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# **SCY-247, A SECOND-GENERATION IV/ORAL TRITERPENOID ANTIFUNGAL: *IN VITRO* ACTIVITY AGAINST A BROAD-SPECTRUM OF FUNGAL PATHOGENS, AND DOSE-DEPENDENT TISSUE DISTRIBUTION *IN VIVO***

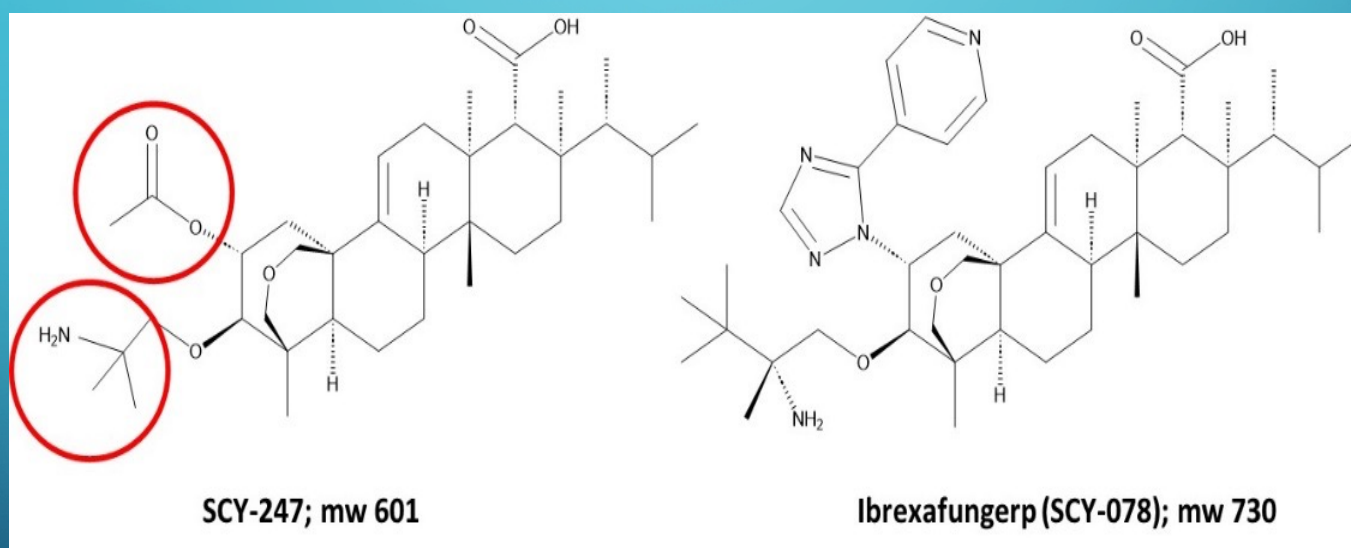
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>30 Fungerp analogs were screened resulting in selection of SCY-247



Structural comparison of Ibrexafungerp with second-generation derivative-SCY-247.

[illegible]

- **Validated MoA- inhibition of glucan synthase**
  - **Not found in human cells**
- **Echinocandins have same MOA (i.e. inhibiting Beta-1,3-glucan synthase. However,**
  - **Differentiated binding vs. echinocandins**
  - **Activity against echinocandin-resistant pathogens**



# SCY-247: MICROBIOLOGY PANEL TESTED

Yeasts		Moulds		Dimorphics
<i>C. albicans</i>		<i>A. flavus</i>		<i>Coccidioides immitis</i>
<i>C. auris</i>		<i>A. fumigatus</i>		<i>Histoplasma spp.</i>
<i>C. glabrata</i>		<i>A. nidulans</i>		<i>Blastomyces spp</i>
<i>C. kefyr</i>		<i>A. terreus</i>		
<i>C. krusei</i>		<i>Acremonium</i>		
<i>C. metapsilosis</i>		<i>Fonsecaea pedrosoi</i>		
<i>C. orthopsilosis</i>		<i>Fusarium oxysporum</i>		
<i>C. parapsilosis</i>		<i>F. solani</i>		
<i>C. tropicalis</i>		<i>Pseudallescheria boydii</i>		
<i>Rhodotorula spp.</i>		<i>Rhizopus oryzae</i>		
<i>Saccharomyces spp.</i>		<i>Scedosporium apiospermum</i>		
<i>Cryptococcus neoformans</i>		<i>S. prolificans</i>		
<i>Trichosporon asahii</i>		<i>Paecilomyces spp.</i>		
<i>Geotrichum capitatus</i>		<i>Trichoderma spp.</i>		
<i>Kodamaea ohmeri</i>				

## SCY-247: MICROBIOLOGY CONT'D

SCY-247 performed well in *in vitro* susceptibility studies, with comparable activity to ibrexafungerp across the entire panel studied

Fungus ( # of isolates)	<i>In Vitro</i> Concentrations	SCY-247 ( $\mu\text{g/ml}$ )
<i>Candida</i> spp. (47)	MIC50	0.5
<i>Aspergillus</i> spp. (20)	MEC50	0.063
Dimorphics* (15 each)	MEC50	<0.25

\**Coccidioides*, *Histoplasma*, *Blastomyces*

# SCY-247: ACTIVITY AGAINST RESISTANT ISOLATES

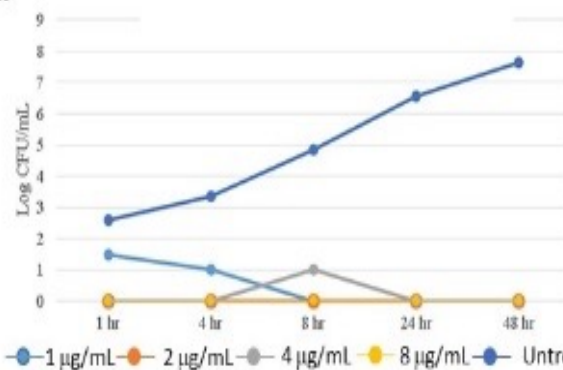
The activity profile of SCY-247 against MDR resistant strains

- The activity of SCY-247 was evaluated against *Candida* and *Aspergillus* isolates shown to be resistant to echinocandins and/or azoles
  - Evaluated in 12 *C. albicans*, 22 *C. glabrata* and 18 *Aspergillus* spp. isolates

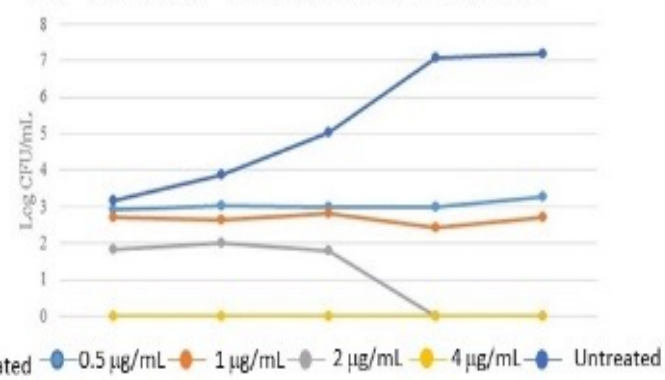
	SCY-247 (µg/ml)
<i>C. albicans</i> (MIC)	0.125 - 4
<i>C. glabrata</i> (MIC)	<0.03 - 1
<i>Aspergillus</i> (MEC)	0.03 - 4

# Growth over 48 hours of *C. albicans* and *C. auris* exposed to SCY-247

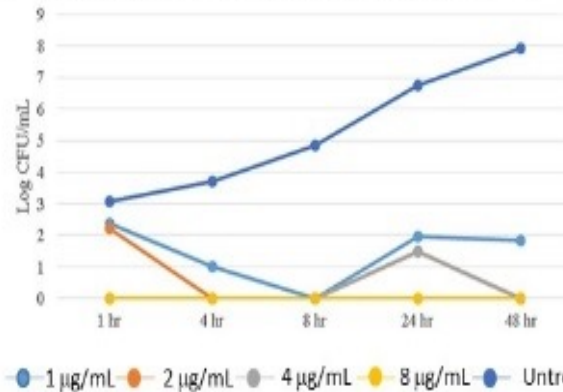
**A.** SCY-247 versus *C. albicans* 11036



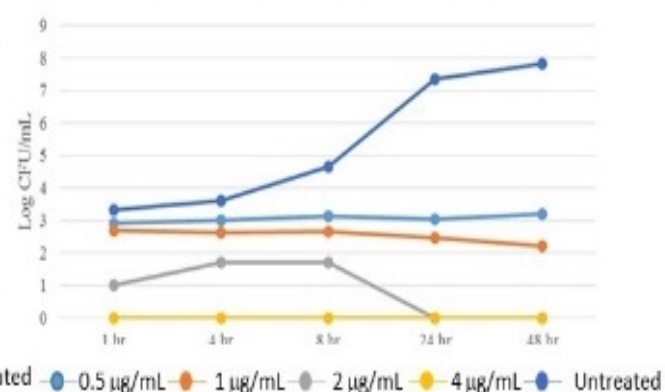
**C.** SCY-247 versus *C. auris* 35653



**B.** SCY-247 versus *C. albicans* 27884

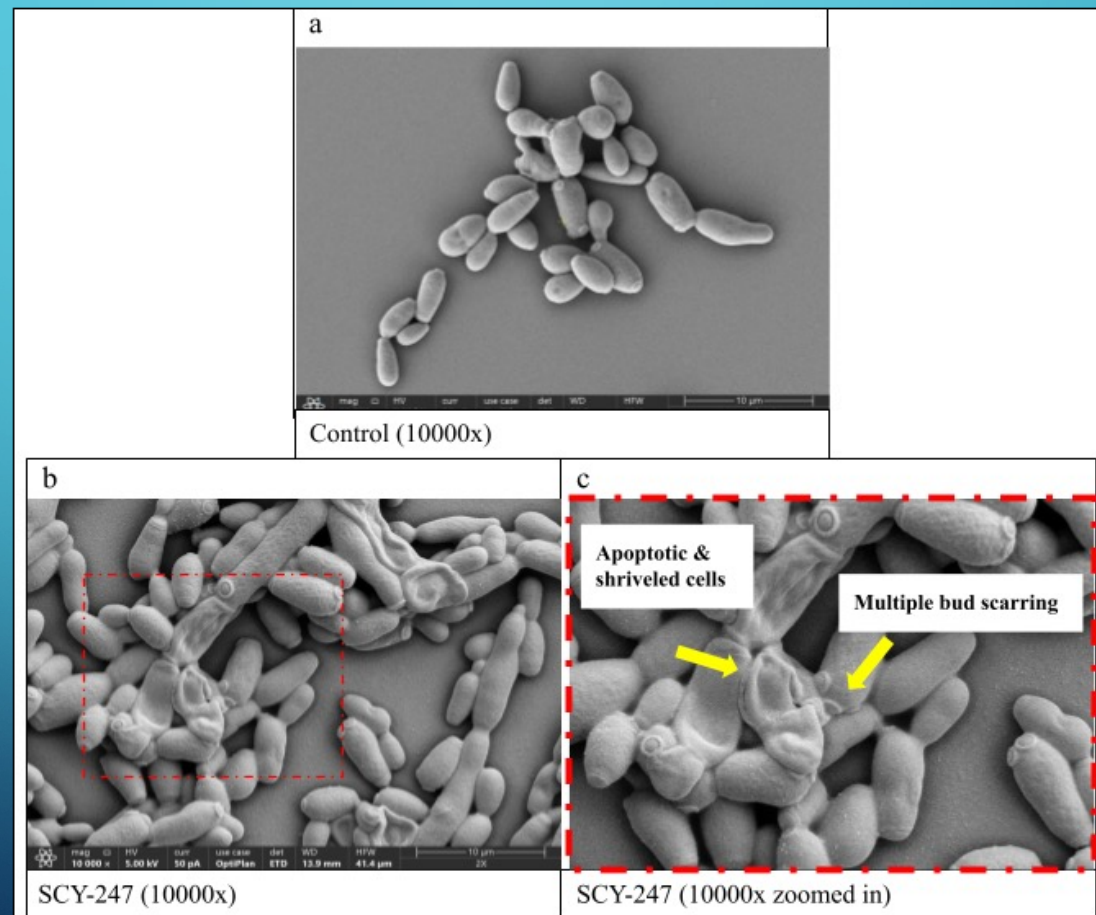


**D.** SCY-247 versus *C. auris* 35646





# SEM images of *Candida auris* 35654 exposed to SCY-247 versus untreated control



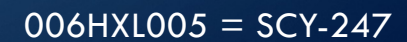


## SCY-247: *IN VITRO* STUDIES KEY FINDINGS

- Broad-spectrum activity against yeasts, moulds and dimorphic fungi
- Potent *in vitro* activity:
  - Dose Dependent Effect
  - *In vitro* fungicidal activity against *Candida*
  - SEM showed that SCY-247 treated *C. auris* cells were enlarged, shriveled, had excessive budding scars, holes in the cell wall, their cytokinesis was inhibited, and apoptosis was observed

# SCY-247: PROFILE COMPARISON TO THE THREE EXISTING ANTIFUNGAL CLASSES

	SCY-247	Echinocandin	Azole	Polyene
Spectrum of Activity	Active vs. <i>Candida albicans</i>	✓	✓	✓
	Active vs. non- <i>albicans</i> <i>Candida</i>	✓		✓
	Active vs. azole-resistant	✓		✓
	Active vs. echinocandin-resistant	✓		✓
	Active vs. <i>Aspergillus</i> spp.	✓	✓	✓
	Extensive Tissue Distribution	✓	✓	✓
Safety	Lack of renal, hepatic, CNS Tox.	✓		✓
	Low risk for DDIs	✓		✓
	Oral/IV Administration	✓	✓	







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