Gilead's PMPA Significantly Reduces HIV Levels in Phase I/II Study

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Oral Version Expected To Enter Clinical Trials Soon

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Gilead Sciences, Inc. (NASDAQ:GILD) announced today data from a Phase I/II study demonstrating that the antiretroviral PMPA significantly reduced human immunodeficiency virus (HIV) RNA levels by greater than 90% after eight doses, with no significant side effects. In this first human study of intravenous (IV) PMPA, the drug was administered as a single agent and resulted in a median decrease in viral load of 1.1 log at the higher of two doses studied.

These data will be presented today at the 10th International Conference on Antiviral Research (ICAR) in Atlanta, Georgia by Patricia Barditch-Crovo, M.D., of The Johns Hopkins University School of Medicine in Baltimore. Gilead plans to begin testing an oral form of PMPA in humans within the next several months.

"The magnitude of HIV viral load reduction after only one week of dosing confirms the significant potency of PMPA," said John C. Martin, Ph.D., President and CEO of Gilead Sciences. "We also are encouraged that PMPA's antiviral activity persisted for an additional week after dosing was discontinued. Based on these encouraging data, Gilead will continue PMPA's development in an oral form."

Phase I/II PMPA Intravenous Study Results

Twenty patients were enrolled in this Phase I/II randomized, double-blind, placebo-controlled, dose-escalation study at The Johns Hopkins University School of Medicine in Baltimore and the University of California, San Francisco (San Francisco General Hospital). All patients enrolled in the study were infected with HIV and had CD4 counts above 200 cells/mm^3. PMPA was administered intravenously, with no other anti-HIV therapies (monotherapy). Patients were randomized to receive placebo (4 patients) or one of two dose levels of PMPA (8 patients at 1 mg/kg and 8 patients at 3 mg/kg). All patients received a single dose of placebo or PMPA, then no treatment for seven days, followed by placebo or PMPA once per day for seven days.

Data presented demonstrated that PMPA reduced HIV RNA levels, a marker of HIV viral load, by a median decrease of 0.6 log in the 1 mg/kg group ($p=0.008$) and a median decrease of 1.1 log in the 3 mg/kg group ($p=0.03$), compared to a median increase of 0.1 log in the placebo group. At both doses, viral load continuously decreased during the PMPA treatment period until completion of seven days of dosing, and decreases in viral load at 3 mg/kg were sustained up to one week after the end of the treatment period. No clinically significant side effects were observed.

Human Testing of Oral PMPA Expected Soon

The Phase I/II study, originally designed to continue to higher dose levels, was stopped because of the significance of the results achieved at the two dose levels studied and because Gilead filed an Investigational New Drug (IND) Application with the U.S. Food and Drug Administration (FDA) to begin studies of the tablet form of PMPA in humans. Preclinical data presented earlier this year demonstrated the prodrug has suitable oral bioavailability (30 percent). In *in vitro* studies, the oral prodrug also has shown greater anti-HIV potency than the parent compound.

Early Data

PMPA belongs to a class of antivirals called nucleotide analogues, which are being developed by Gilead for the treatment of viral diseases. Nucleotides can inhibit viral replication for prolonged periods and have been associated with infrequent development of resistance.

PMPA has shown unprecedented antiviral activity in the prophylaxis and treatment of simian immunodeficiency virus (SIV) infection, a primate model for AIDS. In preclinical studies, primates treated once daily with injections of PMPA either before or after exposure to SIV were completely protected against infection. PMPA also provided 100% protection against the development of SIV infection in primates treated after inoculation of the virus.

Additional studies have demonstrated that PMPA reduced SIV RNA levels by approximately 99% (2 to 3 log decrease) or to below the limit of detection after four weeks. Other data have shown that a topical gel form of PMPA has provided complete protection against SIV when applied intravaginally in primates.

Other Anti-HIV Treatments in Development

GS 840 (adefovir dipivoxil), another oral nucleotide in development at Gilead, has demonstrated antiviral activity against a broad-spectrum of viruses, including HIV, cytomegalovirus (CMV) and hepatitis B virus. GS 840 is being studied in combination with approved anti-HIV agents, including protease inhibitors, for the potential treatment of HIV. One ongoing Phase II/III study, which is planned to enroll up to 400 people infected with HIV, is designed to determine the safety and efficacy of GS 840 when administered in combination with approved antiretroviral therapies for the treatment of patients infected with HIV.

In addition, The Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA), a National Institutes of Health-sponsored organization, is conducting a Phase III study in up to 2,000 patients to determine GS 840's ability, when administered with approved antiretrovirals, to prolong survival and prevent CMV end-organ disease in patients with advanced AIDS.

Gilead Sciences

Gilead Sciences is a biopharmaceutical company dedicated to the discovery, development and commercialization of treatments for human diseases. The company's business and scientific endeavors are focused on making new therapies available to patients, physicians and the healthcare system. Gilead's expertise has resulted in proprietary therapeutics for important viral diseases, including a currently available therapy for cytomegalovirus retinitis, and products in development to treat diseases caused by human immunodeficiency virus, hepatitis B virus, herpes simplex virus, human papillomavirus and influenza virus. Gilead's research programs seek treatments for these and other viral infections, vascular diseases and cancer. Gilead common stock is traded on The Nasdaq Stock Market under the symbol GILD.