



Update on the Development of Brincidofovir (CMX001) for Smallpox and Other Indications

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Dr. Trost presented the structure and described the mechanism of action of brincidofovir (CMX001) as inhibition of replication of multiple dsDNA viruses including adenovirus, CMV and *Variola major*. Dr. Trost described the key attributes of brincidofovir relative to intravenously administered cidofovir (Vistide): improved ease of use, oral bioavailability, increased potency and decreased nephrotoxicity. He explained that brincidofovir has demonstrated a favorable resistance profile for CMV, and has a low risk of significant drug-drug interactions. Dr. Trost stated that it has been administered to more than 900 human subjects, many with life-threatening illnesses caused by dsDNA viruses and has been studied in patients with renal and hepatic impairment as well as pediatric subjects as young as 1 month of age. Dr. Trost described how safety and efficacy data from clinical development of brincidofovir for other indications has informed the smallpox development program and that a Phase 3 study for prevention of CMV in immunocompromised transplant patients is currently enrolling with doses that, scaling from efficacious doses in animal models, are also proposed for treatment of smallpox. Dr. Trost presented the status of the animal efficacy development program including results demonstrating the activity of brincidofovir in a blinded efficacy study in the rabbitpox model in which two different regimens provided a statistically significant survival benefit when treatment was initiated after appearance of clinical signs of infection. Dr. Trost informed the panel that in the first half of 2013, BARDA notified Chimerix of its intention to exercise an option to provide additional funds (Option Segment 1) to further advance the development of brincidofovir for treatment of smallpox. Dr. Trost stated that supported by the work of BARDA's "Animal Model Development Program," Chimerix will initiate pharmacokinetic studies of brincidofovir in the rabbitpox and ectromelia models in the last quarter of 2013 to support dose selection for pivotal efficacy studies. Dr. Trost indicated that if approved brincidofovir will be available in tablet and liquid formulations and that its manufacture has been validated at commercial scale with long term stability of multiple years.

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