SCYNEXIS®

A New Path for Antifungal Treatments

SCY-078

8th Trends in Medical Mycology

Belgrade, Serbia

October 2017

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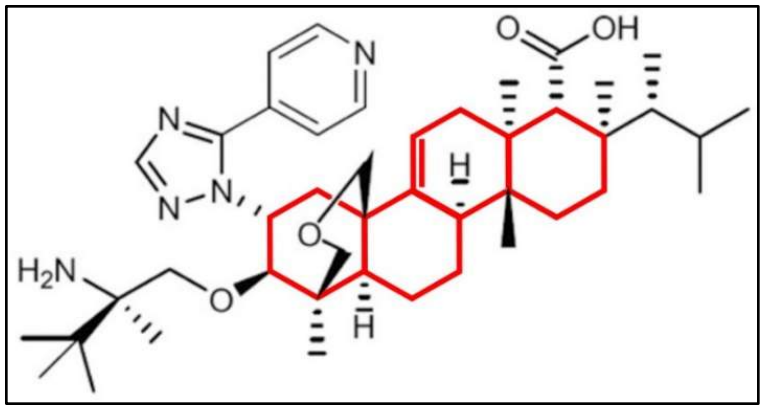
These and other risks are described more fully in SCYNEXIS' filings with the Securities and Exchange Commission, including without limitation, its most recent Annual Report on Form 10-K under the caption "Risk Factors" and other documents subsequently filed with or furnished to the Securities and Exchange Commission. All forward-looking statements contained in this presentation speak only as of the date on which they were made. SCYNEXIS undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

SCYNEXIS at a Glance

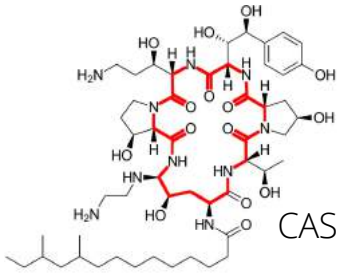
- Company created in 2000
  - Spin-off of Sanofi, initially as a contract service business
  - Transitioned to a biotechnology company in late 2014
- SCY-078 discovered at SCYNEXIS
  - Part of an internal platform of enfumafungin semi-synthetic derivatives (triterpenoids)
    - Glucan synthase inhibitors
- Public Company since May 2014
  - Nasdaq-listed: SCYX
- Based in Jersey City, NJ, USA

SCY-078

Novel Glucan Synthase Inhibitor (GSI)



Structurally district from other GSIs (echinocandins)



- IC_{50} against purified glucan synthase from *C. albicans* is 0.6 ng/mL
- Different enzyme-drug interaction → lower impact of common FKS mutations
- Oral Bioavailability

Key Attributes

- Activity against:
  - *Candida* spp
  - *Aspergillus* spp
  - *Pneumocystis* spp
- Active against azole- and most echinocandin-resistant strains
- ORAL and IV formulations
- Favorable Safety profile > 300 exposed
  - Low risk of Drug-Drug Interactions
- High tissue penetration (V_{dss} > 8 L/kg)

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SCY-078 Addressing Critical Needs

SCY-078

Broad Spectrum
IV and Oral
Active vs. Resistant Strains
High Tissue Penetration

Invasive Candidiasis

- ✓ Activity against resistant strains (azole and echinocandins)
- ✓ Ease of transition from IV to oral, without sacrificing efficacy

Aspergillosis

- ✓ Invasive: Alternative approach to improve outcomes (e.g., combination therapy)
- ✓ Chronic: Oral alternative for azole–resistant strains

Vulvovaginal Candidiasis

- ✓ Oral fungicidal agent with high tissue penetration and activity in vaginal milieu

Prophylaxis

- ✓ Oral, well-tolerated agent with activity vs. *Candida/Aspergillus/Pneumocystis* and low risk for DDIs

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SCY-078 Is Fungicidal against *Candida* Species in Time-Kill Studies

Bernard Scorneaux,[a] David Angulo,[a] Katyna Borroto-Esoda,[a] Mahmoud Ghannoum,[b] Michael Peel,[a] Stephen Wring[a]

Scynexis, Inc., Jersey City, New Jersey, USA[a]; Case Western University, Cleveland, Ohio, USA[b]

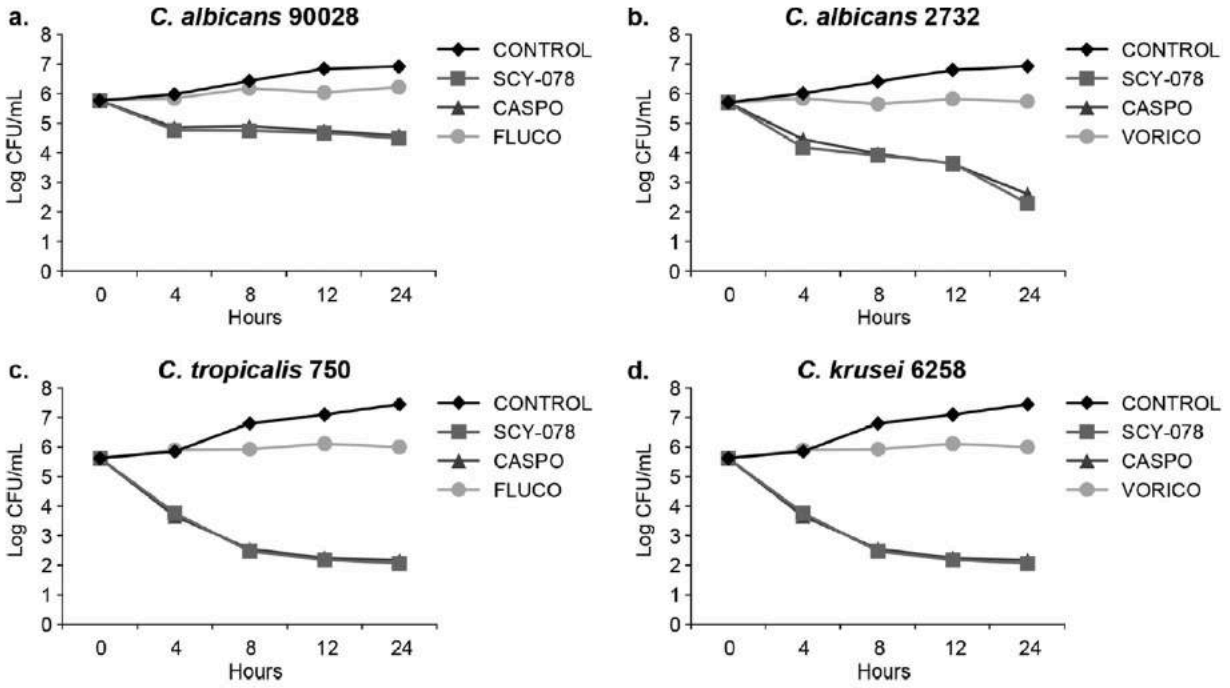

FIG 2 Time-kill curves for SCY-078, caspofungin (CASPO), fluconazole (FLUCO), and voriconazole (VORICO) at 4 times the MIC_{80} against the indicated *Candida* species and a control. 2732, MYA-2732.

Potent and rapid *in vitro* activity against *Candida* spp

Fungicidal against azole-susceptible and resistant isolates

AAC, March 2017 - Volume 61 - Issue 3

Differential Activity of the Oral Glucan Synthase Inhibitor SCY-078 against Wild-Type and Echinocandin-Resistant Strains of *Candida* Species

Michael A. Pfaller,[a] Shawn A. Messer,[a] Paul R. Rhomberg,[a] Katyna Borroto-Esoda,[b] Mariana Castanheira[a]

JMI Laboratories, North Liberty, Iowa, USA[a]; Scynexis, Inc., Jersey City, New Jersey, USA[b]

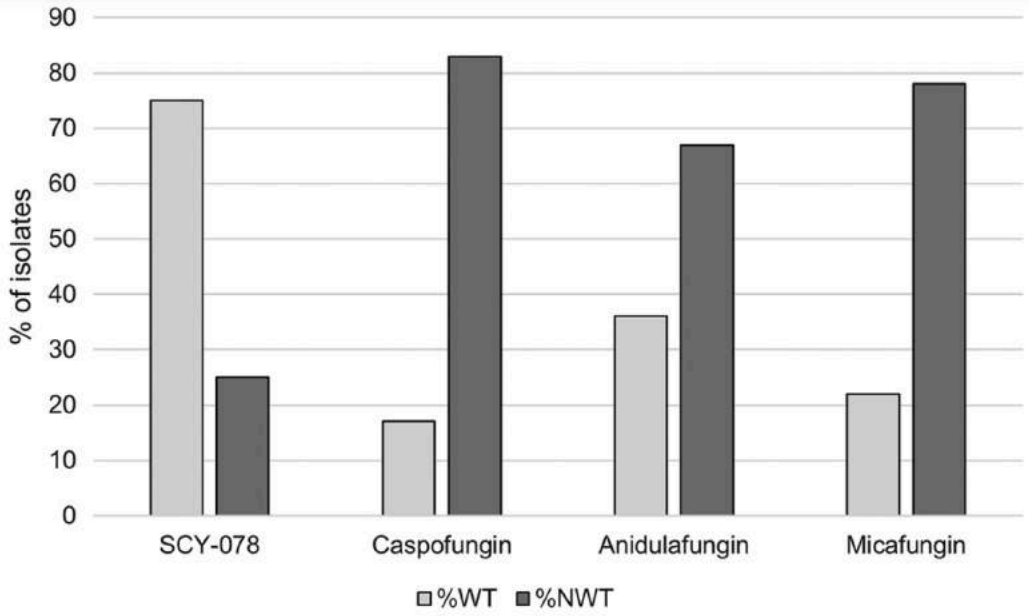

FIG 1 Activity of SCY-078, anidulafungin, caspofungin, and micafungin against strains displaying *FKS* mutations. %WT, percent wild type; %NWT, percent non-wild type (for SCY-078, %NWT is the percent exceeding the wild-type upper-limit value [WT-UL; two 2-fold dilutions higher than the modal MIC value of each WT population]).

SCY-078 is less affected by FKS mutations than echinocandins

(36 isolates)

AAC, August 2017 - Volume 61 - Issue 8

In Vitro Activity of a Novel Glucan Synthase Inhibitor, SCY-078, against Clinical Isolates of *Candida auris*

Elizabeth L. Berkow,[a] David Angulo,[b] Shawn R. Lockhart[a]

Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA[a]; SCYNEXIS, Inc., Jersey City, New Jersey, USA[b]

A collection of 100 isolates of the emerging pathogen *Candida auris*

MIC values of SCY-078 ranged from 0.0625 µg/ml to 2 µg/ml
Mode was 1 µg/ml - MIC50 = 0.5 µg/ml - MIC90 = 1 µg/ml

TABLE 2 SCY-078 MIC data compared to isolates with elevated echinocandin MICs

	MIC (µg/ml) of drug:			
Isolate	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	0.5	0.5	0.5
6	>16	>16	>8	0.5
7	4	>16	1	1

AAC, July 2017 - Volume 61 - Issue 7

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In Vitro Antifungal Activity of SCY-078 Against *Candida parapsilosis*, Including Azole and Echinocandin-resistant Strains

Stephen Barat[1], David Angulo[1], Katyna Borroto-Esoda[1], M. Ghannoum[2]
[1]SCYNEXIS Inc., [2]Center for Medical Mycology, Case Western Reserve University and University Hospitals Case Medical Center

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(μg/mL)	SCY-078 MIC_{50} MIC_{90}	CSP MIC_{50} MIC_{90}	MCF MIC_{50} MIC_{90}	ANF MIC_{50} MIC_{90}
US Study1 2009[a] (N=15)	0.25 0.5	0.5 0.5	NA	NA
US Study 2 2012[b] (N=19)	0.5 2	0.5 1	NA	NA
US Study 3 2013[c] (N=43)	0.5 1	0.5 1	2 2	2 4
US Study 4 2013[d] (N=19)	0.25 0.25	0.25 0.5	1 2	1 2
EU Study 1 2012[e] (N=27)	0.25 0.5	0.5 1	NA	NA
EU Study 2 2015[f] (N=32)	0.25 0.5	NA	0.5 1	NA
EU Study 3 2016[g] (N=36)	1 2	1 2	2 4	2 4

[a]Pfaller et al. JAC 2013, [b]Jimenez-Ortigosa et al. AAC 2014, [c]Pfaller et al. AAC 2017, [d]Shell et al. AAC 2017, [e]Data on file (Eurofin), [f]Marcos-Sabrano et al. JAC 2017 , [g]Borroto-Esoda et al. ASM Microbe 2017

J Antimicrob Chemother
doi:10.1093/jac/dkx010

Journal of Antimicrobial Chemotherapy

The novel oral glucan synthase inhibitor SCY-078 shows *in vitro* activity against sessile and planktonic *Candida* spp.

Laura Judith Marcos-Zambrano[1,2], Marta Gómez-Perosanz[1,2], Pilar Escribano[1,2], Emilio Bouza[1–4] and Jesús Guinea[1–4]*

[1]*Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Madrid, Spain;* [2]*Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain;* [3]*CIBER Enfermedades Respiratorias-CIBERES (CB06/06/0058), Madrid, Spain;* [4]*Medical Department, School of Medicine, Universidad Complutense de Madrid, Madrid, Spain*

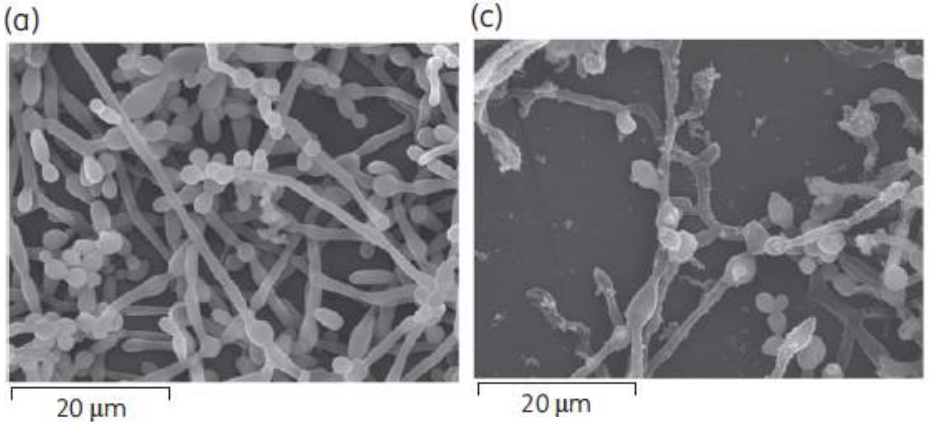

Figure 1. SEM images of the activity of SCY-078 against biofilms
(a) C. albicans, untreated control.
(c) *C. albicans* treated with SCY-078 (0.062 mg/L).

SCY-078 was highly active *in vitro* against invasive *Candida* and *non-Candida* yeast isolates in both sessile and planktonic forms

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SCY-078 PK/PD Target Exposure for Invasive Candidiasis - Preclinical

Target therapeutic exposure, expressed as the plasma AUC_{0-24}, was comparable across 3 murine models, with an upper value of 11.2 µg • h/ml (15.4 µM • h);

TABLE 1 *In vivo* activity of SCY-078 versus *C. albicans* MY1055 and target exposures measured after dose 13 on treatment day 7 in a C′5-deficient DBA/2N murine model of disseminated candidiasis

Study and SCY-078 treatment (mg/kg)[a]	Plasma AUC_{0-24}		Kidney tissue burden (log_{10} CFU/g of tissue)	% animals sterilized[b]	Reduction from sham treatment (log_{10} CFU/g of tissue)
	µg·h/ml	µM·h			
Study A					
12.5	19.7	27.0	2.23	80	4.24
Efficacious	12.9	17.7	2.51	60	4
6.25	6.19	8.48	2.78	40	3.69
Study B					
12.5	16.2	22.2	2.2	100	4.67
Efficacious	9.71a	13.3	2.86	50	4.01
6.25	3.27	4.48	3.52	0	3.35
Study C					
6.25	11.0	15.1	2.61	60	4.35
Efficacy (mean)		15.4			

[a]SCY-078 was administered orally twice daily. Efficacious, projected efficacious exposure assuming linearity regarding both efficacy and plasma exposure. Data are from 3 independent studies.
[b]Five animals per group.

Efficacy target

AAC, April 2017 - Volume 61 - Issue 4

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SCY-078 *In Vitro* Activity vs. *Aspergillus* spp.

Broad activity against *Aspergillus* spp, including azole–resistant strains

- Itraconazole-resistant *Aspergillus* spp (MIC, >4 µg/ml) as determined by CLSI broth microdilution methods

		SCY-078 MEC µg/mL[a] (range)
Wild-type *Aspergillus* spp	*A. fumigatus* (21)	0.25 (0.03-1)
	A. flavus (23)	0.12 (0.06-0.12)
	A. terreus (18)	0.12 (0.03-0.25)
Azole-Resistant *Aspergillus* strains	*A. fumigatus* (6)	(0.03 – 0.5)

[a] MEC that encompasses 90% of isolates tested by CLSI broth microdilution method
Pfaller M. A and Col., J. Antimicrobial Agents and Chemotherapy, 2013; 68(4); 858-863 & 2013; 57(2); 1065-1068.

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Evaluation of 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, PhD 1
1.Center for Medical Mycology, Case Western Reserve University and University Hospitals Cleveland Medical Center, Cleveland, OH; 2. Scynexis Inc., NJ, USA

University Hospitals Cleveland Medical Center
27th ECCMID Vienna, Austria 22 – 25 April 2017

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	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	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	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	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	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	4	>8	0.125	>8	1.03	AD	4	>16	1	>16	1.25	AD	4	4	0.016	1	0.25	SY

SCY-078 in combination with Voriconazole, Isavuconazole and Amphotericin B demonstrates synergistic activity against the majority of *A. fumigatus* isolates tested

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TIMM Trends in Medical Mycology

SCY-078 Antifungal Activity in a Murine Model of Invasive Aspergillosis including Azole-resistant Strains

Stephen Barat[1], Katyna Borroto-Esoda[1], David Angulo[1], Christina Carruthers[1], Kirsty Holden[2], Peter Warn[2]. [1]SCYNEXIS, Inc. USA, [2]Evotec UK

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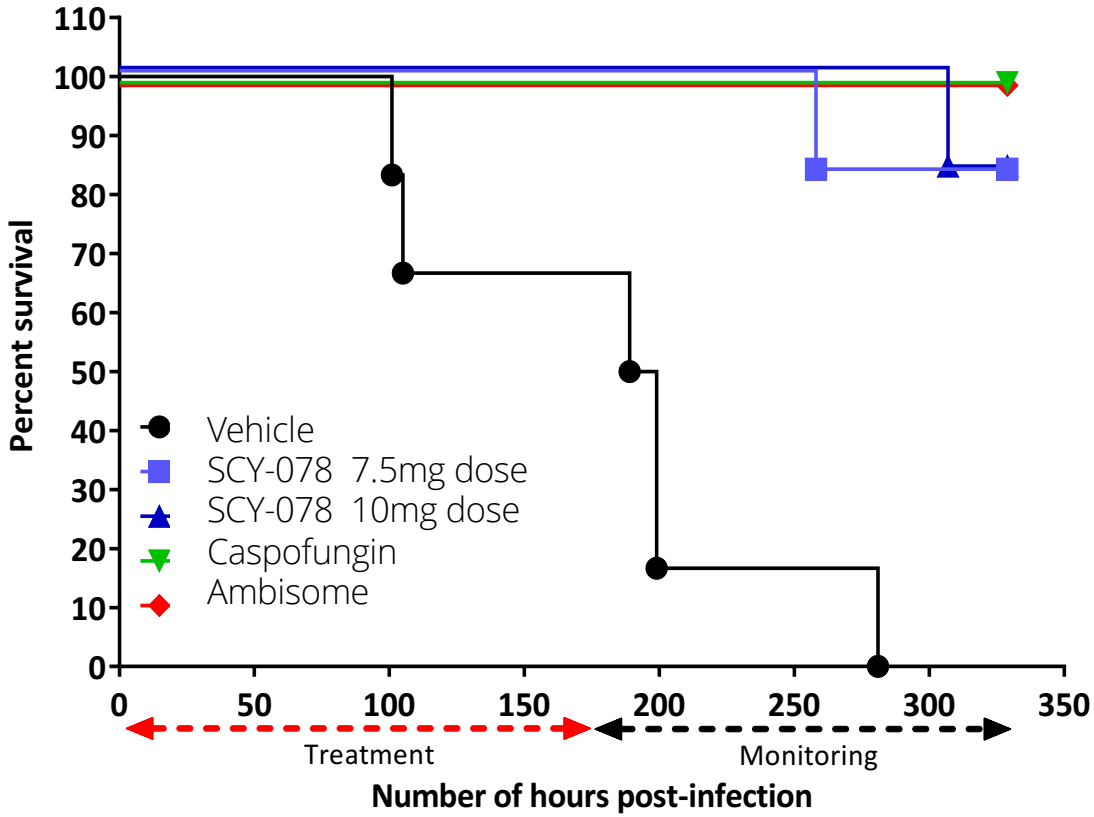
- Neutropenic mice model of disseminated aspergillosis (IV inoculum)
- Treatment for 7 days:
  - SCY-078 PO at 7.5 and 10 mg/kg q12h
  - Caspofungin IP at 5mg/kg
  - Ambisome IV at 10mg/kg
- Observation for 14 days
- SCY-078 exposure needed for efficacy
  - $AUC_{0\text{-}24hr}$ 15 - 20 µM•hr



A. fumigatus (F16216)
Azole-resistant - TR34 L98H

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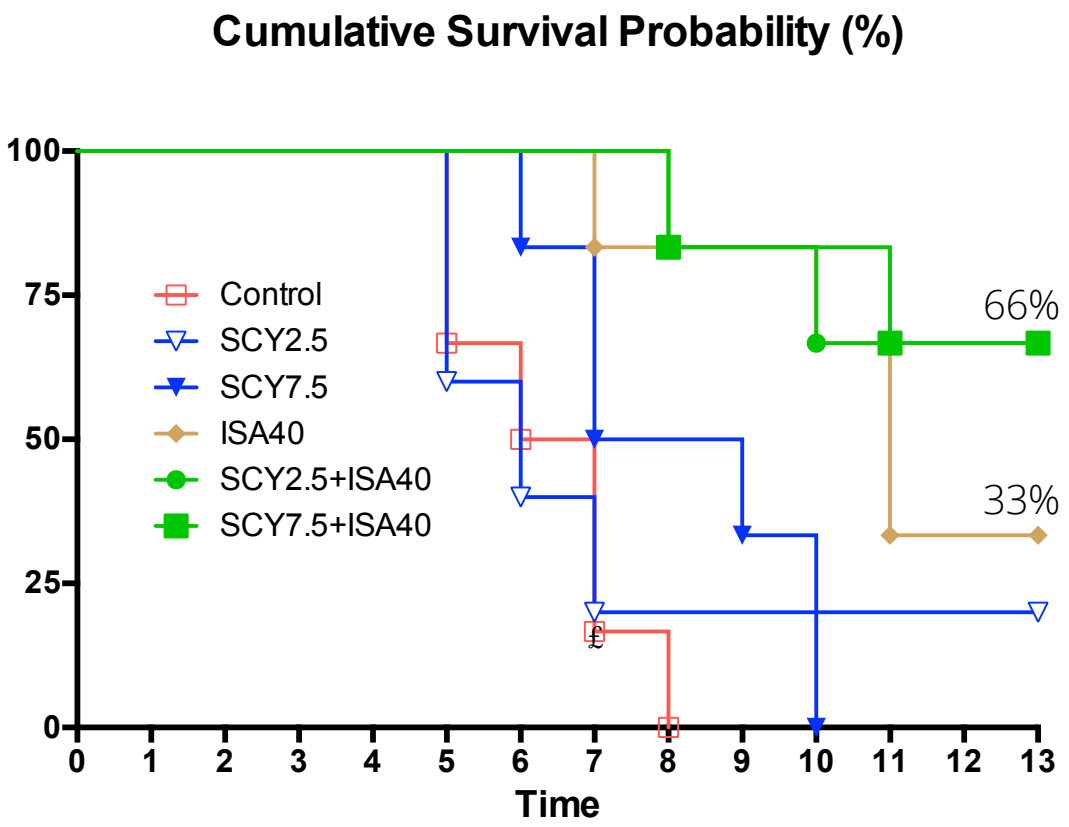
SCY-078 in Combination with Azole for Invasive Pulmonary Aspergillosis -Rabbit Model

- Neutropenic rabbit model of pulmonary aspergillosis
- Treatment for 12 days
- N=6 / group (QD doses):
  - SCY-078 (IV) at 2.5 or 7.5mg/kg
  - Isavuconazole (PO) 40mg/kg
  - SCY-078 2.5 + Isavuconazole
  - SCY-078 7.5 + Isavuconazole
- Preliminary results
- Study conducted at Cornell University, NY by Dr. Tom Walsh



Combination of SCY-078 + Isavuconazole resulted in improved survival

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TIMM Trends in Medical Mycology

SCY-078, a Novel Glucan Synthase Inhibitor, Readily Distributes into Target Organs Associated with Invasive Fungal Infections

Stephen Barat, Katyna Borroto-Esoda, David Angulo, Christina Carruthers SCYNEXIS, Inc. USA

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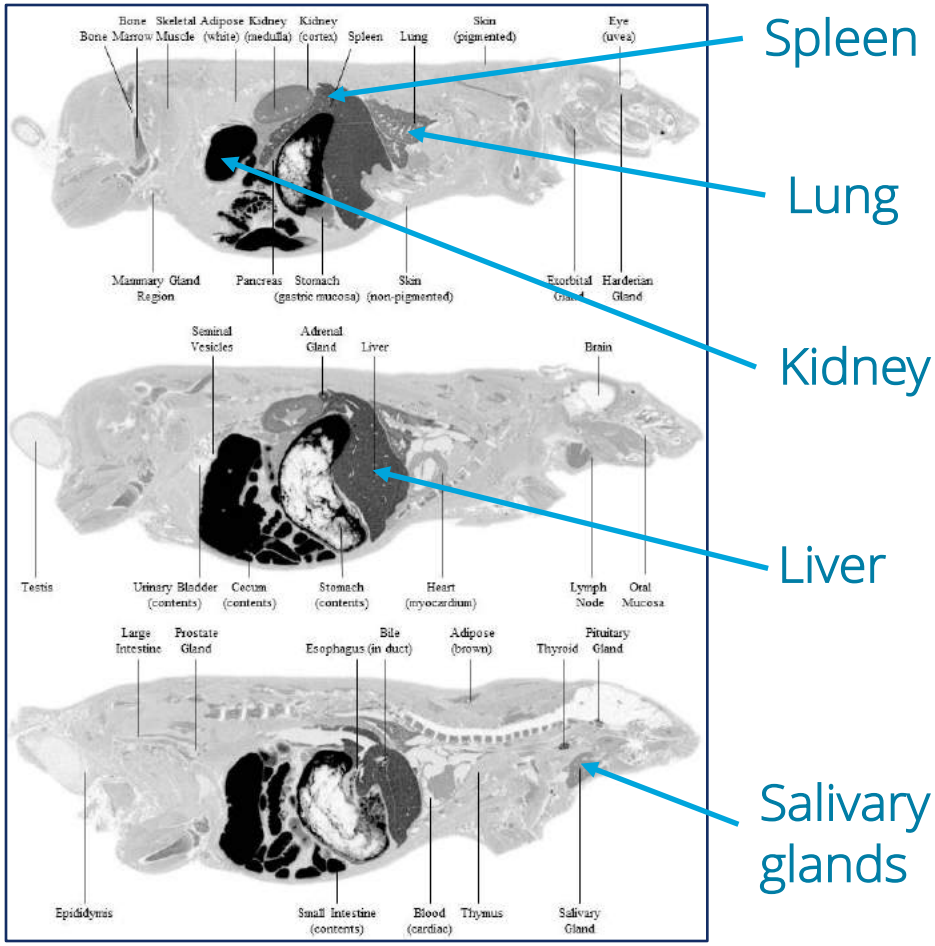
SCY-078 distributes extensively to key tissues associated with invasive fungal infections



Autoradiogram of the Radioactivity Distribution
Rat at 4h Following a Single Oral Dose of [^{14} C]SCY-078

Estimated Volume of Distribution at Steady State (human)

Drug [a]	Vdss L/kg Mean
SCY-078	8.3
Caspofungin	0.15
Micafungin	0.39
Anidulafungin	0.8
L-AMB	0.7
Fluconazole	0.7
Voriconazole	4.6

[a] Felton T. et al, Tissue penetration of antifungal agents. Clin. Microbiol. Rev. 2014, 27(1):68.

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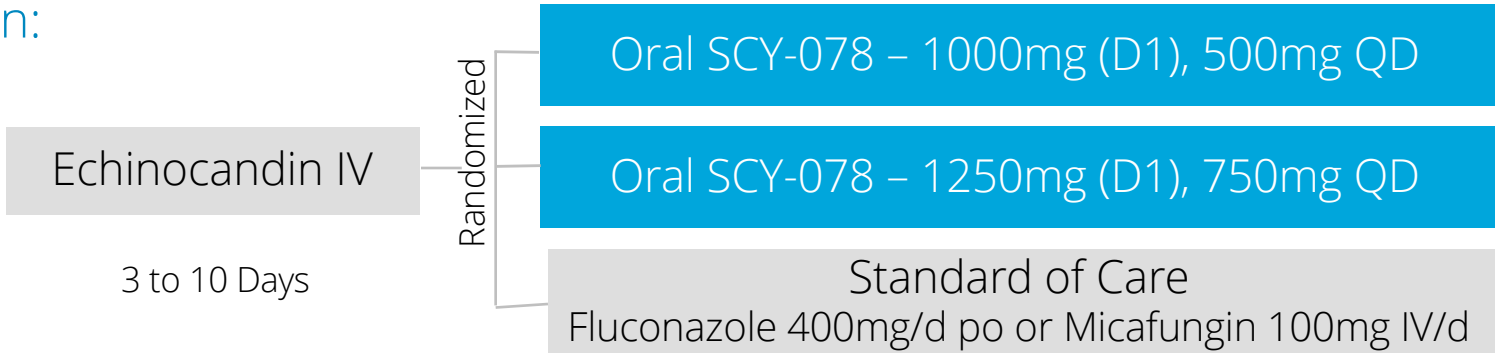
SCY-078 Drug-Drug Interaction and QTc

- SCY-078 is not likely to have clinically meaningful effect on CYP substrates
  - No evidence of effect on rosiglitazone (CYP2C8 substrate) pharmacokinetics
- SCY-078 is not likely to have clinically meaningful effect on Tacrolimus levels
  - SCY-078 co-administration result in <0.4 fold increase in Tacrolimus AUC_{12}
- SCY-078 is not likely to be significantly affected by most CYP inhibitors
  - Diltiazem (moderate inhibitor) had a modest effect on SCY-078 $AUC_{0\text{-}24}$ increased (~2)
- Phase 1 studies: SCY-078 does not have a clinically meaningful effect on the QTcF interval within the range of observed plasma concentrations up to ~4000 ng/mL

SCY-078 - Phase 2 in Invasive Candidiasis (Step Down) - Completed

Design:



Results:

Pop PK = **SCY-078 PO, 750mg QD achieves target exposure** ($AUC_{0\text{-}24hr}$ of 15 µM·hr)
AEs frequency and severity - comparable for all groups

Global Response at EOT	Favorable	Reasons for Unfavorable
SCY-078 500 mg N = 7 n (%)	5 (71.4)	1. Never received study drug 2. Discontinued due to a non-drug related AE
SCY-078 750 mg N = 7 n (%)	6 (85.7)	1. Withdraw consent after one dose
Fluconazole 400 mg N =7 n (%)	5 (71.4)	1. Died (abdominal sepsis) 2. Discontinued (new + blood culture for *Candida* spp)

SCY-078 Phase 2 Study in Moderate and Severe Vulvovaginal Candidiasis (VVC)

27th ECCMID Vienna, Austria 22 – 25 April 2017

M. Roman, MD 1; C. Hernandez, MD 2; D. Blanco, MD 1; G Obrycki 3, S. Helou,, MD 3 D. Angulo: MD 3
1. Hospital Dr. Francisco E. Moscoso Puello, Dominican Republic. 2. Instituto Dermatologico y Cirugia de Piel Calle Federico Velazquez, Dominican Republic. 3. SCYNEXIS, Inc. USA.

70 subjects had cultured-confirmed VVC (per protocol population)

Efficacy Evaluation at Day 24 (per protocol population)					
N Rates %	SCY-078 1250mg (D1), 750mg (D2-3) (n= 24)	SCY-078 1250mg (D1), 750mg (D2-5) (n= 26)	SCY-078 (Combined) (n= 50)	Fluconazole 150mg (D1) (n= 20)	% Δ SCY-078 (combined) vs. Fluconazole
Clinical Cure	19 *79.2%*	19 *73.1%*	38 ***76%***	13 ***65%***	+11%
Efficacy Evaluation at Month 4					
Recurrences Requiring Antifungal Therapy	1 *4.2%*	1 *3.8%*	2 ***4%***	3 ***15%***	-11%

- The rate of mycological eradication at Day 24 and Month 4 was 70% and 74% for the SCY-078 combined arms vs. 65% and 60% for the fluconazole arm
- There were no severe or serious adverse events in any treatment groups. A higher rate of GI adverse events (e.g., nausea, diarrhea) were reported in the SCY-078 treatment arms, which were mild to moderate in severity and transient in nature

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Ongoing Clinical Trials

- FURI: Phase 3, open-label study in patients that are refractory to or intolerant of approved antifungal agents
  - Intended population includes:
    - Invasive candidiasis, including *C.auris*
    - Chronic disseminated candidiasis
    - Severe mucocutaneous candidiasis
  - Sites opened in the US and soon in EU

- DOVE: Phase 2, randomized, double blind, dose-finding study in patients with acute VVC
  - Exploring 5 dose regimens of Oral SCY-078 vs. Fluconazole
  - Sites opened in the US

SCY-078 Summary

- Novel Oral and IV glucan synthase inhibitor
- Spectrum of activity:
  - Broad anti-*Candida* activity
    - Including azole-resistant, ~ 70% FKS mutants (echinocandin-resistant) and *C.auris*
  - Broad anti-*Aspergillus* activity
    - Including azole-resistant
  - Anti-*Pneumocystis* activity
- Extensive tissues distribution
  - High concentrations in key organs such lung, kidney, liver, spleen, mucosa - several fold higher than plasma
- Target exposure attainable with well-tolerated oral doses
- Low risk for DDI and no QTc effect expected