsey immediately if severe skin or hypersensitivity reactions occur, including severe rash or rash accompanied by fever, blisters, mucosal involvement, conjunctivitis, facial edema, angioedema, hepatitis or eosinophilia. Monitor clinical status including laboratory parameters and initiate appropriate therapy.
- **Loss of virologic response due to drug interactions:** See Contraindications and Drug Interactions sections. Consider the potential for drug interactions prior to and during Odefsey therapy and monitor for adverse reactions.
- **Prolongation of QTc interval:** Rilpivirine doses 3 and 12 times higher than the recommended dose can prolong the QTc interval. Consider alternatives to Odefsey in patients at higher risk for Torsade de Pointes or when coadministered with a drug with known risk of Torsade de Pointes.

- **Depressive disorders:** Evaluate patients with severe depressive symptoms to assess if symptoms are due to

Odefsey and if the risks of continued treatment outweigh the benefits. In rilpivirine adult clinical trials (N=686), the incidence of depressive disorders was 9%, Grades 3-4 depressive disorders was 1%, discontinuation due to depressive disorders was 1%, and suicidal ideation and suicide attempt was reported in 4 and 2 subjects, respectively. In a rilpivirine adolescent clinical trial (N=36), the incidence of depressive disorders was 19%, Grades 3-4 depressive disorders was 6%, and suicidal ideation and suicide attempt were reported in 1 subject.

- **Hepatotoxicity:** Hepatic adverse events have been reported, including cases of hepatic toxicity, in patients without pre-existing hepatic disease or other identifiable risk factors. In patients with hepatic abnormalities (e.g., hepatitis, elevated liver-associated tests), order laboratory tests before starting treatment and monitor for hepatotoxicity during treatment; consider testing and monitoring in all patients.

Adverse reactions

Adverse reactions for Descovy and Odefsey:

- **Common adverse reactions** (incidence ≥5%; all Grades) in clinical studies of FTC/TAF in combination with other antiretroviral agents were nausea (10%), diarrhea (7%), headache (6%), and fatigue (5%).

Additional adverse reactions for Odefsey:

- **Most common adverse reactions** (incidence ≥2%, Grades 2-4) in clinical studies of rilpivirine in combination with other antiretroviral agents were depressive disorders (2%), insomnia (2%) and headache (2%).

Drug interactions

Drug interactions for Descovy and Odefsey:

- **Prescribing information:** Consult the full prescribing information for more information on potentially significant drug interactions, including clinical comments.
- **Drugs affecting renal function:** Coadministration with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC and tenofovir and the risk of adverse reactions.

Additional drug interactions for Descovy:

- **Metabolism:** Drugs that inhibit P-gp can increase the concentrations of components of Descovy. Drugs that induce P-gp can decrease the concentrations of components of Descovy, which may lead to loss of efficacy and development of resistance.

Additional drug interactions for Odefsey:

- **Metabolism:** Drugs that induce CYP3A or P-gp and drugs that increase gastric pH can decrease the concentrations of components of Odefsey. Drugs that inhibit CYP3A or P-gp can increase the concentrations of components of Odefsey.
- **QT prolonging drugs:** Consider alternatives to Odefsey in patients taking a drug with known risk of Torsade de Pointes.

Dosage and administration

Information for Descovy and Odefsey:

- **Dosage for patients 12 years and older (≥35 kg):** 1 tablet taken orally once daily.
  - **Descovy:** take with or without food, in combination with other antiretroviral agents.
  - **Odefsey:** take with a meal, as a single-tablet regimen.
- **Renal impairment:** Not recommended in patients with CrCl <30 mL/min.

- **Testing prior to initiation:** Test patients for HBV infection and assess CrCl, urine glucose and urine protein.

Additional information for Odefsey:

- **Testing after initiation:** In virologically-suppressed patients, additional monitoring of HIV-1 RNA and regimen tolerability is recommended.

Pregnancy and lactation

Information for Descovy and Odefsey:

- **Pregnancy:** There are insufficient data on use during pregnancy. In animal studies, no adverse developmental effects were observed. 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

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercialises 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 benefits of switching patients from regimens containing Truvada to regimens containing Descovy. Further, there is a possibility of unfavorable results from other clinical trials involving Descovy (FTC/TAF)-based regimens. 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 June 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 Atripla, Complera, Descovy, Odefsey, and Truvada, including **BOXED WARNINGS**, are available at www.gilead.com.*

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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

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