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# ECCMID SCY-078 Scientific Data Presentation Conference Call

April 25, 2017

4:05pm ET

# Forward-Looking Statements

Certain statements regarding SCYNEXIS, Inc. (the “Company”) made in this presentation constitute forward-looking statements, including, but not limited to, statements regarding our business strategies and goals, plans and prospects, market size, adoption rate, potential revenue, clinical validity and utility, growth opportunities, future products and product pipeline. Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from our expectations. These risk and uncertainties include, but are not limited to: our ability to successfully develop SCY-078, including our ability to obtain FDA approval for SCY-078; the expected costs of studies and when they will begin; and our reliance on third parties to conduct our clinical studies. Forward-looking statements may be identified by the use of the words “anticipates,” “expects,” “intends,” “plans,” “could,” “should,” “would,” “may,” “will,” “believes,” “estimates,” “potential,” or “continue” and variations or similar expressions. These statements are based upon the current expectations and beliefs of management and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks and uncertainties include, but are not limited to, risks and uncertainties discussed in the Company's most recent reports filed with the Securities and Exchange Commission ("SEC") including under the caption “Risks Factors” in the Company’s annual report on Form 10-K, which factors are incorporated herein by reference. Readers are cautioned not to place undue reliance on any of these forward-looking statements. The Company undertakes no obligation to update any of these forward-looking statements to reflect events or circumstances after the date of this presentation, or to reflect actual outcomes.

# Agenda

| | |
|---|---|
| Objectives and Introductions | Marco Taglietti, M.D. |
| ECCMID SCY-078 *In Vitro* Data | Mahmoud Ghannoum Ph.D. |
| ECCMID SCY-078 Clinical Data | Oliver Cornely, M.D. |
| Summary | David Angulo, M.D. |
| Q&A Session | |

# Objectives

- To provide an update on recent R&D data presented at ECCMID 2017 in Vienna, Austria
  - Eight SCY-078 presentations
    - SCY-078 demonstrating activity against emerging global health threat, *Candida auris*
    - *In vitro* combination of SCY-078 and azoles and Amphotericin B, demonstrating synergy against *Aspergillus* spp.
    - SCY-078 activity against *Candida* spp. and *Candida* in biofilm
    - Clinical efficacy of oral SCY-078 in Invasive Candidiasis and Vulvovaginal Candidiasis
    - Two Drug-Drug Interactions demonstrating SCY-078 minimal interactions

# Introductions

- Mahmoud Ghannoum, Ph.D.
  - Professor and Director of the Center for Medical Mycology at Case Western Reserve University and University Hospitals Cleveland Medical Center, Cleveland, OH, USA
  - To discuss SCY-078 *in vitro* data presented at ECCMID
- Oliver Cornely, M.D.
  - Professor of Internal Medicine and Medical Director, Clinical Trials Center Cologne, University of Cologne, Cologne, Germany
  - To discuss SCY-078 clinical data presented at ECCMID
- David Angulo, M.D.
  - Chief Medical Officer, SCYNEXIS, Inc.
  - To provide an ECCMID SCY-078 summary

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# ECCMID SCY-078 *In Vitro* Presentations

Mahmoud Ghannoum, Ph.D.

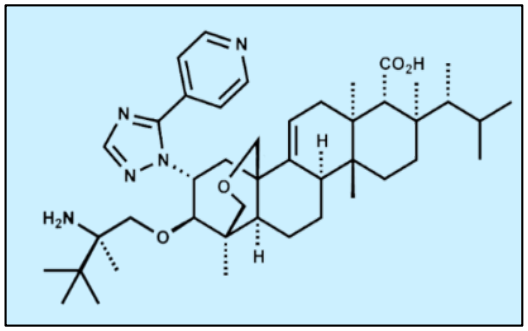
*Disclosure: Dr. Ghannoum receives grant/research support and is a consultant to SCYNEXIS.*

# The emerging *Candida auris*: antifungal activity of SCY-078, a novel glucan synthesis inhibitor, on growth morphology and biofilm formation

*E Larkin, C Hager, J Chandra, PK Mukherjee, M Retuerto, I Salem, L Long, N Isham, L Kovanda, K Borroto-Esoda, S Wring, D Angulo and MA Ghannoum.*

- *Candida auris* is an emerging MDR yeast species
- It causes invasive infections with high mortality
- It has reduced susceptibility to the three major classes of available antifungals (azoles, polyenes, and echinocandins)
- Infections have been found globally
- SCY-078 is a novel IV/oral semi-synthetic triterpenoid antifungal weighing 730 Da
- MOA- inhibition of Beta 1,3 D glucan synthase inhibition; its binding properties are different than echinocandins

Triterpenoid- SCY-078



Caspofungin

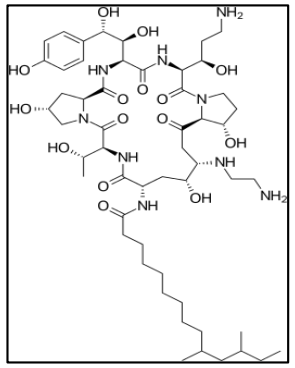


Figure 1. SCY-078 chemical structure versus Caspofungin

MIC values for SCY-078 and antifungal comparators against a panel of *C. auris* clinical isolates (n=16)

| | MIC (µg/mL) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | SCY-078 | AFG | MFG | CAS | 5FC | FLU | ISA | ITC | POS | VRC | AMB |
| Range | 0.5-2 | 0.125-0.25 | 0.25-2 | 0.25-1 | 0.5-1 | 1->64 | 0.004-0.25 | <0.063-1 | 0.25-1 | <0.063-1 | 0.5-8 |
| $MIC_{50}$ | 1 | 0.125 | 1 | 0.5 | 0.5 | 16 | 0.063 | 0.5 | 0.25 | 0.5 | 2 |
| $MIC_{90}$ | 1 | 0.25 | 1 | 1 | 1 | >64 | 0.125 | 1 | 0.5 | 1 | 4 |

# The emerging *Candida auris*: antifungal activity of SCY-078, a novel glucan synthesis inhibitor, on growth morphology and biofilm formation

## SCY-078 demonstrated potent *in vitro* activity against *Candida auris*

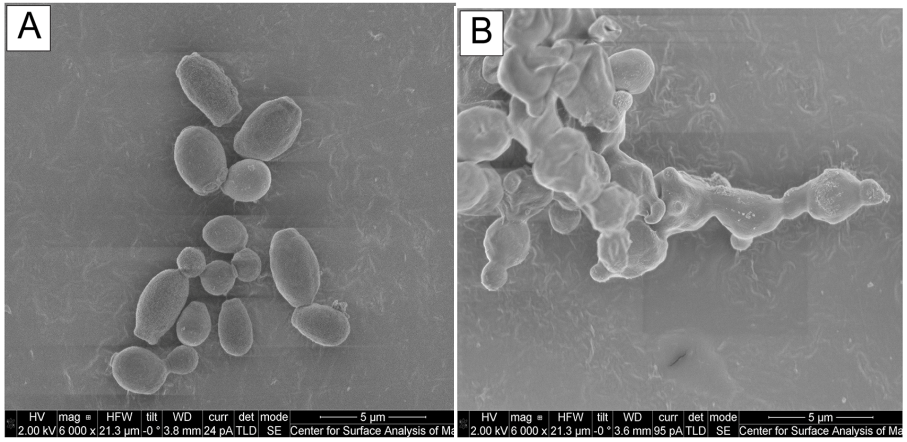



**Figure 3**. Scanning electron micrograph of *C. auris* treated with: (A) no drug (control) and (B) SCY-078, at 1X MIC (0.5 mg/L)

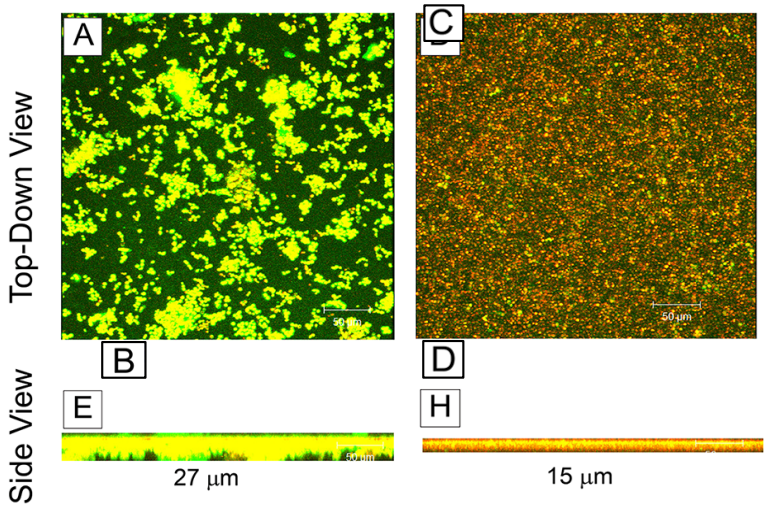



**Figure 4.** Confocal scanning laser microscopy analyses of the effect of SCY-078 on biofilms formed by *C. auris* exposed to: (A, B) no drug (control) and (C, D) SCY-078, at 4 mg/L

## CONCLUSIONS

- SCY-078 had potent antifungal activity against C. *auris*, with a susceptibility profile similar to that of echinocandins and activity against C. *auris* biofilm
- SCY-078, the first orally bioavailable 1,3-β-D-glucan synthase inhibitor, could be an important addition to the armamentarium against this MDR pathogen.



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#EV0123

# Evaluation of the antifungal activity of SCY-078 in combination with other antifungals against *Aspergillus* strains

*Lisa Long, BA 1; Emily L. Larkin, BA 1; Katyna Borroto-Esoda, PhD 2; Steve Wring, PhD 2; David Angulo, MD 2; and Mahmoud A. Ghannoum, Ph.D.*

## SCY-078 is synergistic in combination with an Azoles or Amphotericin B and may provide a new therapeutic approach to treatment of *Aspergillus* infections

Table 1. MIC values (µg/mL) alone & in combination for SCY-078 with other antifungal agents against *A. fumigatus* (test performed in duplicate, representative value displayed)

| | SCY-078 with Isavuconazole (ISA) | | | | | | SCY-078 with Voriconazole (VRC) | | | | | | SCY-078 with Amphotericin B (AmB) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | MIC Alone | | MIC Combo | | FICI | Interpretation* | MIC Alone | | MIC Combo | | FICI | Interpretation* | MIC Alone | | MIC Combo | | FICI | Interpretation* |
| Strain | SCY-078 | ISA | SCY-078 | ISA | SCY-078 + ISA | | SCY-078 | VRC | SCY-078 | VRC | SCY-078 + VRC | | SCY-078 | AmB | SCY-078 | AmB | SCY-078 + AmB | |
| WT 20438 | 4 | 1 | 0.016 | 0.5 | 0.50 | SY | 4 | 1 | 0.125 | 0.25 | 0.27 | SY | 4 | 4 | 0.016 | 0.5 | 0.13 | SY |
| WT 28378 | 4 | 1 | 0.125 | 0.25 | 0.28 | SY | 4 | 0.25 | 0.5 | 0.16 | 0.19 | SY | 4 | 2 | 0.016 | 0.5 | 0.25 | SY |
| WT 28382 | 4 | 1 | 0.063 | 0.25 | 0.27 | SY | 8 | 0.5 | 0.5 | 0.125 | 0.31 | SY | 4 | 4 | 0.016 | 1 | 0.25 | SY |
| WT 28401 | 4 | 1 | 0.25 | 0.25 | 0.31 | SY | 8 | 2 | 0.25 | 0.5 | 0.28 | SY | 4 | 4 | 0.016 | 1 | 0.25 | SY |
| Azole-R 28383 | 4 | >8 | 0.063 | >8 | 1.02 | AD | 8 | >16 | 0.031 | >16 | 1.00 | AD | 4 | 2 | 0.125 | 2 | 1.03 | AD |
| Azole-R 28500 | 4 | >8 | 0.125 | >8 | 1.03 | AD | 4 | >16 | 1 | >16 | 1.25 | AD | 4 | 4 | 0.016 | 1 | 0.25 | SY |

SY= Synergistic, AD= Additive



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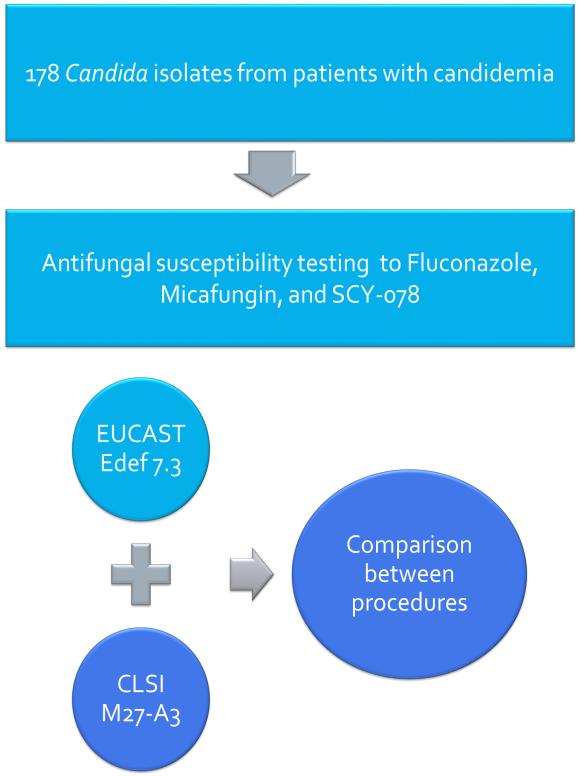
# Activity of SCY-078 against *Candida* spp. obtained by EUCAST and CLSI procedures

*L.J. Marcos-Zambrano[1,2], M Gómez-Perosanz[1,2], P. Escribano[1,2,3], E. Bouza[1,2,3,4], J. Guinea[1,2,3,4]*

We studied the antifungal activity of SCY-078 (an orally bioavailable 1,3-beta-D-glucan synthesis inhibitor), micafungin and fluconazole against 178 yeasts isolates causing fungemia in patients recently admitted to Gregorio Marañón hospital in Madrid, Spain, from Jan 2014 to Dec 2015.




| CLSI M27-A3 | Fluconazole | | Micafungin | | SCY-078 | |
|---|---|---|---|---|---|---|
| | CLSI | EUCAST | CLSI | EUCAST | CLSI | EUCAST |
| *C. albicans* (55) | 0.178 | 0.273 | 0.008 | 0.016 | 0.029 | 0.065 |
| *C. parapsilosis* (33) | 0.422 | 0.5 | 0.458 | 0.656 | 0.206 | 0.266 |
| *C. glabrata* (31) | 2.287 | 7.153 | 0.011 | 0.030 | 0.168 | 0.365 |
| *C. tropicalis* (8) | 0.25 | 0.353 | 0.035 | 0.051 | 0.066 | 0.353 |
| *C. krusei* (12) | 10.07 | 22.627 | 0.051 | 0.06 | 0.395 | 0.445 |
| Other *Candida* spp. (26) | 1.026 | 1.205 | 0.036 | 0.053 | 0.369 | 0.556 |
| Non-*Candida* (13) | 10.886 | 20.88 | 9.33 | 11.61 | 4.66 | 7.19 |
| FLC-R *Candida* isolates (24) | 19.5 | 24.6 | 0.043 | 0.049 | 0.291 | 0.423 |
| *fks*-mutant *Candida* isolates (9) | 0.925 | 1.714 | 0.169 | 0.734 | 0.338 | 0.793 |

## CONCLUSIONS

- SCY-078 is a promising drug with high in vitro antifungal activity against Candida and other yeast isolates causing fungemia
- CLSI and EUCAST standard procedures were comparable and suitable for antifungal susceptibility testing of this compound



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# The Novel Oral Glucan Synthase Inhibitor, SCY-078 shows in vitro activity against Candida spp. Biofilm

*L.J. Marcos-Zambrano, M Gómez-Perosanz, P. Escribano, E. Bouza, J. Guinea*

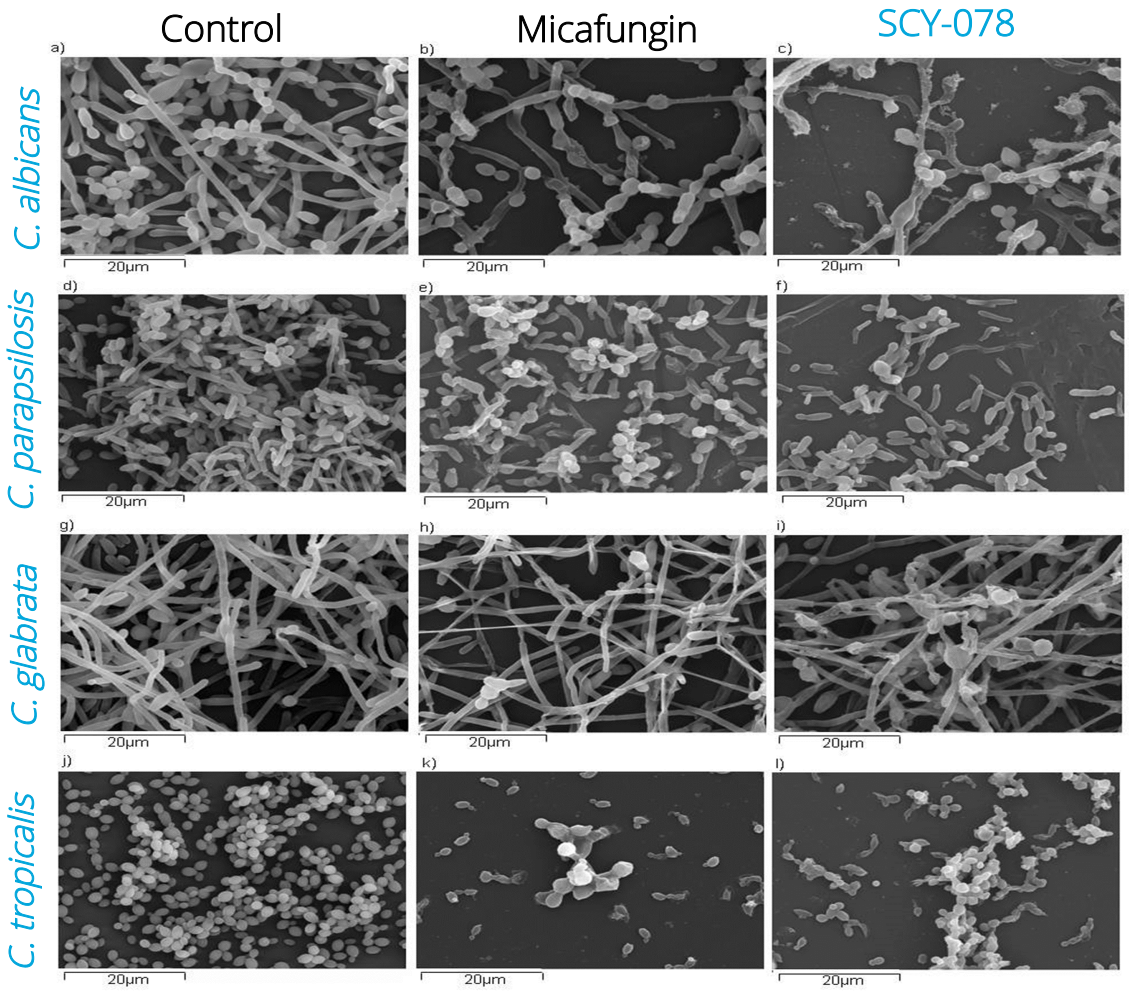
We studied the antifungal activity of SCY-078 and micafungin against the sessile forms of 178 Candida and non-Candida isolates causing fungemia in patients recently admitted to a large European hospital in Madrid, Spain

**ISOLATES**
C. albicans n= 55
C. parapsilosis n= 33
C. glabrata n=31
C. tropicalis n= 8
C. krusei n=12
Candida spp. n=26
Non-Candida yeasts n=13
Fluconazole resistant isolates n= 24
Echinocandin resistant isolates n= 9

Biofilm susceptibility to micafungin and SCY-078 by XTT

Determination of sessile MIC ($SMIC_{80}$) as 80% reduction of metabolic activity in comparison with untreated control

Scanning electron microscopy of 4 randomly chosen isolates.
C. albicans n=1
C. parapsilosis n=1
C. glabrata n=1
C. tropicalis n=1




## CONCLUSION

Our study showed that SCY-078 has a high in vitro activity against Candida invasive isolates in sessile forms (biofilms) comparable to micafungin



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# ECCMID SCY-078 Clinical Presentations

Oliver Cornely, M.D.

*Disclosure: Dr. Cornely receives grant/research support and is a consultant to SCYNEXIS.*

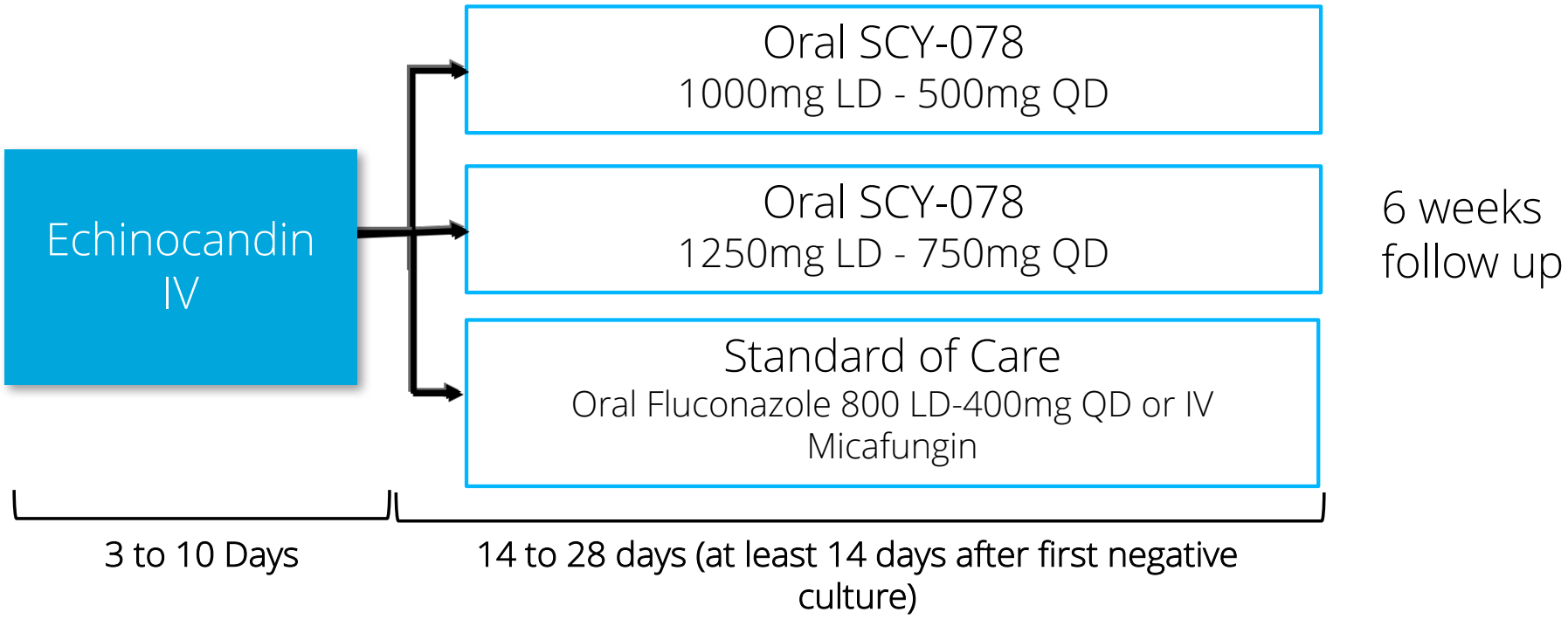
# SCY-078: Phase 2 Study in Invasive Candidiasis

## A Prospective, Phase 2, Multicenter, Open-Label, Randomized, Comparative Study to Estimate the Safety, Tolerability, Pharmacokinetics, and Efficacy of Oral SCY-078 vs. Standard-of-Care Following Initial Intravenous Echinocandin Therapy in the Treatment of Invasive Candidiasis (including Candidemia) in Hospitalized Non-neutropenic Adults (Mycoses Study Group 010)

*P. Pappas, University of Alabama at Birmingham*
*J. Pullman, Mercury Street Medical at Butte, MT*
*G. Thompson, University of California-Davis at Sacramento, CA*
*W. Powderly, A. Spec  Washington University School of Medicine at San Louis, MO*
*E. Tobin, Albany Medical Center at Albany, NY*
*J. Vazquez, Georgia Regents University at Augusta, GA*
*S. Wring, D.Angulo , S. Helou Scynexis, Inc. USA*
*and the Investigators of the Mycoses Study Group*

# SCY-078: Study 202 Invasive Candidiasis

- Primary Endpoints
  - Pharmacokinetics: Orally administered 750mg/day estimated to achieve the target exposure in ~ 85% of the IC population at steady state.
  - Safety, Tolerability
- Secondary Endpoints
  - Efficacy at end of antifungal therapy and relapse rates during follow up



# SCY-078: Study 202 Invasive Candidiasis - Results

| Global Response ITT | | SCY-078 500 mg N = 7 n (%) | SCY-078 750 mg N = 7 n (%) | Fluconazole 400 mg N =7 n (%) | Micafungin 100 mg N=1 n (%) |
|---|---|---|---|---|---|
| End of Treatment | Favorable | 5 (71.4) | 6 (85.7) | 5 (71.4) | 1 (100) |
| | Unfavorable | 2 | 1 | 2 | |
| | Reasons for unfavorable | • Never received study drug<br>• Discontinued due to a not drug related AE | • Withdraw consent after 1 dose | • Died - abdominal sepsis<br>• Discontinued - new + culture | |
| End of Follow up | Relapse* | 1<br>New positive blood culture during the 2 week FU period | 0 | 0 | |

* No imputation - Approximately 50% of the patients were "lost to follow up" before end of study.

# SCY-078: Study 202 Invasive Candidiasis - Results

## SCY-078 achieved target AUC at 1250mg loading dose, 750 mg maintenance dose

### 1250 mg (1st day), 750 mg (maintenance dose)

| Probability of $AUC_{0-24}$ >= 15.4 uM*hr (%) | Median $AUC_{0-24}$ | 90% PI of $AUC_{0-24}$ |
|---|---|---|
| 84.46 | 27.06 | 10.42 – 64.27 |

# SCY-078: Phase 2 Vulvovaginal Candidiasis Study Results

A multicenter, randomized, evaluator-blinded, active-controlled study to evaluate the safety and efficacy of oral SCY-078 in subjects with moderate to severe vulvovaginal candidiasis

*M. Roman, MD; C. Hernandez, MD; D. Blanco, MD; G Obrycki, S. Helou MD D. Angulo: MD*

| Efficacy Evaluation at Day 24 (per Protocol Population) | | | | | |
|---|---|---|---|---|---|
| N<br>Rates % | SCY-078<br>(3-Days)<br>(n= 24) | SCY-078<br>(5-Days)<br>(n= 26) | SCY-078<br>(Combined)<br>(n= 50) | Fluconazole<br>(n= 20) | % Δ SCY-078<br>(combined) vs.<br>Fluconazole |
| Clinical Cure | 19<br>*79.2%* | 19<br>*73.1%* | 38<br>*76%* | 13<br>*65%* | 11% |
| Clinical Cure Updated FDA Definition | 17<br>*70.8%* | 18<br>*69.2%* | 35<br>*70%* | 11<br>*55%* | 15% |
| **Efficacy Evaluation at Month 4** | | | | | |
| Recurrences Requiring Antifungal Therapy | 1<br>*4.2%* | 1<br>*3.8%* | 2<br>*4%* | 3<br>*15%* | -11% |

#P1738

#P1713

# SCY-078 showed no clinically meaningful effects on Tacrolimus or Rosiglitazone

*Angulo David, Murphy Gail, Atiee George, Corr Christy, Willett Michael, Wring Steve*

#P1713- PK Rosiglitazone Co-administered with SCY-078 vs. Rosiglitazone Alone

| Treatment | $AUC_{0\text{-}Inf}$ (h*nM)[a] | $C_{max}$ (nM)[a] | $T_{max}$ (h)[b] |
|---|---|---|---|
| Test (Rosiglitazone + SCY-078) | 1451 | 235.1 | 1.0 |
| Reference (Rosiglitazone Alone) | 1461 | 295.6 | 0.53 |
| GMR[c] Test/Reference (90% CI) | 0.99 (0.90, 1.10) | 0.80 (0.70, 0.90) | |

[a]LS Geometric Mean and its 95% CI were calculated based on linear model: log(PK Result)=Sequence of Treatment. ; [b]Median (Min-Max).; [c]Geometric Means Ratio, GMR

#P1738- PK Tacrolimus Co-administered with SCY-078 vs. Tacrolimus Alone

| Treatment | $AUC_{0\text{-}inf}$ (ng•h/mL)[a] | $AUC_{0\text{-}24hr}$ (ng•h/mL)[a] | $C_{max}$ (ng/mL)[a] | $T_{max}$ (h)[b] |
|---|---|---|---|---|
| Test (Tacrolimus + SCY-078) | 116.9 | 63.22 | 8.29 | 2.0 |
| Reference (Tacrolimus Alone) | 82.50 | 46.16 | 8.03 | 2.0 |
| GMR[d] | 1.42 (1.25, 1.61) | 1.37 (1.21, 1.56) | 1.03 (0.89, 1.20) | |

[a] LS geometric Mean and its 95% CI were calculated based on linear mixed effects model: (log PK Result)= treatment + subject
[b] Median (Min - Max).
[c] GMR = Geometric Means Ratio, GMR Test/Reference (90% CI).



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# ECCMID SCY-078 Summary

David Angulo M.D.

# ECCMID SCY-078 Summary

- ✓ SCY-078 demonstrating activity against emerging global health threat, *Candida auris*
- ✓ *In vitro* combination of SCY-078 and azoles and Amphotericin B, demonstrating synergy against *Aspergillus* spp.
- ✓ SCY-078 activity against *Candida* spp. and *Candida* in biofilm
- ✓ Evidence of anti-*Candida* activity of oral SCY-078 in Invasive Candidiasis and Vulvovaginal Candidiasis
- ✓ Two Drug-Drug Interaction studies showing SCY-078's minimal interactions

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# Thank You
# Q&A