DOSE-RESPONSE RELATIONSHIP OF SUBCUTANEOUS LONG-ACTING HIV CAPSID INHIBITOR GS-6207

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Background:
GS-6207, a potent, first-in-class, multi-stage inhibitor of HIV-1 capsid function is in development as a long-acting agent for treatment of HIV-1 infection. The safety, antiviral activity and pharmacokinetics of GS-6207 were evaluated in people living with HIV (PLWH) in this Phase 1b study.

Methods:
This is an ongoing, Phase 1b, randomized, double-blinded, placebo-controlled dose-ranging study of GS-6207 in HIV capsid-inhibitor naive PLWH not on antiretrovirals. A single subcutaneous dose of GS-6207 (20,50,150,450, or 750mg; n=6/cohort) or placebo (n=2/cohort) was administered. The primary endpoint was maximum reduction of plasma HIV-1 RNA through post-dose day 10 (D10). Safety was assessed using laboratory tests and adverse event (AE) reporting. We present antiviral activity, safety, and dose-response relationship for the 20 to 450mg dose cohorts; enrollment of the 750mg cohort is ongoing.

Results:
All PLWH who received GS-6207 had greater reductions in HIV-1 RNA by D10 versus placebo ($p<0.0001$). The 50 to 450mg groups had numerically greater mean reductions in HIV-1 RNA through D10 (range: 1.8-2.2 $\log_{10}$copies/mL) than the 20mg group (1.4 $\log_{10}$copies/mL). At these doses, the inhibitory quotients on D10 ranged from 0.7-9.9. Using a maximum effect (E_{max}) model for GS-6207 (SC 20-450mg) and antiviral activity, E_{max} was ~2.1 $\log_{10}$copies/mL decline in HIV-1 RNA, and a ~10mg dose inhibited viral replication by 50%. One participant experienced a serious AE (Grade 3) of atrial fibrillation after using methamphetamine; no other SAEs, Grade 3/4 AEs, AEs leading to discontinuation, or clinically relevant Grade 3/4 laboratory abnormalities were reported. Most common AEs were injection site reactions that were mostly mild and transient (50%).

Conclusions:

In PLWH, GS-6207 demonstrated potent antiviral activity, with up to a 2.2 log10 copies/mL decline at Day 10, and was generally safe and well tolerated. These results support further clinical evaluation of GS-6207 as a long-acting antiretroviral agent.

Disclosure
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