Ibrexafungerp (formerly SCY-078) Demonstrates Activity Against *Candida auris*: *In Vitro*, *In Vivo* and Clinical Case Studies of Candidemia

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Objectives

Candida auris is a growing global threat; a pathogen associated with high mortality (up to 60%), multi-drug resistance, the ability to spread from person-to-person and surface-to-person, presenting high risk for outbreaks in healthcare facilities. Ibrexafungerp is a novel IV/oral glucan synthase inhibitor (triterpenoid) antifungal with activity against *Candida*, *Aspergillus* and *Pneumocystis* spp, in Phase 3 development. Given the potent activity of ibrexafungerp against *Candida* spp., Scynexis has embarked on a development program to understand the activity and effectiveness against *Candida auris*. We will present the current preclinical and clinical data sets of ibrexafungerp against *Candida auris*.

Methods

In vitro studies tested ibrexafungerp against >100 clinical isolates of *C. auris*. Other *in vitro* studies evaluated the effects of ibrexafungerp against *C. auris* biofilms. *In viv*o activity against *C.auris* was evaluated using a disseminated murine model and a cutaneous infection guinea pig model. In humans, an ongoing open-label trial of ibrexafungerp for treatment of patients with infections caused by *C. auris* (the CARES study) has been initiated in the USA and India.

Results

In vitro and in vivo studies demonstrated that ibrexafungerp is active against *C. auris*, including MDR strains. The MIC mode for ibrexafungerp was 1ug/ml and the MIC_{50} and MIC_{90} were 0.5 and 1 ug/ml, respectively. Many echinocandin resistant *C. auris* isolates have shown susceptibility to ibrexafungerp. Further, ibrexafungerp has been shown to reduce biofilm thickness. In animal models of *C. auris* infection, treatment with ibrexafungerp resulted in improved survival and reduced fungal burden in both the murine model of disseminated infection and the guinea pig model of cutaneous infection as compared to untreated controls. In humans, two patients with difficult to treat *C. auris* candidemias were enrolled in the CARES study and responded positively to oral ibrexafungerp with eradication of the infection.

Conclusion

This data demonstrates that ibrexafungerp possess potent *in vitro* and *in vivo* activity as well as promising clinical activity. Therefore, continued clinical evaluation of ibrexafungerp as an option to treat *C. auris* infections is warranted.