Gilead Sciences Commences Human Clinical Testing of Systemic PMPA for HIV

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Gilead Sciences, Inc. (NASDAQ:GILD) announced today the commencement of human clinical studies of PMPA. In preclinical testing, PMPA has demonstrated potent activity against simian immunodeficiency virus (SIV) infection, a primate model for human immunodeficiency virus (HIV), the causative agent of AIDS.

The Phase I/II randomized, double-blind, placebo-controlled human study is planned to assess the safety, tolerance, pharmacokinetics and anti-HIV activity of PMPA when administered by intravenous infusion to HIV-infected patients. The study is designed to enroll a total of 40 patients with CD4 cell counts greater than 200 cells/mm3 at The Johns Hopkins University School of Medicine in Baltimore and the University of California, San Francisco (San Francisco General Hospital).

Dosing will consist of an initial intravenous infusion of PMPA, at one of up to four different dose levels, or placebo. One week later, patients may then be eligible to receive PMPA or placebo once per day for seven days. Patients will be monitored for four weeks, and anti-HIV activity will be measured by changes in CD4 cell counts and plasma HIV RNA levels.

PMPA is a member of a new class of antiviral therapeutics based on nucleotides, the building blocks of DNA and RNA. PMPA is known to inhibit reverse transcriptase, an enzyme essential to HIV replication. Nucleotide analogues such as PMPA are characterized by their ability to inhibit viral replication for long periods of time in a variety of cell types and to potentially form protective reservoirs of active drug inside cells. These characteristics offer the potential for infrequent dosing and prophylactic use in humans.

PMPA Active in SIV Preclinical Models of Treatment and Prophylaxis

In preclinical studies, PMPA had potent activity in both the treatment and prophylaxis of SIV infection. In primates chronically infected with SIV, PMPA reduced SIV RNA levels by approximately 99% (2 to 3 log decreases) or to below the limit of detection. These data were presented at the Ninth International Conference on Antiviral Research in Japan in May 1996. At the same conference, other data were presented demonstrating that PMPA, when administered intravaginally in a topical gel, completely prevented the transmission of SIV to female primates exposed intravaginally to the virus. These data suggest that PMPA may be useful in protecting against HIV transmission in humans.

An earlier study (Science, November 1995) demonstrated that PMPA provided 100% protection against the development of SIV infection in primates treated by subcutaneous injection for four weeks beginning either 48 hours before or up to 24 hours after exposure to the virus. No evidence of SIV infection was found in treated primates after monitoring for up to 52 weeks. These data suggest that PMPA may be protective when taken prophylactically at the time of known accidental HIV exposure by healthcare workers or others, and maternal-fetal transmission by newborn infants.

In these preclinical studies, PMPA was well tolerated and there were no observed toxicities. It should be noted, however, that data obtained from preclinical models are not necessarily predictive of outcomes in human clinical trials.

PMPA is chemically similar to another Gilead nucleotide product candidate, GS 840 (adefovir dipivoxil), which is now in pivotal Phase II/III human clinical testing for the treatment of HIV infection. Data from placebo-controlled Phase I/II studies demonstrated that treatment with GS 840 produced sustained decreases in viral load (HIV RNA) and increases in CD4 cell counts, a marker of immune system function.

Gilead retains worldwide rights to develop and commercialize PMPA. Gilead licensed rights to PMPA and other nucleotide analogues from the Institute of Organic Chemistry and Biochemistry (IOCB) in the Czech Republic and from the REGA Stichting Research Institute (REGA) in Belgium. IOCB and REGA were the first to synthesize antiviral nucleotide analogues and characterize their activity. Gilead Sciences maintains ongoing collaborations with both IOCB and REGA regarding a portfolio of nucleotide candidates.

Gilead's first product, VISTIDE® (cidofovir injection), received marketing clearance by the U.S. Food and Drug Administration

in June 1996 for the treatment of cytomegalovirus (CMV) retinitis in patients with AIDS. In addition, the Company has other nucleotide product candidates in human testing for the potential treatment of viral diseases caused by CMV, HIV, hepatitis B virus, herpes simplex virus and human papillomavirus.

Gilead Sciences is a leader in the discovery and development of a new class of human therapeutics based on nucleotides, the building blocks of DNA and RNA. The Company's research and development efforts encompass three interrelated programs: small molecule antivirals, cardiovascular therapeutics and genetic code blockers for cancer and other diseases. Gilead's expertise in each of these areas has also resulted in the discovery of non-nucleotide product candidates that expand the Company's technology platforms. Gilead common stock is traded on The Nasdaq Stock Market under the symbol GILD.