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SAFETY AND PK OF SUBCUTANEOUS GS-6207, A NOVEL HIV-1 CAPSID INHIBITOR

Jennifer E. Sager1, Rebecca Begley1, Martin Rhee1, Steve K. West1, John Ling1, Scott D. Schroeder1, Winston C. Tse1, Anita Mathias1
1Gilead Sciences, Inc, Foster City, CA, USA

Background:
GS-6207, a selective, multi-stage inhibitor of HIV-1 capsid function, is in development for the treatment of HIV-1 infection. GS-6207 is characterized by potent antiviral activity, low predicted human clearance, and low aqueous solubility, making it well suited for an extended-release parenteral formulation. This Phase 1 study evaluated the safety, tolerability and pharmacokinetics (PK) of a subcutaneous (SC) suspension of GS-6207 in healthy volunteers.

Methods:
This is a randomized, blinded, placebo-controlled healthy volunteer study with staggered single dose escalation cohorts. Within each cohort, subjects were randomized (4:1) to receive single SC doses of GS-6207 (n=8/cohort) or placebo (N=2/cohort), at 30, 100, 300 or 450 mg. PK parameters will be estimated and summarized by dose and dose proportionality will be assessed. Safety, tolerability and PK will be evaluated for at least 24 weeks post-dose.

Results:
40 subjects received a single SC dose of GS-6207 (N=32) or placebo (N=8). The study is ongoing with interim safety and PK data available through at least 20 weeks (Cohort 1, 30 mg), 16 weeks (Cohort 2, 100 mg), 8 weeks (Cohort 3, 300 mg) and 4 weeks (Cohort 4, 450 mg). PK parameters for Cohorts 1 and 2 have been estimated. Analysis for Cohorts 3 and 4 is ongoing. The PK profile of SC GS-6207 is consistent with sustained delivery. Tmax values ranged from 21 to 35 days (Cohorts 1 and 2). The median apparent terminal t1/2 was between 30 to 38 days and concentrations are measureable for at least 16 weeks, to date (Cohorts 1 and 2). The increase in exposure (Cmax and AUC) between 30 and 100 mg GS-6207 was approximately dose proportional. To date, there have been no deaths, serious adverse events, or Grade 3 or 4 adverse events (AEs). Most AEs were mild (Grade 1) and resolved.

Conclusion:
Based on the interim data, GS-6207 was safe and well tolerated following single SC doses of up to 450 mg in healthy subjects. Sustained delivery supports a dosing interval of at least 3 months. The safety and PK of GS-6207 supports evaluation of its antiviral activity in HIV-infected participants.