**INTRODUCTION**

Last year data were presented on the Idenix protease inhibitor program, which showed better selectivity and activity as compared to first generation protease inhibitors. The compound series also exhibited a favorable early PK profile in preclinical species. Idenix has advanced two novel macrocyclic HCV protease inhibitors, IDX136 and IDX316, as well as their pharmacokinetic profile in the mouse, rat and monkey.

**METHODS**

IC₅₀ (50% inhibition concentration) determination: Cleavage of a synthetic peptide by recombinant HCV NS3-4A protease activity from human 1a, 2a, 2a, and 3a was measured in the presence of compound.

Binding kinetics: The binding kinetics of IDX316 to NS3-4A were determined by surface plasmon resonance. Association (kₐ) was fast, and dissociation (kₐ) was slow, with a dissociation half-life (t½) of nearly 17 minutes.

**RESULTS**

 IDX316 binds to protease tightly, with an equilibrium constant (Kᵢ) less than 3 nM, as determined by surface plasmon resonance. Association (kₐ) was fast, and dissociation (kₐ) was slow, with a dissociation half-life (t½) of nearly 17 minutes.

**DISCUSSION**

The plasma half-life of IDX316 ranged from 4.0 to 5.2 h in mice, rats and monkeys.

The oral bioavailability of IDX316 was nearly 20% in mice, rats and monkeys.

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**REFERENCES**