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PRELIMINARY PROFILE OF THE ANTIVIRAL ACTIVITY, METABOLIC EFFECTS AND SAFETY OF DMP-450, A NOVEL CYCLIC UREA PROTEASE INHIBITOR

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OBJECTIVE: DMP-450 is a non-peptidomimetic, water-soluble, cyclic urea that is a selective inhibitor of HIV-1 protease. DMP-102 is a Phase I/II, randomized, indinavir-controlled, dose escalation study to evaluate the antiviral activity and safety of DMP-450.

METHODS: Antiretroviral-naïve patients with HIV RNA >10 000 copies/ml and unrestricted CD4 counts were randomized to receive DMP-450 at three different doses or indinavir 800 mg three times daily, in combinations with stavudine and lamivudine. Fifteen patients (12 DMP-450, three indinavir) were enrolled in each cohort at the following doses: Cohort 1 (a) 750 mg three times daily; Cohort 2 (b) 1250 mg twice daily; and Cohort 3 (c) 1250 mg three times daily. Patients receiving indinavir are known as (d).

RESULTS: Enrolment has been completed and the treatment periods range from 2–36 weeks. The median logviral load at baseline is (a) 4.60, (b) 5.00, (c) 4.25 and (d) 4.66. Preliminary data indicate that DMP-450 is well tolerated and no significant laboratory toxicities have been observed. Most adverse events have been mild and self-limited. At the time of abstract submission, the number of patients who have completed through week 4 are (a) 12, (b) 6, (c) 11 and (d) 6. The week 4 mean log₁₀ viral load change from baseline has been (a) –1.82, (b) –2.39 (c) –2.24 and (d) –2.25. Week 12 data are available for (a), (c) and (d) patients (*n*=12, 10 and 4 respectively). Week 12 log₁₀ viral load change from baseline has been (a) –2.64, (c) –3.05 and (d) –2.89. Week 4 data show that patients receiving

indinavir demonstrated a statistically significant increase in total serum cholesterol compared to all three DMP450 doses. The study is ongoing and updated data will be presented.

CONCLUSION: To date, DMP-450 appears to have good antiviral activity and tolerability at all doses tested.

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