Retrovirology

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Oral presentation

Development of Bevirimat (PA-457): first-in-class HIV maturation inhibitor

Graham P Allaway*

Address: Panacos Pharmaceuticals Inc., Gaithersburg, Maryland, USA
* Corresponding author

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Bevirimat is the first in a new class of HIV drugs called maturation inhibitors that specifically inhibit the last step in processing of Gag, the conversion of capsid-SP1 (p25) to capsid (p24). Following bevirimat treatment, viral particles released from infected cells have abnormal core structures and are non-infectious. The compound is a potent inhibitor of HIV-1 replication and retains activity against drug resistant isolates. It is synergistic with most approved drugs in vitro. Bevirimat is metabolized by glucuronidation and has minimal potential for clinically significant drug interactions.

Bevirimat has good oral bioavailability and long half-life (2.5–3 days) in humans, making it suitable for once-daily oral dosing. It has been well tolerated in clinical studies, following administration to more than 300 people for up to 2 weeks. In a Phase 2a study, 10 days of bevirimat monotherapy at 200 mg/day resulted in >1 log median viral load reduction. A Phase 2b study was recently initiated where bevirimat is being studied in combination with approved drugs in a dose escalation format, in order to identify optimal dose(s) for Phase 3 clinical trials.