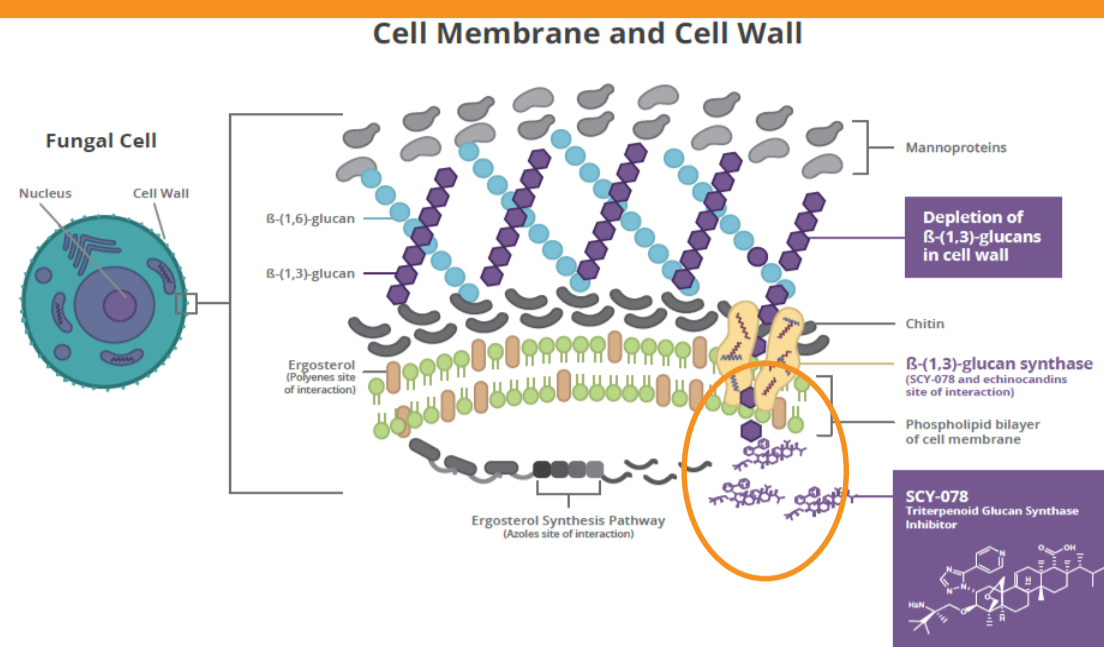


SCY-078: A first-in-class, orally-bioavailable, glucan synthase inhibitor has broad spectrum activity against *Candida*, *Aspergillus* and *Pneumocystis* spp.

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BACKGROUND

SCY-078 is a first-in-class oral and intravenous (IV) triterpenoid glucan synthase inhibitor with differentiated bindings from the echinocandins and broad activity against *Candida*, *Aspergillus* and *Pneumocystis* spp., currently in clinical development for the treatment of various fungal infections. *In vitro* studies show that SCY-078 has potent, cidal activity against wild-type and drug-resistant *Candida* strains, including the emerging pathogen multidrug-resistant *C. auris*. Activity *in vivo* has been shown in animal models of infection with *Candida*, *Aspergillus* and *Pneumocystis* spp. The pre-clinical profile of SCY-078 supports continued development of SCY-078 as a next generation antifungal agent.



METHODS

The *in vitro* activity of SCY-078 has been evaluated against ≈1500 wild-type (WT) and drug-resistant *Candida* spp. isolates and ≈500 WT and azole-resistant *Aspergillus* spp. across eight independent laboratories. The *in vivo* activity of SCY-078 has been evaluated across seven independent laboratories in murine models of invasive candidiasis, invasive aspergillosis and pneumocystis pneumonia. SCY-078 was also evaluated in a rabbit model of pulmonary aspergillosis, given alone and in combination with isavuconazole. The determination of efficacy across these studies was based on survival, kidney and/or lung fungal burden, serum galactomannan index (GMI) and/or nuclei and asci counts, as appropriate for each model. Plasma exposure was assessed across the dose ranges of each study in order to guide exposures in clinical studies.

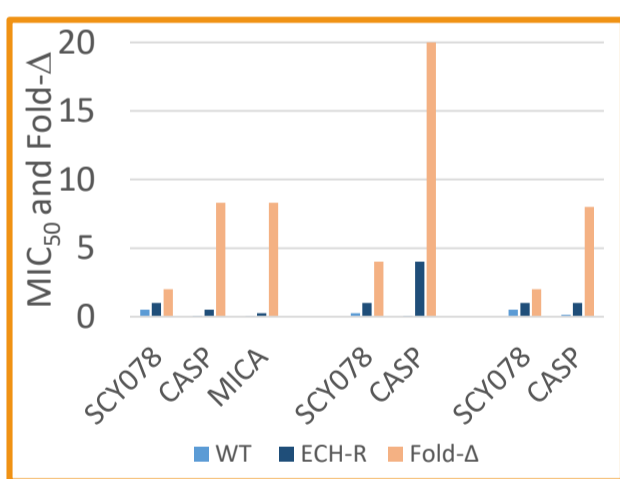
RESULTS

SCY-078 *In Vitro* Activity Against *Candida* and *Aspergillus* spp.^a

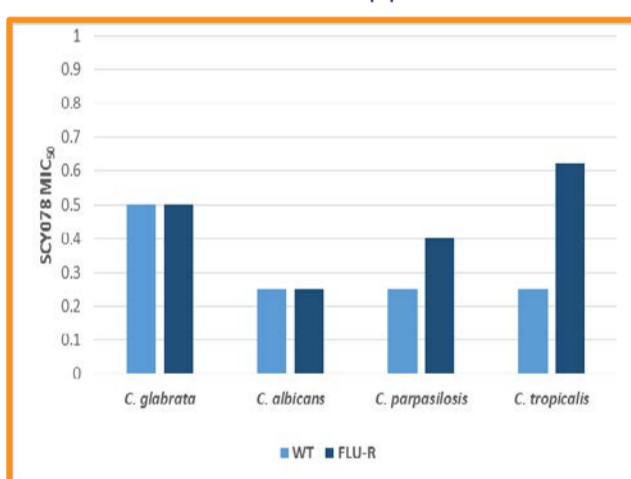
<i>Candida</i> Species	N	*MIC ₉₀	<i>Aspergillus</i> Species	N	*MEC ₉₀
<i>C. glabrata</i>	343	0.25 - 4	<i>A. fumigatus</i>	175	0.008 - 0.25
<i>C. albicans</i>	258	0.06 - 0.25	<i>A. flavus</i>	102	<0.06 - 4
<i>C. tropicalis</i>	186	0.25 - 1	<i>A. niger</i>	56	0.009 - 0.06
<i>C. parapsilosis</i>	181	0.25 - 1	<i>A. terreus</i>	99	0.125
<i>C. krusei</i>	130	0.5 - 2	Azole-R	18	0.03 - 0.5
<i>C. auris</i>	116	1			

*Represents the range of MIC₉₀/MEC₉₀ values obtained across 7 independent laboratories

SCY-078 Demonstrated Superior Activity vs ECHs Against Isolates with *fks* Mutations^b



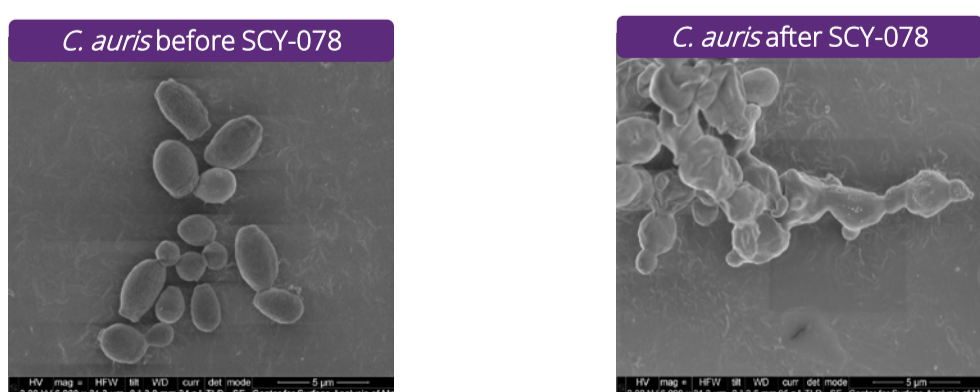
SCY-078 Demonstrated Potent Activity Against FLU-resistant *Candida* spp.^c



SCY-078 activity against a panel of *C. auris* isolates with elevated ECH MICs^e

<i>C. auris</i> Isolate	Minimum Inhibitory Concentration (μg/ml)			
	Anidulafungin	Caspofungin	Micafungin	SCY-078
1	8	1	4	1
2	16	1	4	1
3	1	16	1	1
4	2	16	2	1
5	4	.5	.5	0.5
6	>16	>16	>8	0.5
7	4	>16	1	1

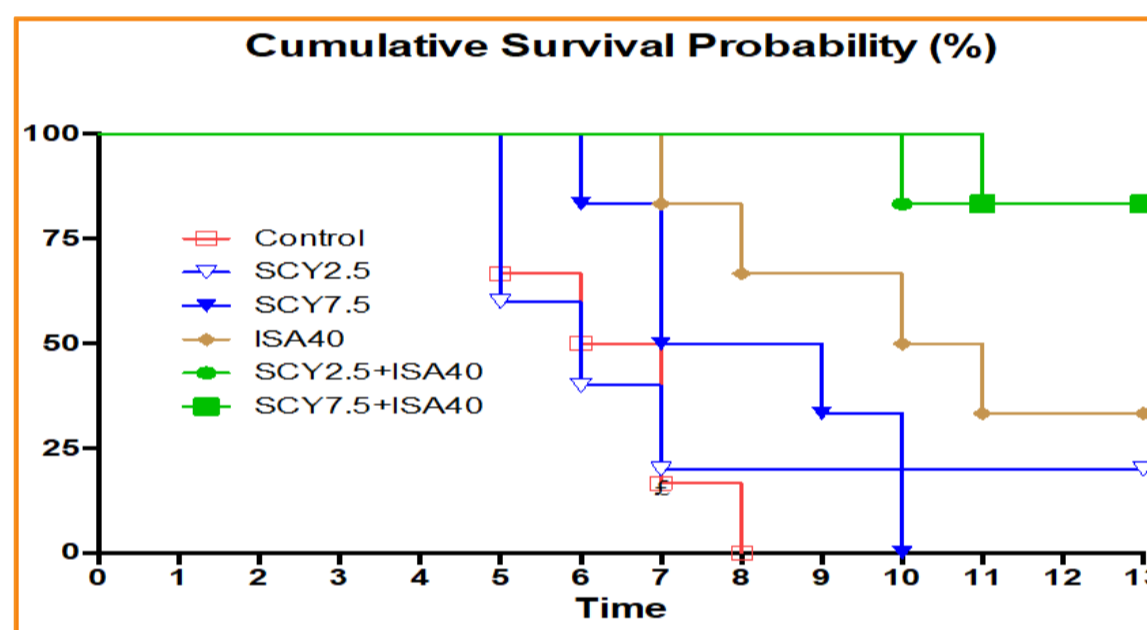
Scanning Electron Micrographs Showing Cidal Activity of SCY-078^f



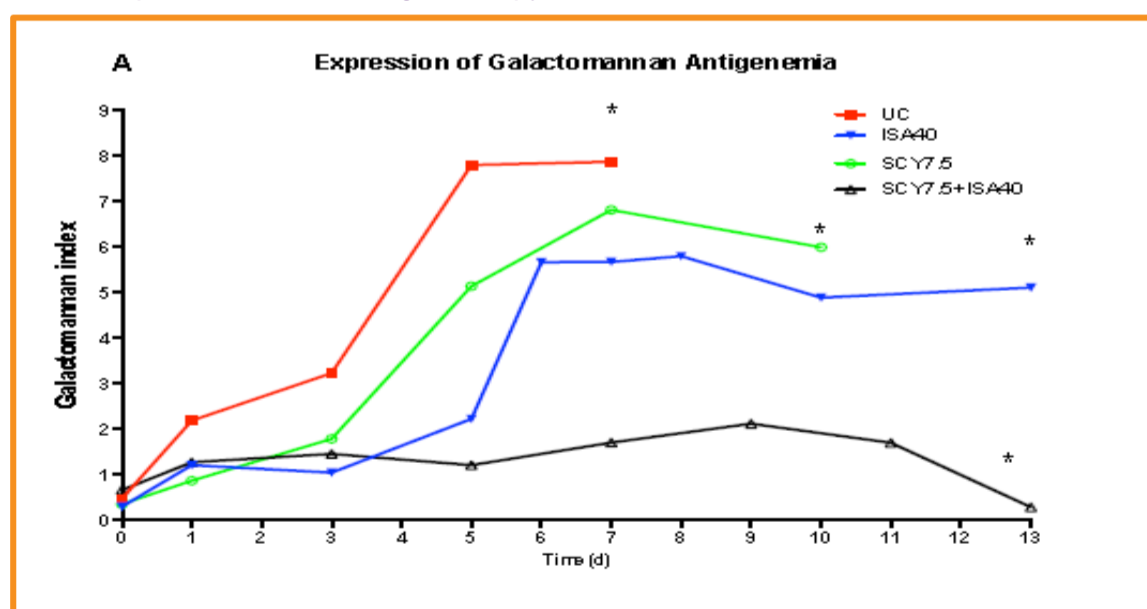
CONCLUSION

SCY-078's broad spectrum activity, high potency and flexibility for IV and PO dosing support its continued development as a new antifungal agent.

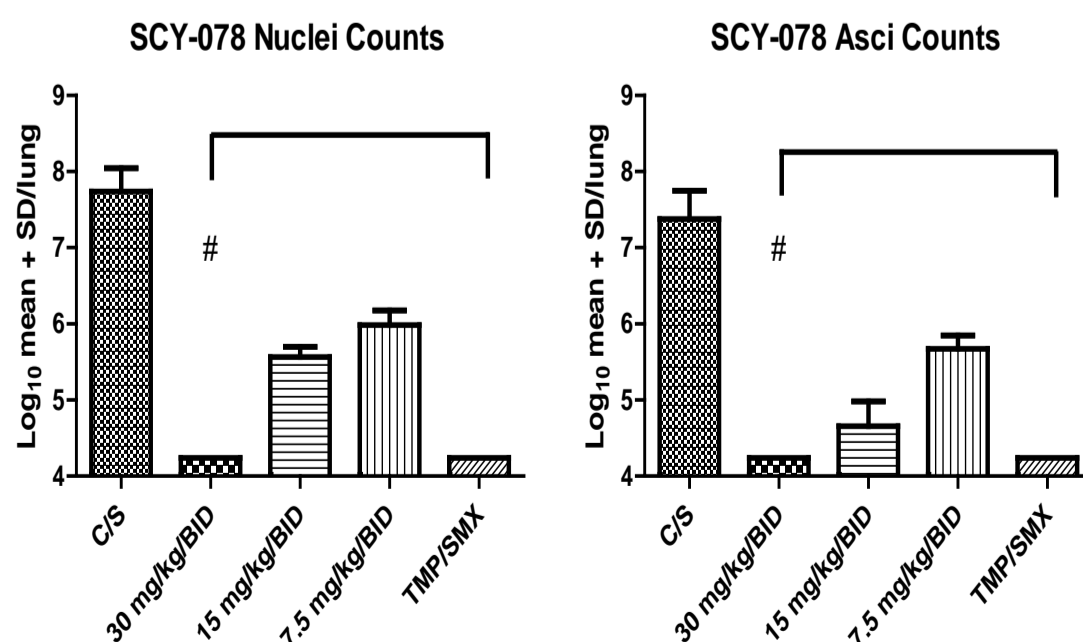
SCY-078 Activity in a Rabbit Model of Pulmonary Aspergillosis^d



Lower GMI in rabbits treated with combination regimen of SCY7.5+ISA40 in comparison to that of single therapy of SCY7.5, ISA40, and untreated controls^d



SCY-078 Activity in a Murine Model of Pneumocystis^g



^aData on file

^bBorroto-Esoda et al. 2016, 13th ASM conference on Candidiasis; poster #45

^cBorroto-Esoda et al. 2016, 13th ASM conference on Candidiasis; poster #44

^dWalsh et al. 8th Advances Against Aspergillosis 2018

^eBerkow et al. AAC July, 2017

^fHager et al. 2018 ASM Microbe; poster #497

^gAshbaugh et al. 2018, 28th ECCMID; poster #969

