Introduction

- Ritonavir (RTV), a HIV protease inhibitor (PI), is a weak cytochrome P450 (CYP) substrate

- GS-9350, a novel pharmacoenhancer without anti-HIV activity

Saraha et al. (2010) reported that GS-9350 as a single agent was metabolically inactive in humans, and coadministration of RTV significantly reduced anti-HIV activity.

- CYP3A inhibition data described were generated using industry and FDA recommended methods.

SAR of P2 Region

GS-9350 was successfully co-formulated with elvitegravir/emeritam/tenofovir/DRGO (QUAD) is smaller in size than ATRIPLA.

Results and Discussion (cont'd)

GS-9350 was successfully co-formulated with elvitegravir/emtricitabine/tenofovir (ATR) in Phase I study in HIV-infected patients.

Clinical Studies

- GS-9350 is a potent, selective, mechanism-based CYP3A inhibitor that blocks a single activity and has limited activity against CYP2C19, CYP2D6, and CYP3A4.

- GS-9350 has reduced potential than ritonavir for alterations in drug interactions due to enzyme inhibition or induction.

- GS-9350 was used as a single agent, with other agents, or with elvitegravir/emtricitabine/tenofovir (ATR) in HIV patients.

Conclusions

- GS-9350 is being evaluated in Phase I studies in HIV-infected patients.

Acknowledgments

- Yuli Wang, Chris Yang, Leah Tong, Quynh Iwata and Bill Lee
- Srini Ramanathan, David Warren, Kitty Yale and Andrew Cheng

References

3. Xu L and Desai MC: Pharmacokinetic enhancers for HIV drugs. Curr Opinion in
4. Desoxy-Ritonavir served as the lead compound for SAR studies. GS-9350 is a potent, selective, mechanism-based CYP3A inhibitor that blocks a single activity and has limited activity against CYP2C19, CYP2D6, and CYP3A4.

5. Impact of lipophilic enhancers on the absolute bioavailability of atazanavir coformulated with ritonavir, elvitegravir/emtricitabine/tenofovir, and GS-9350.


9. GS-9350 is a potent, selective, mechanism-based CYP3A inhibitor that blocks a single activity and has limited activity against CYP2C19, CYP2D6, and CYP3A4.

10. GS-9350 is a potent, selective, mechanism-based CYP3A inhibitor that blocks a single activity and has limited activity against CYP2C19, CYP2D6, and CYP3A4.


12. Xu L and Desai MC: Pharmacokinetic enhancers for HIV drugs. Curr Opinion in