



Session 12 – New Antifungals

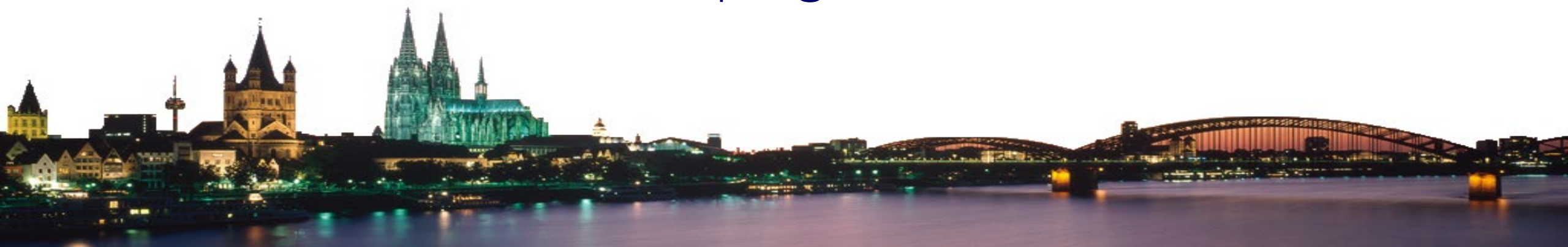
Novel approaches for the Treatment of Aspergillosis and Mucormycosis

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- Received consultancy, service, speaker fees and/or travel support fees from:
 - Akademie für Infektionsmedizin
 - Hikma
 - Pfizer
 - Scynexis



Limitations of Available Antifungals



Route of administration

Echinocandins and AMB only for IV administration

No IV formulation of 5-FC on the market



Multidrug-resistant fungi

Rare fungi with intrinsic resistances

Resistance development against 5-FC

MDR *Candida* spp.

Use of azoles in agriculture



Tissue penetration

Limited options in CNS infections

Low concentrations in different compartments

Organ toxicity of azoles and AMB



Toxicity, intolerance, drug interactions

CYP interactions limiting use in vulnerable pts

Heme toxicity of 5-FC

Solvent agents such as cyclodextrin

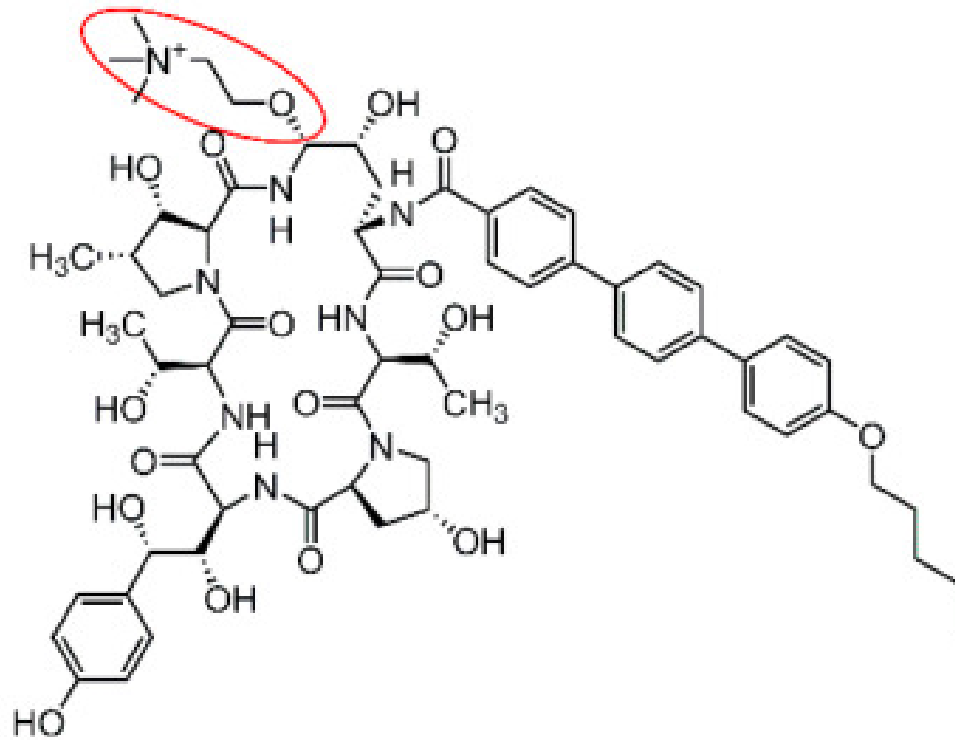


- Recently approved antifungals
 - (Rezafungin)
 - (Ibrexafungerp)

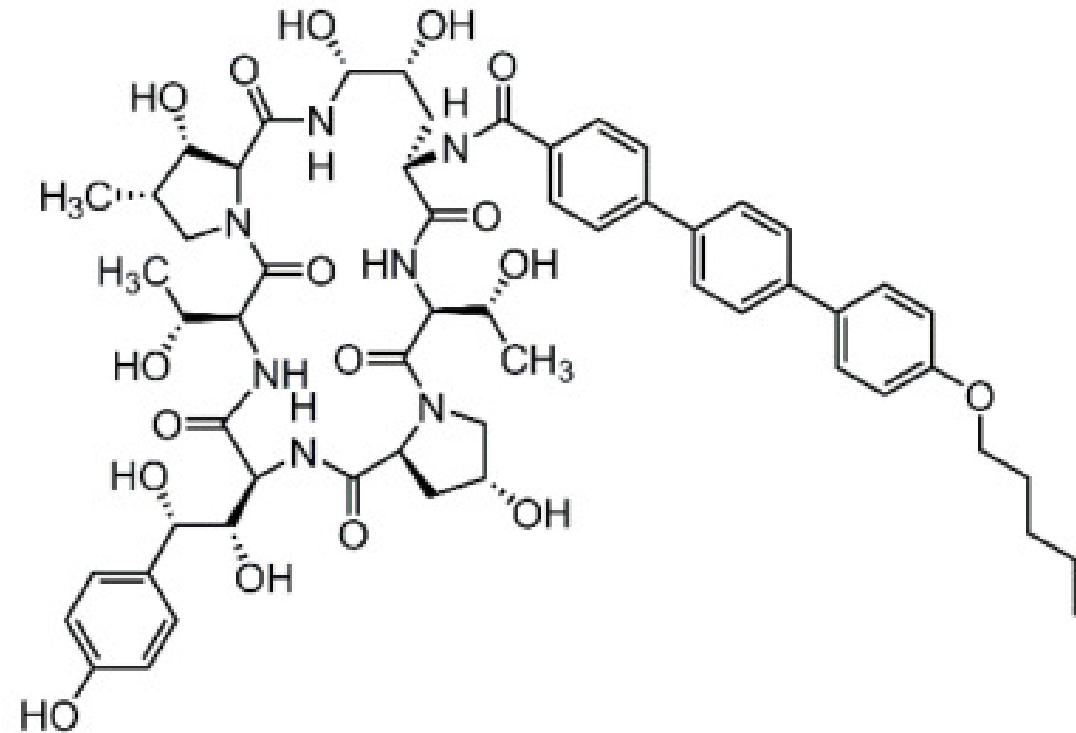


- Antifungals in late stage of clinical development
 - Fosmanogepix
 - Olorofim
 - Opelconazole

- **Class:** Echinocandin with extended half-life



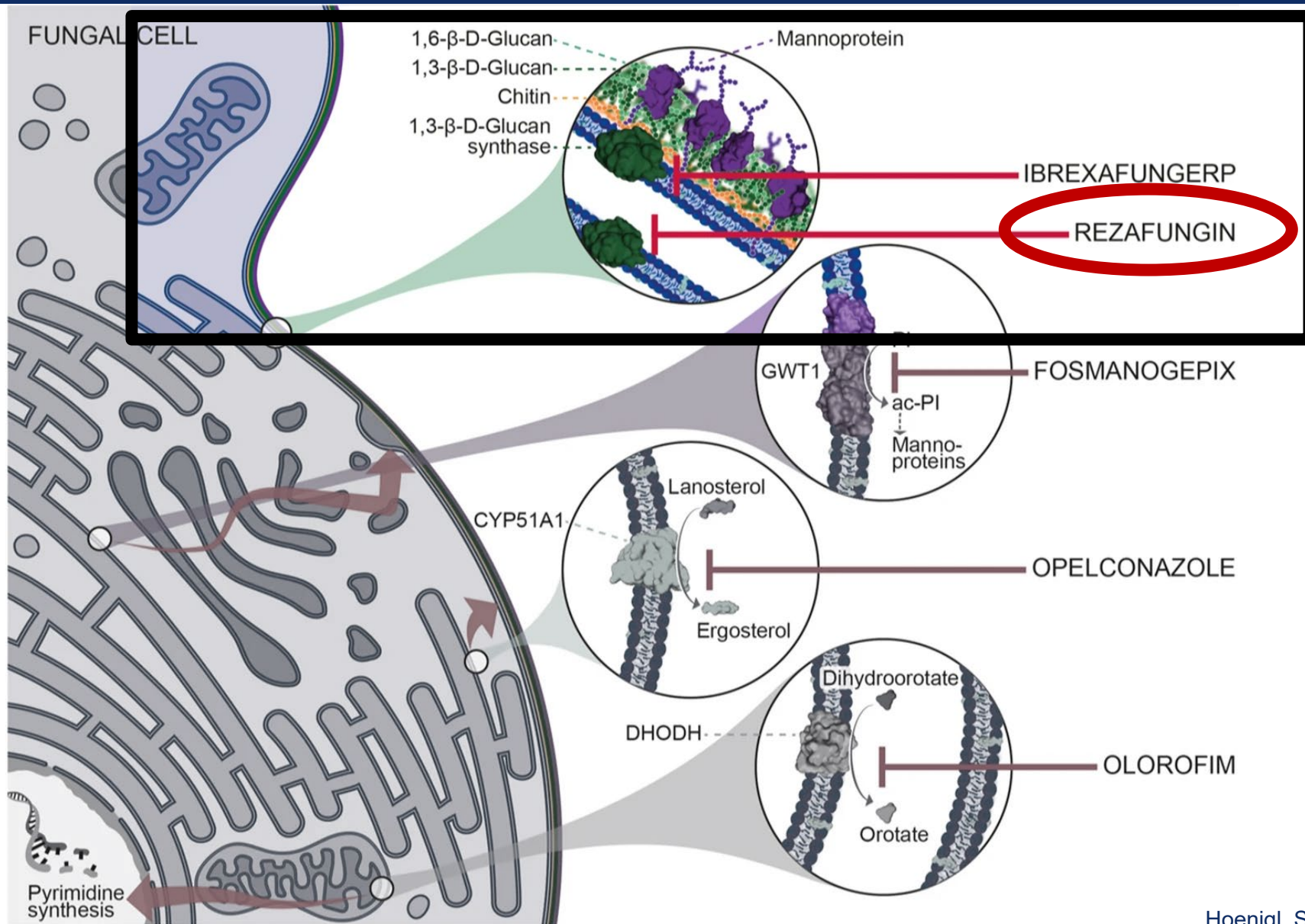
rezafungin




anidulafungin



Rezafungin (CD101; Cidara/Melinta/Mundipharma)






- **Class:** Echinocandin with extended half-life
- **Mechanism of Action:** (1-3)- β -D-glucan synthase inhibitor
- **Form of Application:** IV 




Rezafungin (CD101; Cidara/Melinta/Mundipharma)




-  *Aspergillus calidoustus*
- Aspergillus fumigatus*
- Azole-resistant *A. fumigatus*
- Aspergillus flavus*
- Aspergillus lentulus*
- Aspergillus nidulans*
- Aspergillus niger*
- Aspergillus terreus*
- Aspergillus tubingensis*

-  *Cunninghamella*
- Lichtheimia*
- Mucor*
- Rhizopus*

-  *Fusarium spp.*

-  *Alternaria alternata*
- Cladosporium spp.*
- Paecilomyces variotii*
- Purpureocillium lilacinum*
- Scopulariopsis spp.*
- Rasamsonia spp.*


-  *Scedosporium spp.*
- Lomentospora prolificans*

-  *Candida albicans*
- Candida auris*
- Candida dubliniensis*
- Candida glabrata*
- Candida krusei*
- Candida lusitaniae*
- Candida parapsilosis*
- Candida tropicalis*

-  *Cryptococcus gattii*
- Cryptococcus neoformans*

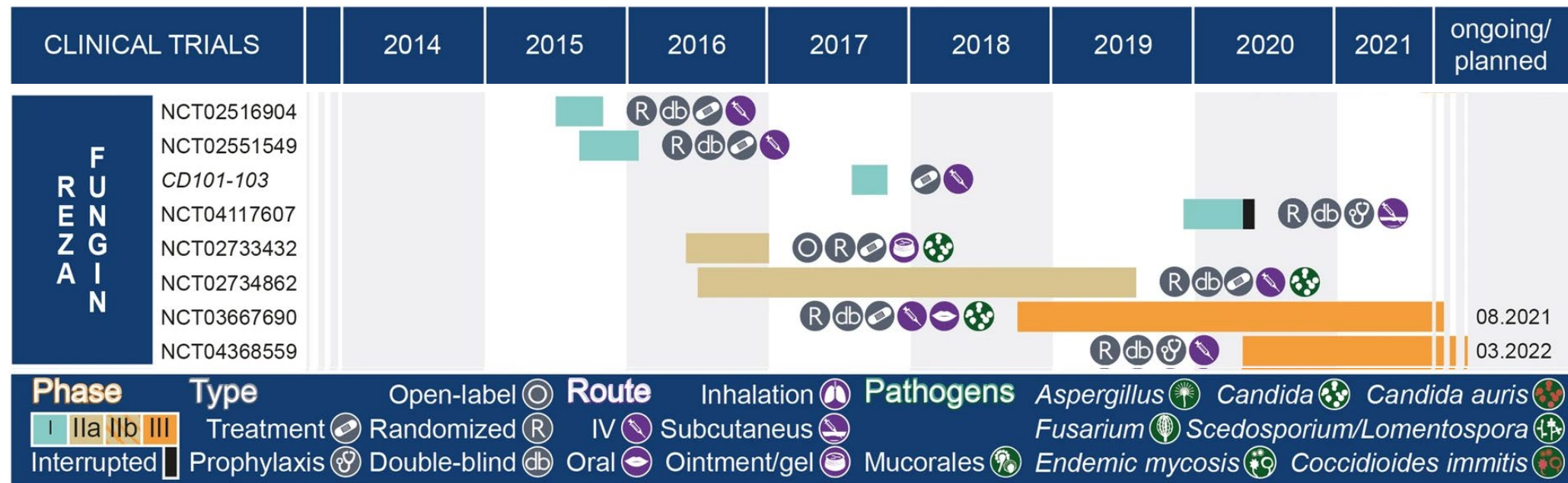
-  *Trichosporon asahii*
- Exophiala dermatitidis*
- Malassezia furfur*

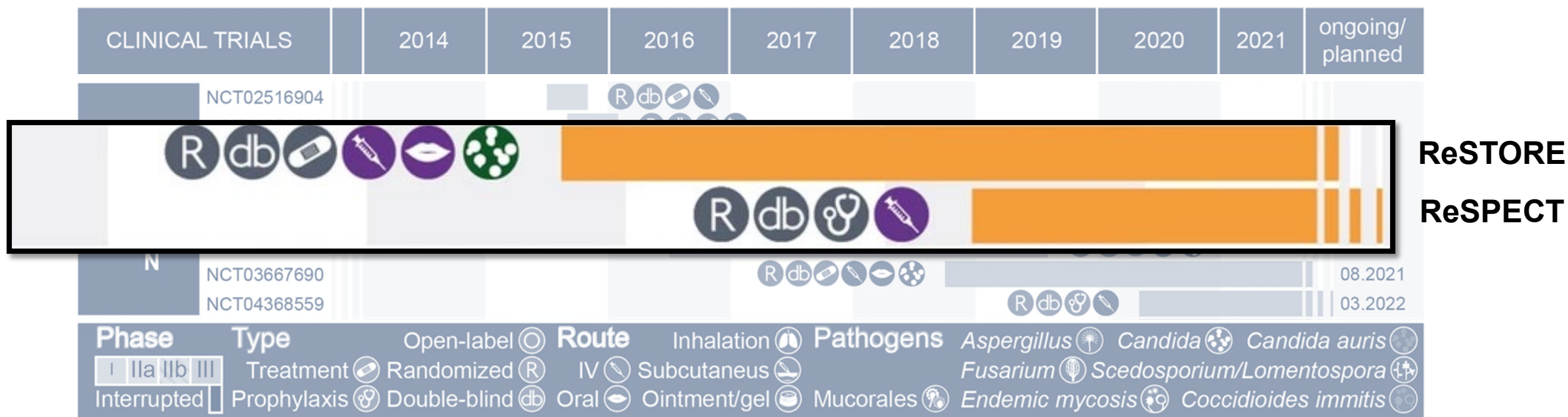
-  *Pneumocystis jirovecii*

-  *Blastomyces dermatitidis*
- Coccidioides immitis*
- Histoplasma capsulatum*
- Fonsecaea pedrosoi*
- Madurella mycetomatis*
- Talaromyces marneffeii*
- Phialophora verrucosa*

⊖ isolates with FKS mutations









Rezafungin versus caspofungin for treatment of candidaemia and invasive candidiasis (ReSTORE): a multicentre, double-blind, double-dummy, randomised phase 3 trial

George R Thompson III, Alex Soriano, Oliver A Cornely, Bart Jan Kullberg, Marin Kollef, Jose Vazquez, Patrick M Honore, Matteo Bassetti, John Pullman, Methee Chayakulkeeree, Ivan Poromanski, Cecilia Dignani, Anita F Das, Taylor Sandison, Peter G Pappas, on behalf of the ReSTORE trial investigators

ongoing/
planned

ReSTORE
ReSPECT

08.2021
03.2022

Phase

I IIa IIb III

Interrupted

Prophylaxis

Randomized (R)

IV

Subcutaneous

Oral

Ointment/gel

Mucorales

Endemic mycosis

Pathogens

Aspergillus

Candida

Candida auris

Fusarium

Scedosporium/Lomentospora

Coccidioides immitis



- Multicentre, randomized (1:1) phase III trial
- Candidaemia and invasive candidiasis, N=222
- Intravenous rezafungin once weekly (2 to 4 doses) vs. caspofungin for ≤ 4 weeks
- Global cure at D14: 55/93 (59%) with rezafungin, 57/94 (61%) with caspofungin
- 30D all-cause mortality: 22/93 (24%) with rezafungin, 20/94 (21%) with caspofungin
- TEAE: at least one in 89/98 (91%) with rezafungin and 83/98 (85%) with caspofungin
- Most common TEAEs: were pyrexia, hypokalaemia, pneumonia, septic shock, and anaemia observed in $\geq 5\%$ of patients in either group
- SAEs: 55 (56%) patients with rezafungin and 52 (53%) with caspofungin
- Conclusion: Rezafungin was non-inferior to caspofungin for the primary endpoints of day-14 global cure and 30-day all-cause mortality



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PRESS RELEASES

CIDARA THERAPEUTICS AND MELINTA THERAPEUTICS ANNOUNCE FDA APPROVAL OF REZZAYO™ (REZAFUNGIN FOR INJECTION) FOR THE TREATMENT OF CANDIDEMIA AND INVASIVE CANDIDIASIS

March 22, 2023

REZZAYO™ (rezafungin for injection), for intravenous use
Initial U.S. Approval: 2023

-----INDICATIONS AND USAGE-----

REZZAYO is an echinocandin antifungal indicated in patients 18 years of age or older who have limited or no alternative options for the treatment of candidemia and invasive candidiasis. Approval of this indication is based on limited clinical safety and efficacy data for REZZAYO. (1, 12.4, 14)




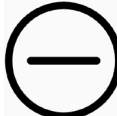

PRESS RELEASES

CIDARA THERAPEUTICS ANNOUNCES
EUROPEAN APPROVAL OF REZZAYO®
(REZAFUNGIN) FOR THE TREATMENT OF
INVASIVE CANDIDIASIS IN ADULTS

December 22, 2023

INDICATIONS AND USAGE
REZZAYO is an echinocandin antifungal indicated in patients 18 years of age or older who have limited or no alternative options for the treatment of candidemia and invasive candidiasis. Approval of this indication is based on limited clinical safety and efficacy data for REZZAYO. (1, 12.4, 14)



 Advantages	 Limitations
<p>Favorable safety profile</p> <p>Once weekly IV application</p> <p>High tissue concentrations, enhanced penetration into abdominal abscesses </p> <p>Limited DDI</p>	<p>Poor CNS and urinary tract penetration</p> <p>IV only, SC and topical formulations failed</p> <p>No role in <i>Cryptococcus</i> spp., <i>Mucorales</i> and other rare molds or rare yeasts, endemic fungi</p>



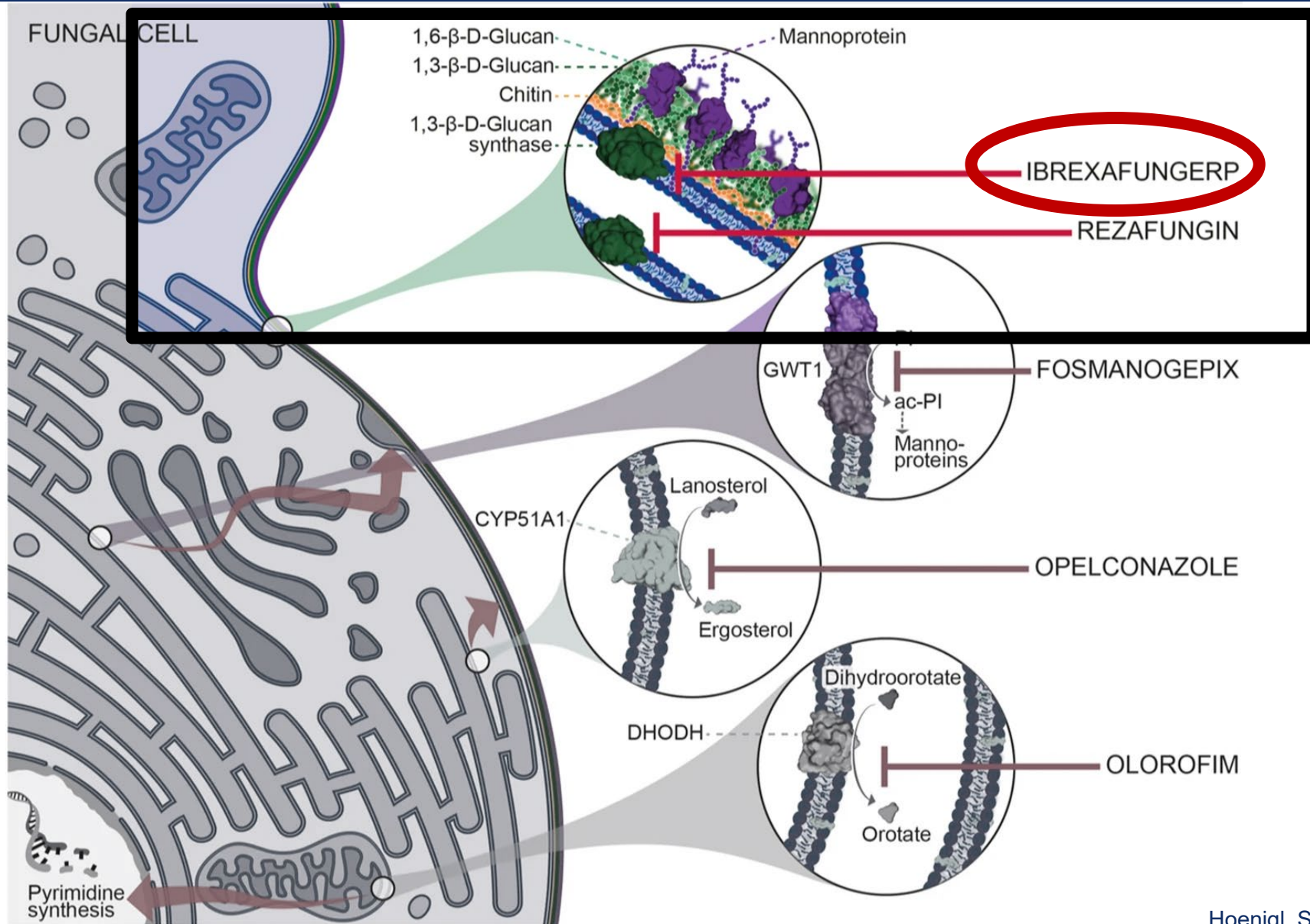
Future Roles: in case of early discharge or prolonged therapy, azole-resistance or intolerance, outpatient setting, prophylaxis





- **Class:** Triterpenoids, -fungerps



Ibrexafungerp (SCY-078; Scynexis/GSK)







- **Class:** Triterpenoids, -fungerps
- **Mechanism of Action:** Oral (1-3)- β -D-glucan synthase inhibitor
- **Form of Application:** PO  (and IV )



Ibrexafungerp (SCY-078; Scynexis/GSK)

	<i>Aspergillus calidoustus</i>	█
	<i>Aspergillus fumigatus</i>	█
	Azole-resistant <i>A. fumigatus</i>	█
	<i>Aspergillus flavus</i>	█
	<i>Aspergillus lentulus</i>	█
	<i>Aspergillus nidulans</i>	█
	<i>Aspergillus niger</i>	█
	<i>Aspergillus terreus</i>	█
	<i>Aspergillus tubingensis</i>	█

	<i>Candida albicans</i>	█
	<i>Candida auris</i>	█
	<i>Candida dubliniensis</i>	█
	<i>Candida glabrata</i>	█
	<i>Candida krusei</i>	█
	<i>Candida lusitanae</i>	█
	<i>Candida parapsilosis</i>	█
	<i>Candida tropicalis</i>	█

may overcome
echinocandin
resistance

Combination  ?

	<i>Cunninghamella</i>	█
	<i>Lichtheimia</i>	█
	<i>Mucor</i>	█
	<i>Rhizopus</i>	█

	<i>Cryptococcus gattii</i>	█
	<i>Cryptococcus neoformans</i>	█


	<i>Trichosporon asahii</i>	█
	<i>Exophiala dermatitidis</i>	█
	<i>Malassezia furfur</i>	█

	<i>Fusarium spp.</i>	█
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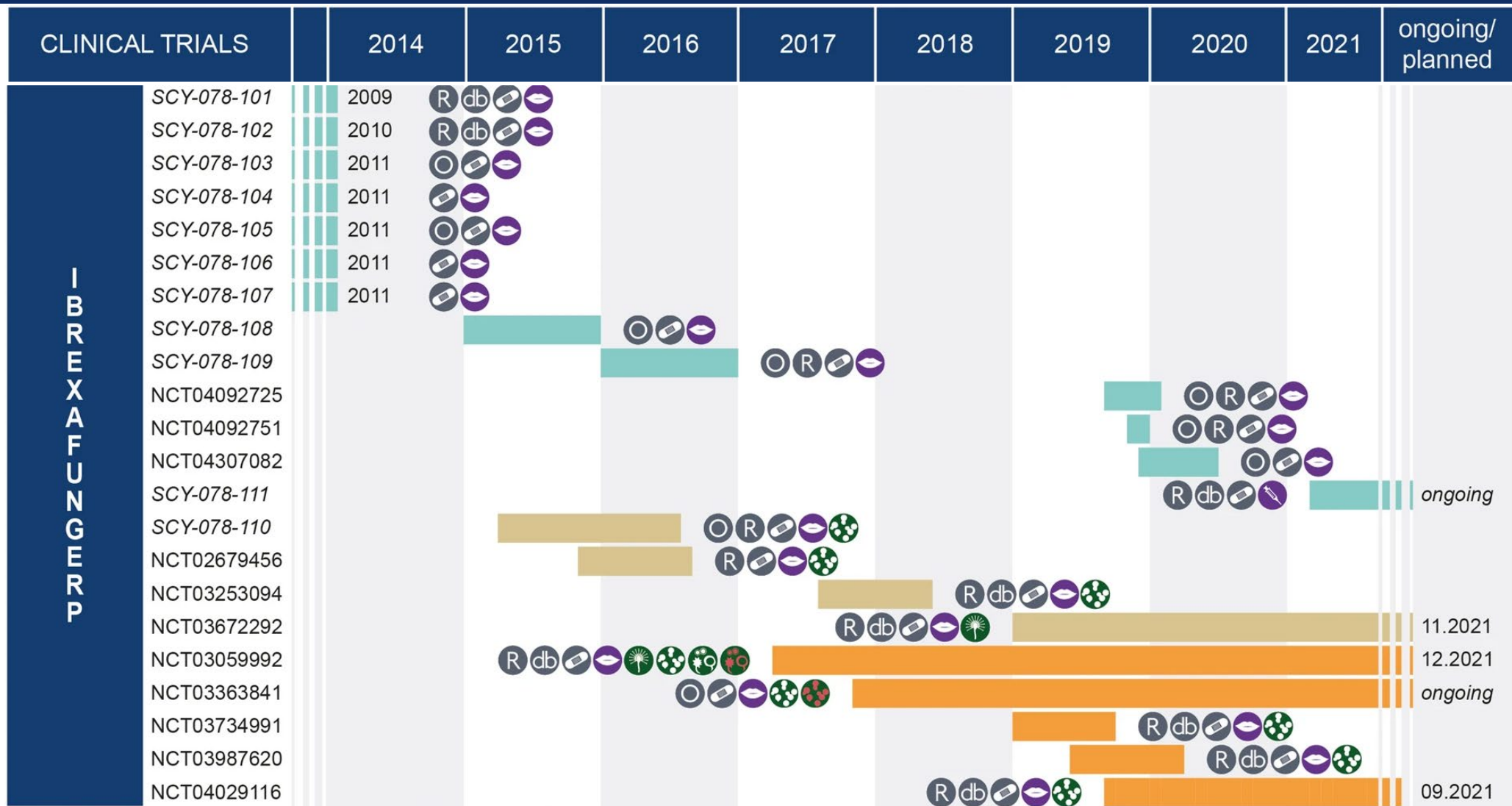
	<i>Pneumocystis jirovecii</i>	█
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	<i>Alternaria alternata</i>	█
	<i>Cladosporium spp.</i>	█
	<i>Paecilomyces variotii</i>	█
	<i>Purpureocillium lilacinum</i>	█
	<i>Scopulariopsis spp.</i>	█
	<i>Rasamsonia spp.</i>	█

	<i>Blastomyces dermatitidis</i>	█
	<i>Coccidioides immitis</i>	█
	<i>Histoplasma capsulatum</i>	█
	<i>Fonsecaea pedrosoi</i>	█
	<i>Madurella mycetomatis</i>	█
	<i>Talaromyces marneffeii</i>	█
	<i>Phialophora verrucosa</i>	█

	<i>Scedosporium spp.</i>	█
	<i>Lomentospora prolificans</i>	█



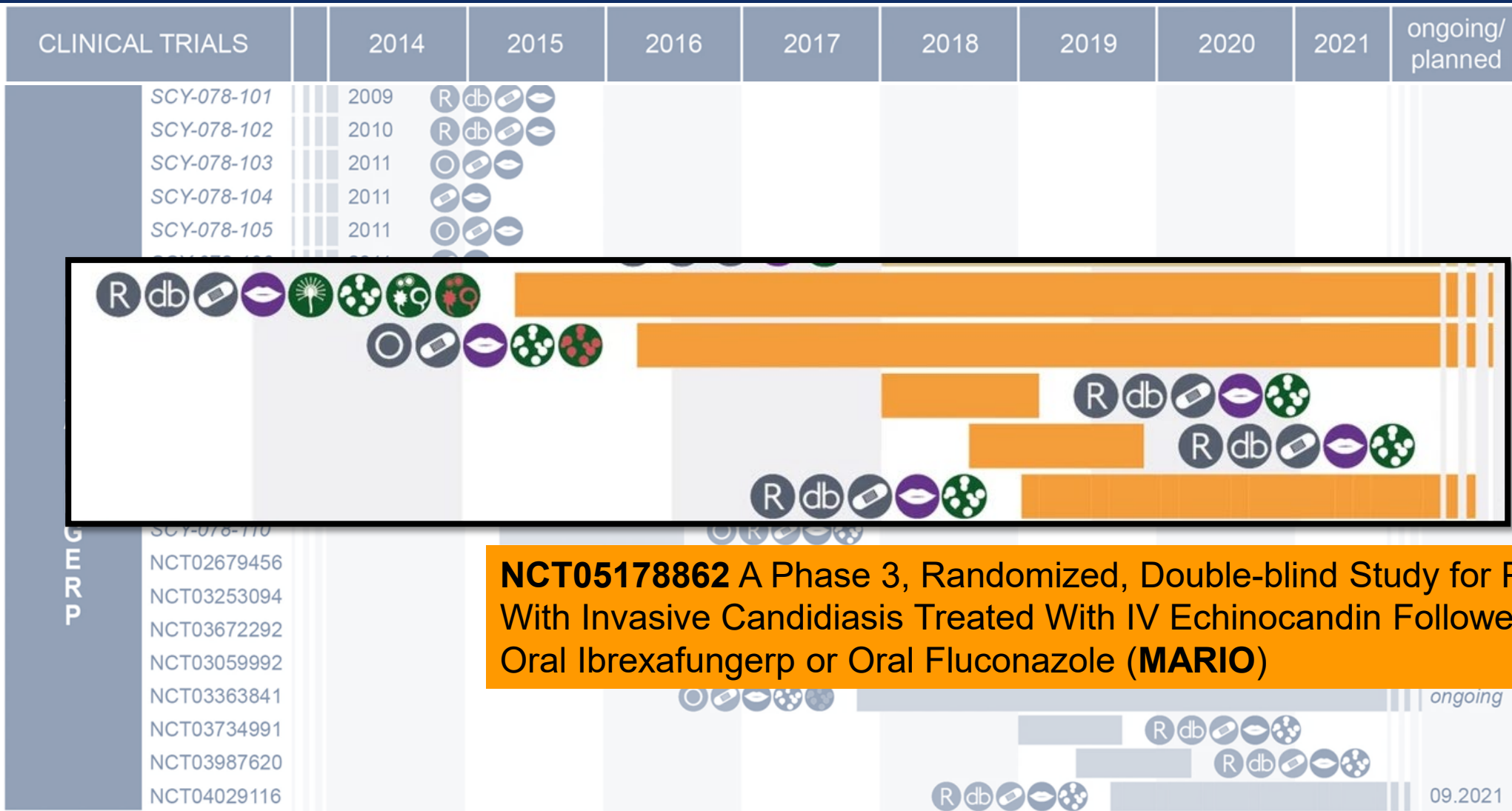
IBREXAFUNGERP

Phase I IIa IIb III | **Type** Treatment | **Open-label** | **Route** Inhalation | **Pathogens** Aspergillus | Candida | Candida auris | Fusarium | Scedosporium/Lomentospora | Mucorales | Endemic mycosis | Coccidioides immitis

Interrupted | **Prophylaxis** | **Randomized** R | **IV** | **Subcutaneous** | **Oral** | **Ointment/gel** | **Double-blind** db



Ibrexafungerp (SCY-078; Scynexis/GSK)



FURI
CARES
VANISH 303
VANISH 306
CANDLE

NCT05178862 A Phase 3, Randomized, Double-blind Study for Patients With Invasive Candidiasis Treated With IV Echinocandin Followed by Either Oral Ibrexafungerp or Oral Fluconazole (**MARIO**)

Phase I IIa IIb III
Type Treatment Randomized Double-blind
Route Open-label IV Subcutaneous Oral
Pathogens Aspergillus Candida Candida auris Fusarium Scedosporium/Lomentospora Mucorales Endemic mycosis Coccidioides immitis



CLINICAL TRIALS	2014	2015	2016	2017	2018	2019	2020	2021	ongoing/ planned
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SCY-078-101	2009
SCY-078-102	2010
SCY-078-103	2011
SCY-078-104	2011
SCY-078-105	2011



BREXAFEMME® (ibrexafungerp tablets), for oral use
Initial US Approval: 2021

-----INDICATIONS AND USAGE-----
 BREXAFEMME is a triterpenoid antifungal indicated for the treatment of adult and post-menarchal pediatric females with vulvovaginal candidiasis (VVC). (1)

CARES
VANISH 303
VANISH 306
CANDLE

SCY-078-110	
NCT02679456	
NCT03253094	
NCT03672292	
NCT03059992	
NCT03363841	
NCT03734991	
NCT03987620	
NCT04029116	

Phase	Type	Open	Other	Route	Indication
I IIa IIb III	Treatment	Randomized (R)	IV	Subcutaneous	Fusarium
Interrupted	Prophylaxis	Double-blind (db)	Oral	Ointment/gel	Mucorales
					Endemic mycosis
					Candida auris
					Scedosporium/Lomentospora
					Coccidioides immitis



CLINICAL TRIALS	2014	2015	2016	2017	2018	2019	2020	2021	ongoing/ planned
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SCY-078-105	2011



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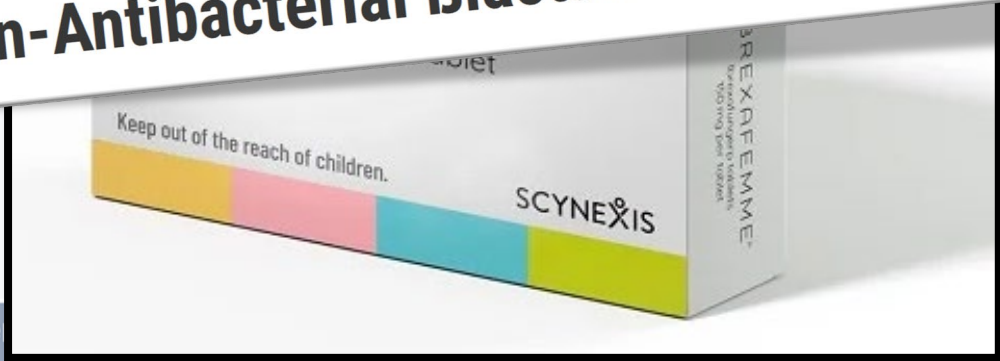


September 27, 2023

COMPANY ANNOUNCEMENT

SCYNEXIS Issues a Voluntary Nationwide Recall of BREXAFEMME® (ibrexafungerp tablets) Due to Potential for Cross Contamination with a Non-Antibacterial β lactam Drug Substance



SCY-078-101
NCT02679
NCT03253
NCT03672
NCT03059
NCT03363841
NCT03734991
NCT03987620
NCT04029116



CARES
VANISH 303
VANISH 306
CANDLE

Phase	Type	Open	Randomized (R)	Subcutaneous	Mucorales	Endemic mycosis	Coccidioides immitis
I IIa IIb III	Treatment	☐	☑	☐	☑	☑	☑
Interrupted	Prophylaxis	☑	☑	☑	☑	☑	☑

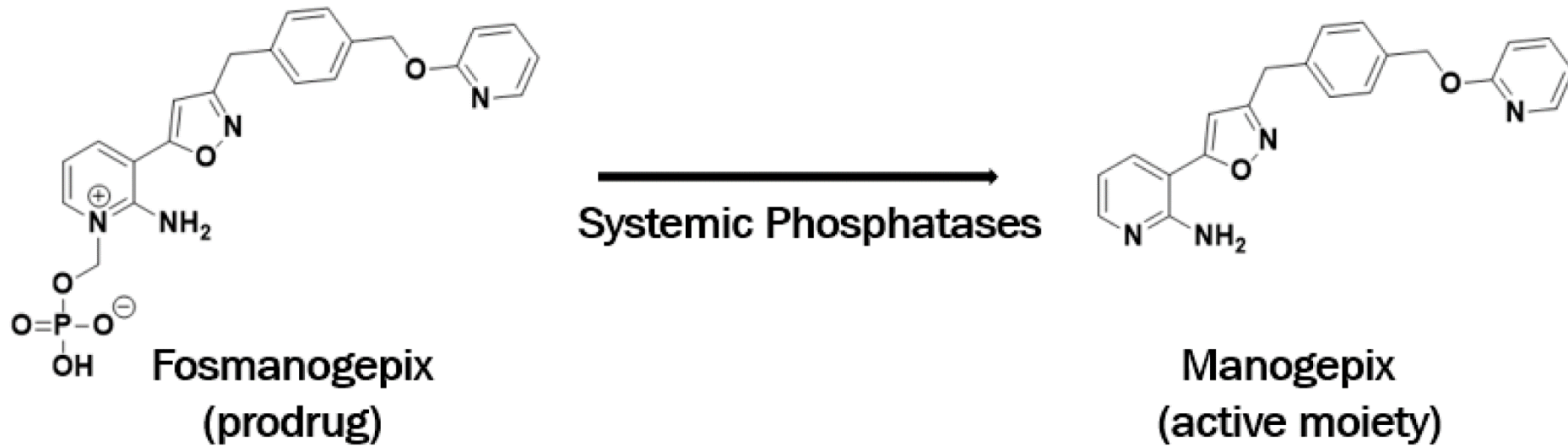


 Advantages	 Limitations
<p>Oral (and IV) formulation</p> <p>Favourable safety profile</p> <p>Broad antifungal activity including azole-resistant and cryptic <i>Aspergillus</i> spp.</p> <p>Alternate binding site, limited cross-resistance with echinocandins</p>	<p>Absorption characteristics in pts with mucositis, acid suppression therapy etc.</p> <p>Poor CNS penetration</p> <p>DDI with strong CYP inducers/inhibitors</p>



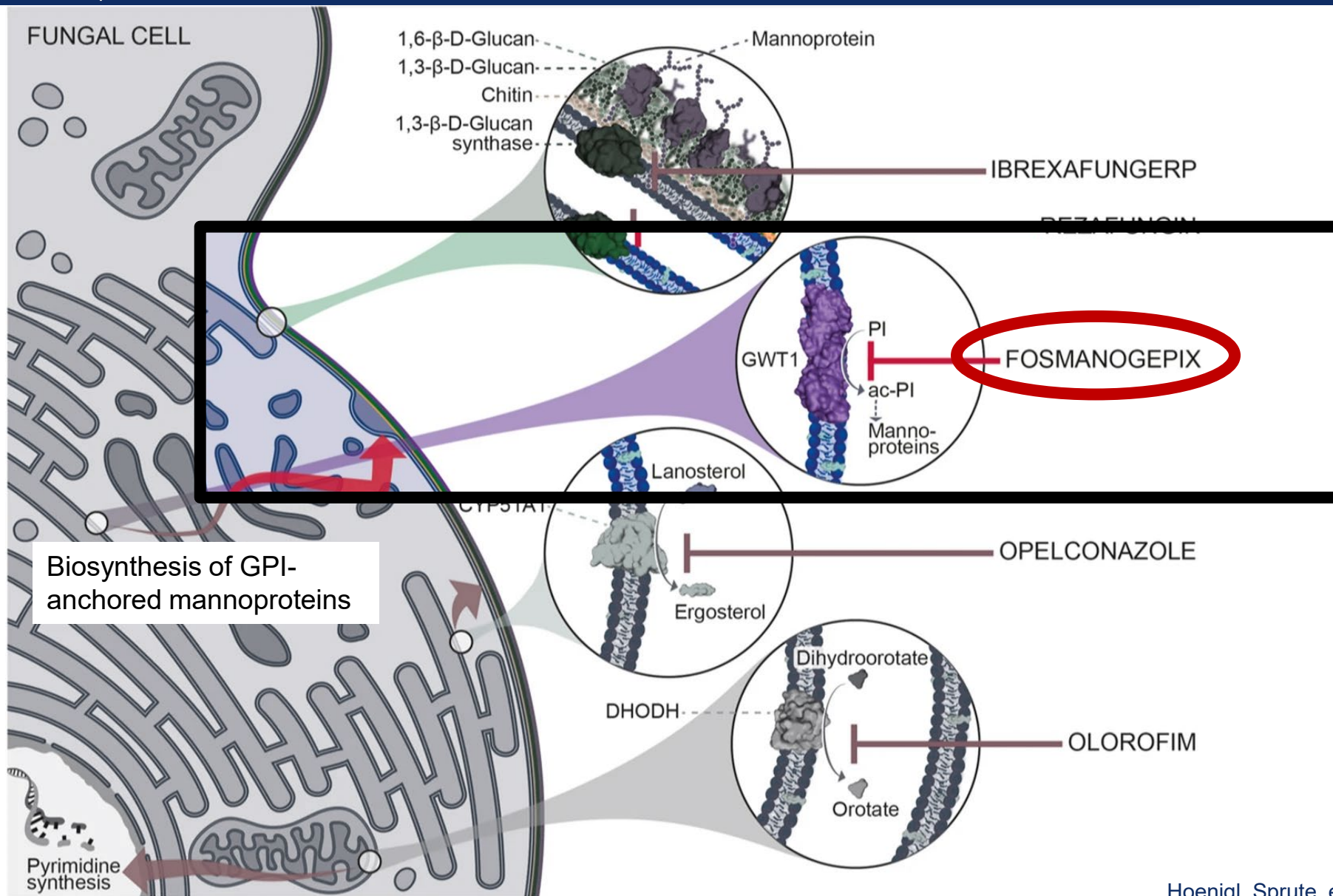
Future Roles: Combination therapy for IA, oral step-down therapy, prophylaxis for IC, IA, and *Pneumocystis* pneumonia

- **Class:** N-phosphonoxymethyl (pro)drug







Fosmanogepix (APX001; Amplyx/Pfizer/Basilea)





- **Class:** N-phosphonooxymethyl (pro)drug
- **Mechanism of Action:** targets GPI-anchored protein maturation through inhibition of the fungal inositol acyltransferase Gwt1
- **Form of Application:** IV  and PO  (bioavailability >90%)




comparable to
isavuconazole


	<i>Aspergillus calidoustus</i>	Green
	<i>Aspergillus fumigatus</i>	Green
	Azole-resistant <i>A. fumigatus</i>	Green
	<i>Aspergillus flavus</i>	Green
	<i>Aspergillus lentulus</i>	Green
	<i>Aspergillus nidulans</i>	Green
	<i>Aspergillus niger</i>	Green
	<i>Aspergillus terreus</i>	Green
	<i>Aspergillus tubingensis</i>	Green

	<i>Cunninghamella</i>	Orange
	<i>Lichtheimia</i>	Orange
	<i>Mucor</i>	Orange
	<i>Rhizopus</i>	Orange


	<i>Fusarium spp.</i>	Green
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	<i>Alternaria alternata</i>	Orange
	<i>Cladosporium spp.</i>	Green
	<i>Paecilomyces variotii</i>	Green
	<i>Purpureocillium lilacinum</i>	Green
	<i>Scopulariopsis spp.</i>	Green
	<i>Rasamsonia spp.</i>	Green

	<i>Scedosporium spp.</i>	Green
	<i>Lomentospora prolificans</i>	Green

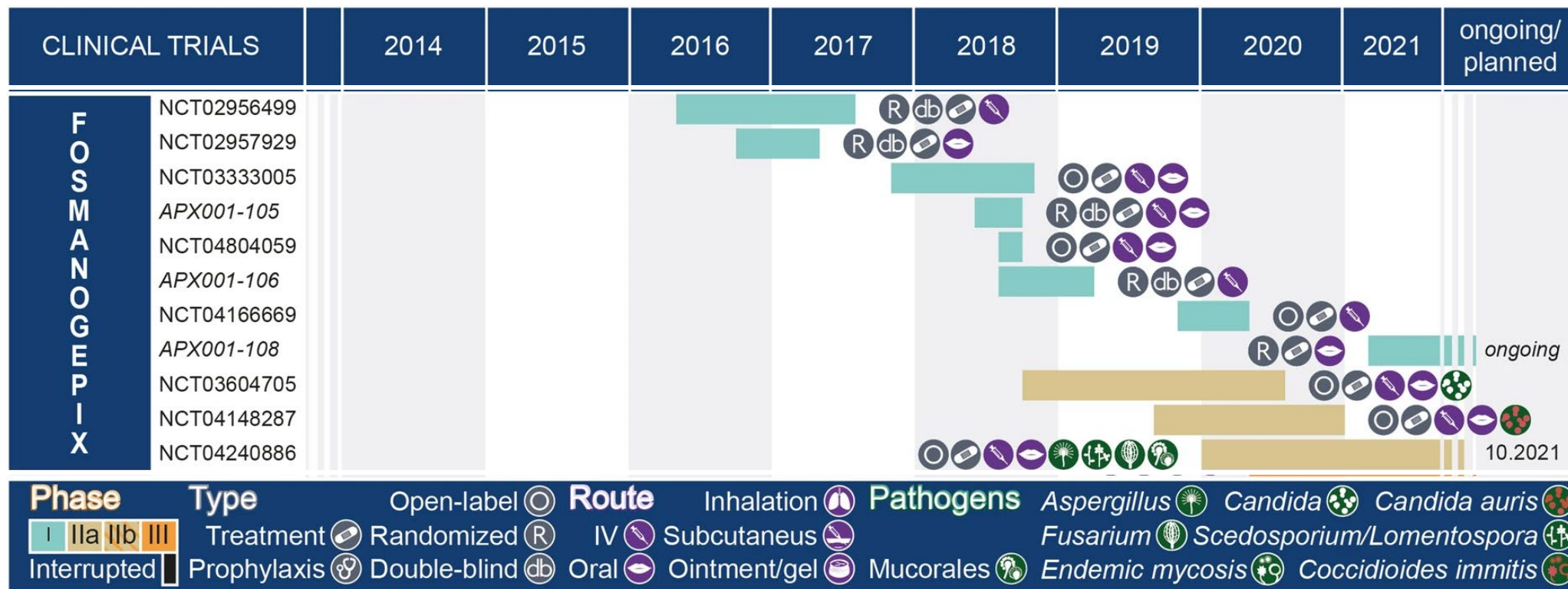
	<i>Candida albicans</i>	Green
	<i>Candida auris</i>	Red
	<i>Candida dubliniensis</i>	Green
	<i>Candida glabrata</i>	Green
	<i>Candida krusei</i>	Red
	<i>Candida lusitanae</i>	Green
	<i>Candida parapsilosis</i>	Green
	<i>Candida tropicalis</i>	Green

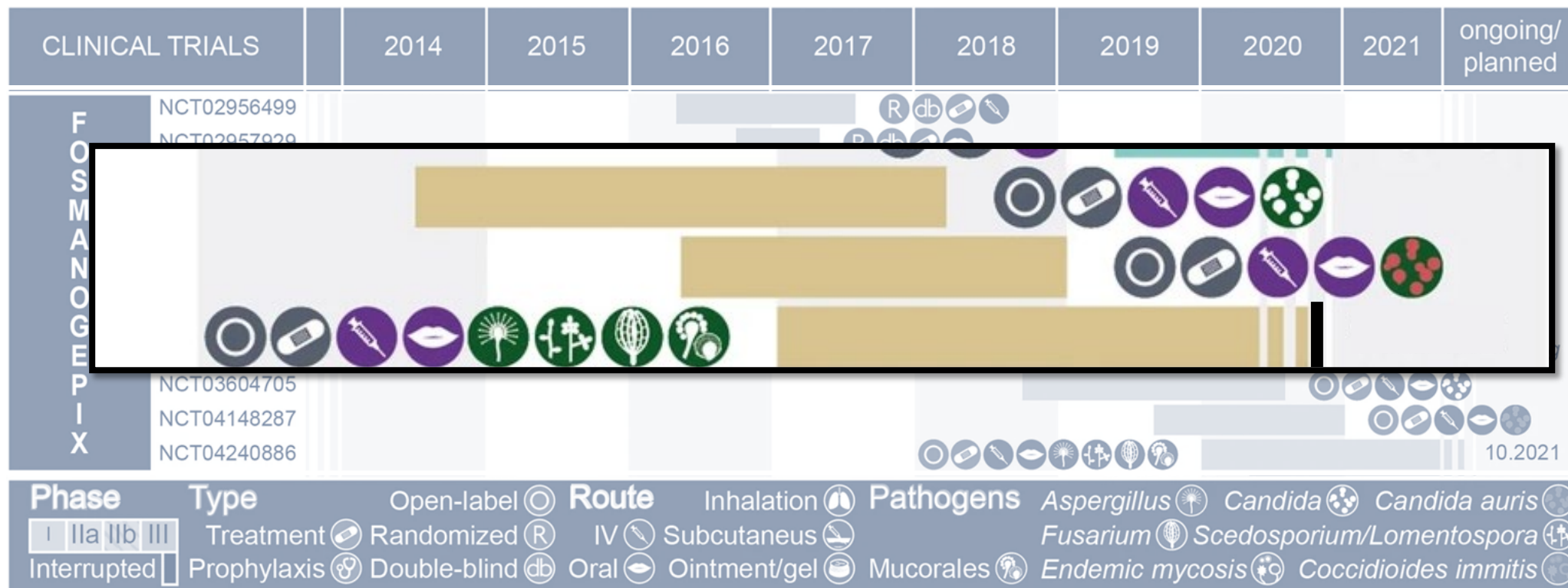
	<i>Cryptococcus gattii</i>	Green
	<i>Cryptococcus neoformans</i>	Green

	<i>Trichosporon asahii</i>	Green
	<i>Exophiala dermatitidis</i>	Green
	<i>Malassezia furfur</i>	Green

	<i>Pneumocystis jirovecii</i>	Green
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	<i>Blastomyces dermatitidis</i>	Green
	<i>Coccidioides immitis</i>	Red
	<i>Histoplasma capsulatum</i>	Green
	<i>Fonsecaea pedrosoi</i>	Green
	<i>Madurella mycetomatis</i>	Green
	<i>Talaromyces marneffeii</i>	Green
	<i>Phialophora verrucosa</i>	Green





NCT03604705

APEX

AEGIS



CLINICAL TRIALS

FOSMANOGEPIX

NCT02956499
NCT02957020

NCT03604705
NCT04148287
NCT04240886

Phase Type

I IIa IIb III Treatment
Interrupted Prophylaxis

Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Amplyx Pharmaceuticals, Inc. (owned by Pfizer Inc.)

Medicine Studied: Fosmanogepix (PF-07842805 or APX001)

Protocol Number: C4791010 (APX001-202)

Dates of Study: 04 January 2020 to 09 May 2022

Title of this Study: A Study of Fosmanogepix in Participants With Invasive Mold Infections
[A Phase 2, Open-Label Study to Evaluate the Safety and Efficacy of APX001 in the Treatment of Patients With Invasive Mold Infections Caused by Aspergillus Species or Rare Molds]

Date(s) of this Report: 27 March 2023

2020	2021	ongoing/ planned

NCT03604705
APEX
AEGIS

10.2021

Candida auris
Aspergillus/Lomentospora
Cryptosporidium parvum
Coccidioides immitis



AEGIS: Open-label Study of APX001 for Treatment of Patients With Invasive Mold Infections Caused by *Aspergillus* or Rare Molds

Patients with limited/no treatment options, N=21

- All-cause mortality after 42d was 5/21 (25%) for fosmanogepix vs. 45% (expected rate)
- All-cause mortality after 84d was 9/25 (36%), considered not related to fosmanogepix
- Most common AEs: Nausea 13/21 (62%), diarrhoea 10/21 (48%), vomiting 9/21 (43%), lack of appetite 7/21 (33%), oedema 6/21 (29%), fever 5/21 (24%)
- SAEs: Neutropenic fever 3/21 (14%), BSI 2/21 (10%), cardiac arrest 2/21 (10%), diarrhoea 2/21 (10%), ARDS 2/21 (10%)
- Terminated in May 2022 by the sponsor to prioritize a randomized comparative Phase 3 trial in the same indication



CLIN

F
O
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P
I
X

Phase

I IIa IIb

Interrupted

Ad hoc announcement pursuant to Art. 53 LR

Basilea announces acquisition of fosmanogepix, a phase-3-ready broad-spectrum antifungal

Allschwil, Switzerland, November 13, 2023

Basilea Pharmaceutica Ltd, Allschwil (SIX: BSLN), a commercial-stage biopharmaceutical company committed to meeting the needs of patients with severe bacterial and fungal infections, announced today that it has entered into an asset purchase agreement with Amplyx Pharmaceuticals, Inc., an affiliate of Pfizer Inc., to acquire the rights to fosmanogepix, a clinical-stage broad-spectrum antifungal candidate. In addition, Basilea has acquired the rights to a preclinical antifungal compound.

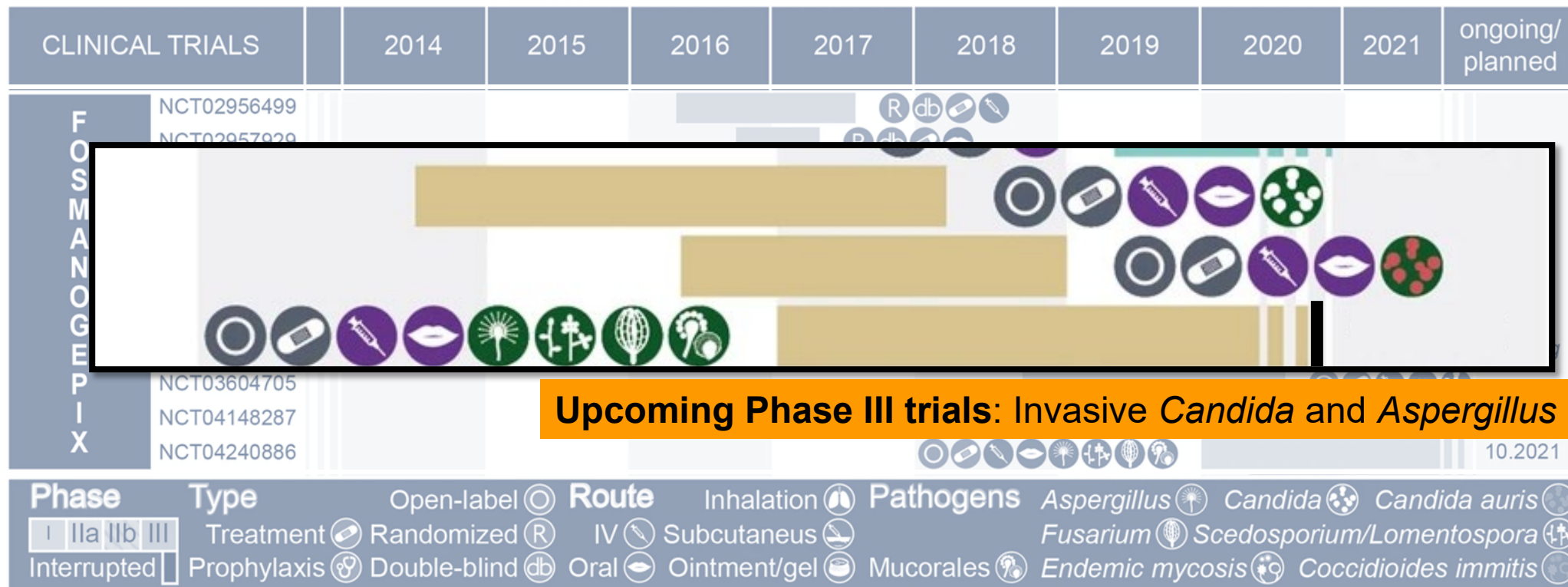
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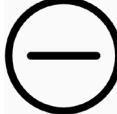
APEX

AEGIS

Candida Candida auris
Fusarium Scedosporium/Lomentospora
Mucorales Endemic mycosis Coccidioides immitis





 Advantages	 Limitations
<p>Oral and IV formulations with high oral bioavailability</p> <p>Broad antifungal spectrum</p> <p>Broad tissue distribution including CNS</p> <p>So far limited DDI (under investigation)</p>	<p>No activity against <i>C. krusei</i></p> <p>Efflux-mediated azole cross-resistance?</p> <p>Variable activity against <i>Mucorales</i></p>



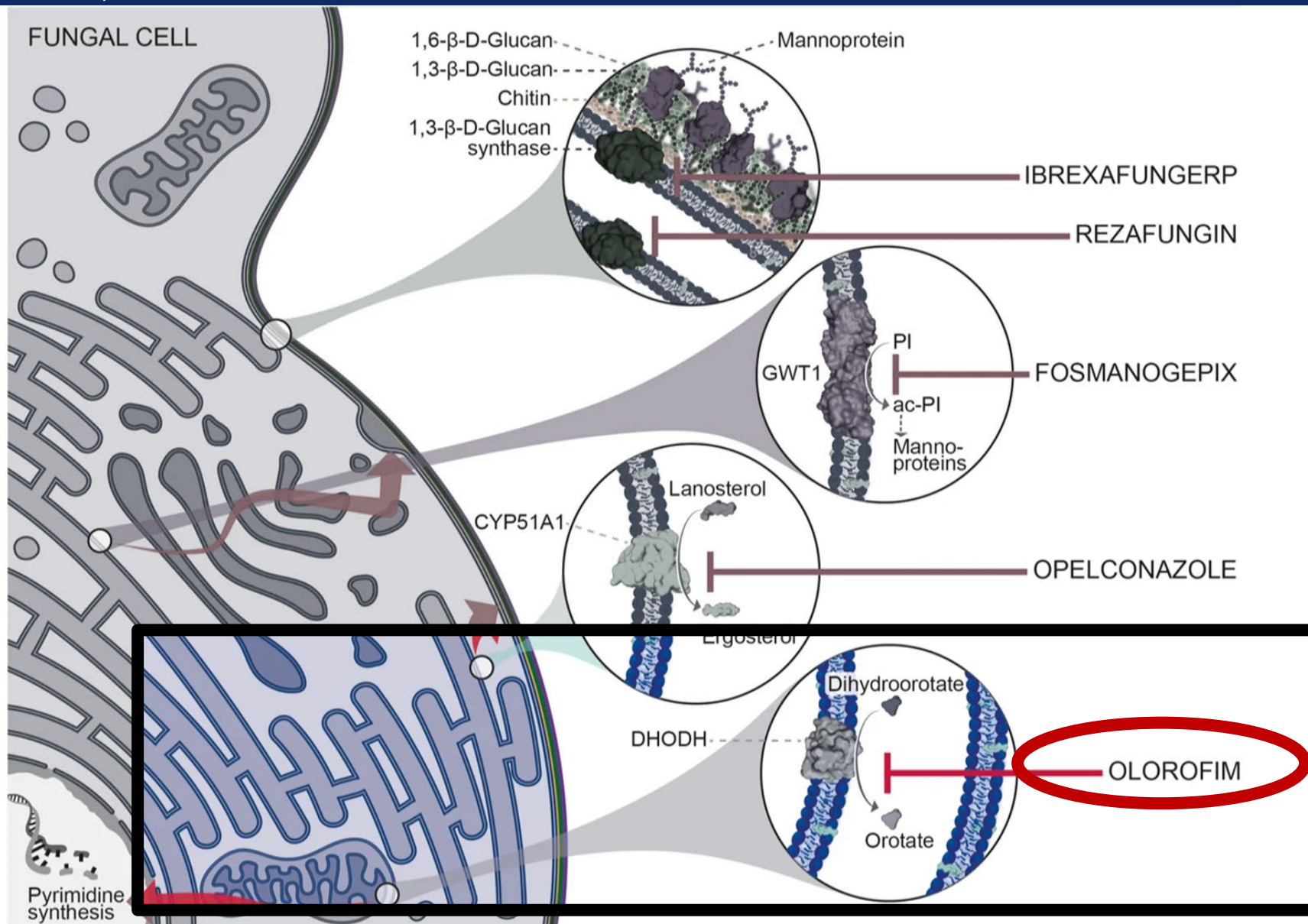
Future Roles: Resistant IA, difficult-to-treat invasive rare mold infections






- **Class:** Orotomide



Olorofim (F901318; F2G/Shionogi)






- **Class:** Orotomide
- **Mechanism of Action:** Inhibition of dihydroorotate dehydrogenase, targets pyrimidine synthesis
- **Form of Application:** PO  (and IV  and inhaled )



Olorofim (F901318; F2G/Shionogi)


	<i>Aspergillus calidoustus</i>	Green
	<i>Aspergillus fumigatus</i>	Green
	Azole-resistant <i>A. fumigatus</i>	Green
	<i>Aspergillus flavus</i>	Green
	<i>Aspergillus lentulus</i>	Green
	<i>Aspergillus nidulans</i>	Green
	<i>Aspergillus niger</i>	Green
	<i>Aspergillus terreus</i>	Green
	<i>Aspergillus tubingensis</i>	Green

	<i>Cunninghamella</i>	Red
	<i>Lichtheimia</i>	Red
	<i>Mucor</i>	Red
	<i>Rhizopus</i>	Red

	<i>Fusarium spp.</i>	Orange
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	<i>Alternaria alternata</i>	Red
	<i>Cladosporium spp.</i>	Green
	<i>Paecilomyces variotii</i>	Green
	<i>Purpureocillium lilacinum</i>	Orange
	<i>Scopulariopsis spp.</i>	Green
	<i>Rasamsonia spp.</i>	Green


	<i>Scedosporium spp.</i>	Green
	<i>Lomentospora prolificans</i>	Green

	<i>Candida albicans</i>	Red
	<i>Candida auris</i>	Red
	<i>Candida dubliniensis</i>	Red
	<i>Candida glabrata</i>	Red
	<i>Candida krusei</i>	Red
	<i>Candida lusitaniae</i>	Red
	<i>Candida parapsilosis</i>	Red
	<i>Candida tropicalis</i>	Red

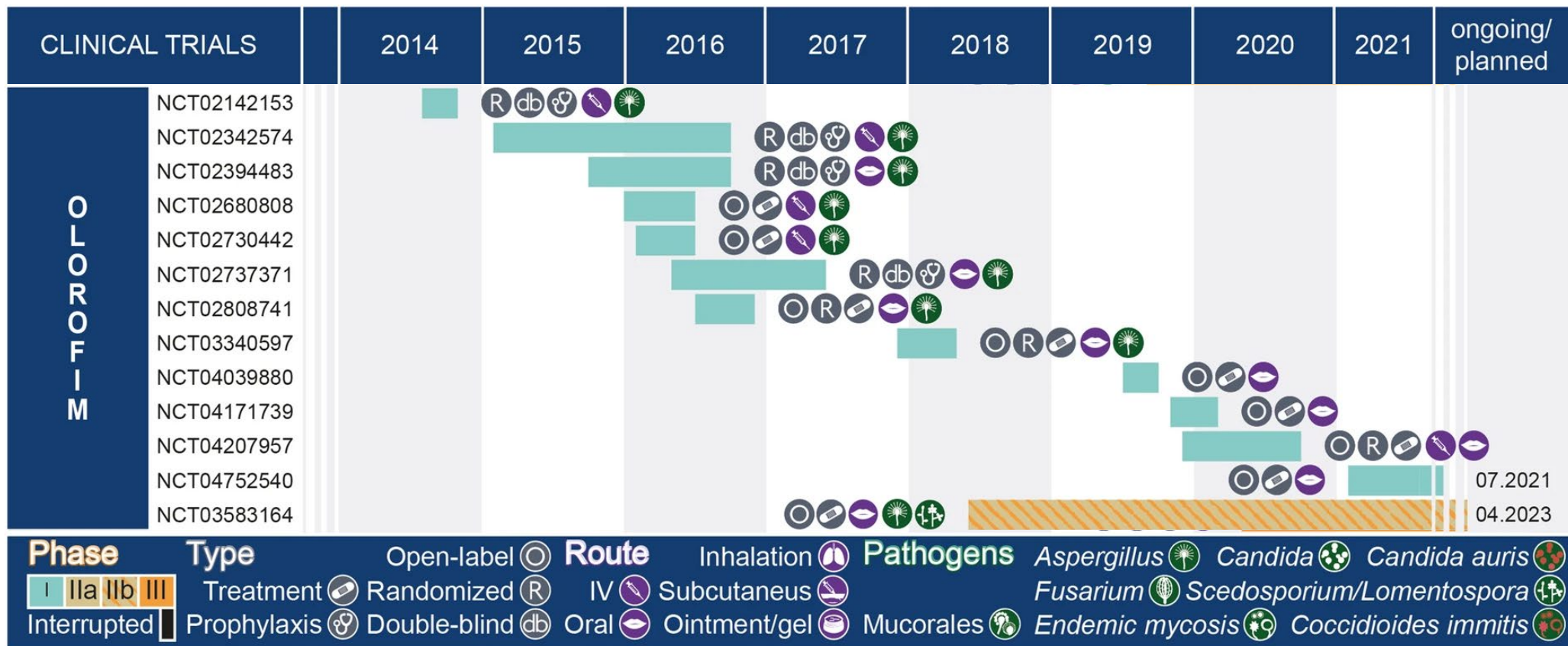
	<i>Cryptococcus gattii</i>	Red
	<i>Cryptococcus neoformans</i>	Red

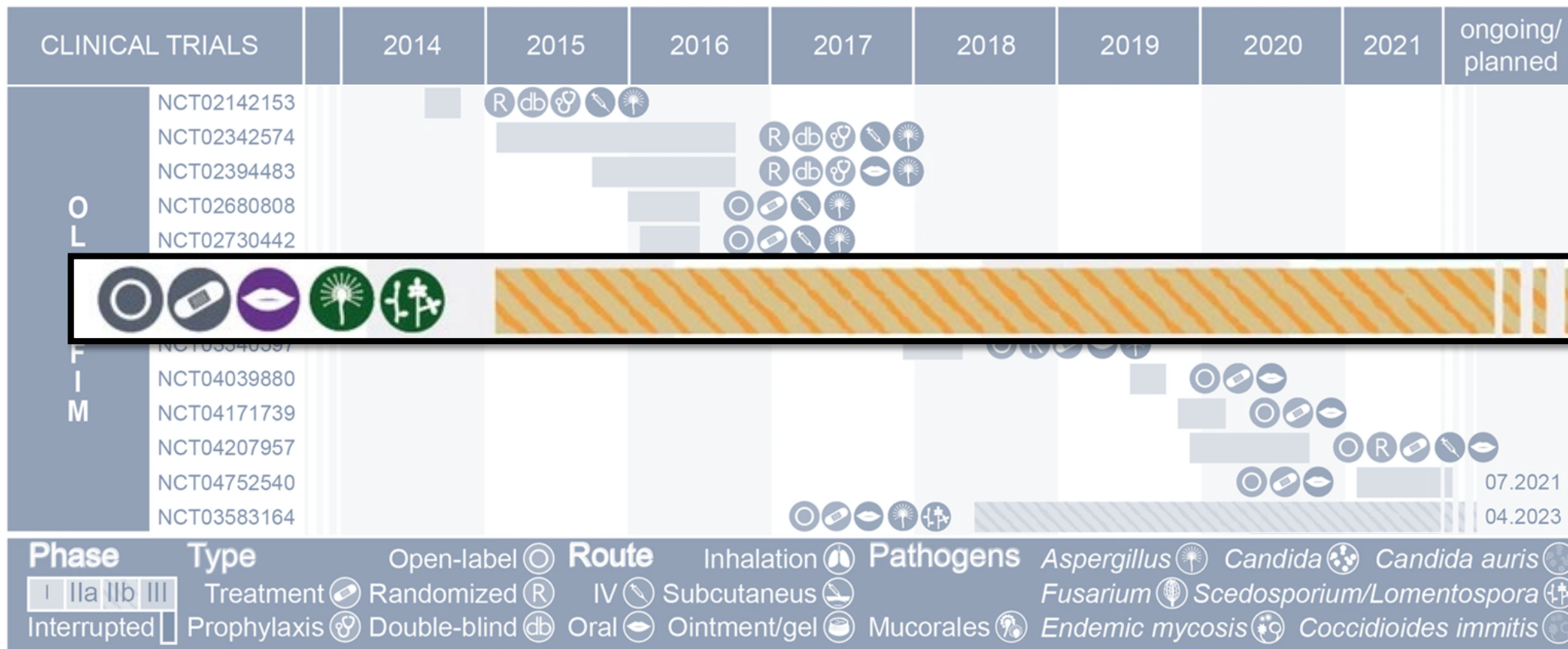
	<i>Trichosporon asahii</i>	Red
	<i>Exophiala dermatitidis</i>	Red
	<i>Malassezia furfur</i>	Red

	<i>Pneumocystis jirovecii</i>	Red
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	<i>Blastomyces dermatitidis</i>	Green
	<i>Coccidioides immitis</i>	Green
	<i>Histoplasma capsulatum</i>	Green
	<i>Fonsecaea pedrosoi</i>	Red
	<i>Madurella mycetomatis</i>	Green
	<i>Talaromyces marneffeii</i>	Green
	<i>Phialophora verrucosa</i>	Green







**FORMULA
-OLS**



F2G and Shionogi Present Full Data Set from Pivotal Phase 2b Study at Trends in Medical Mycology (TIMM) 2023 Demonstrating Positive Therapeutic Responses in Patients with Invasive Fungal Infections Treated with Oral Olorofim

Published: Oct 21, 2023

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-OLS

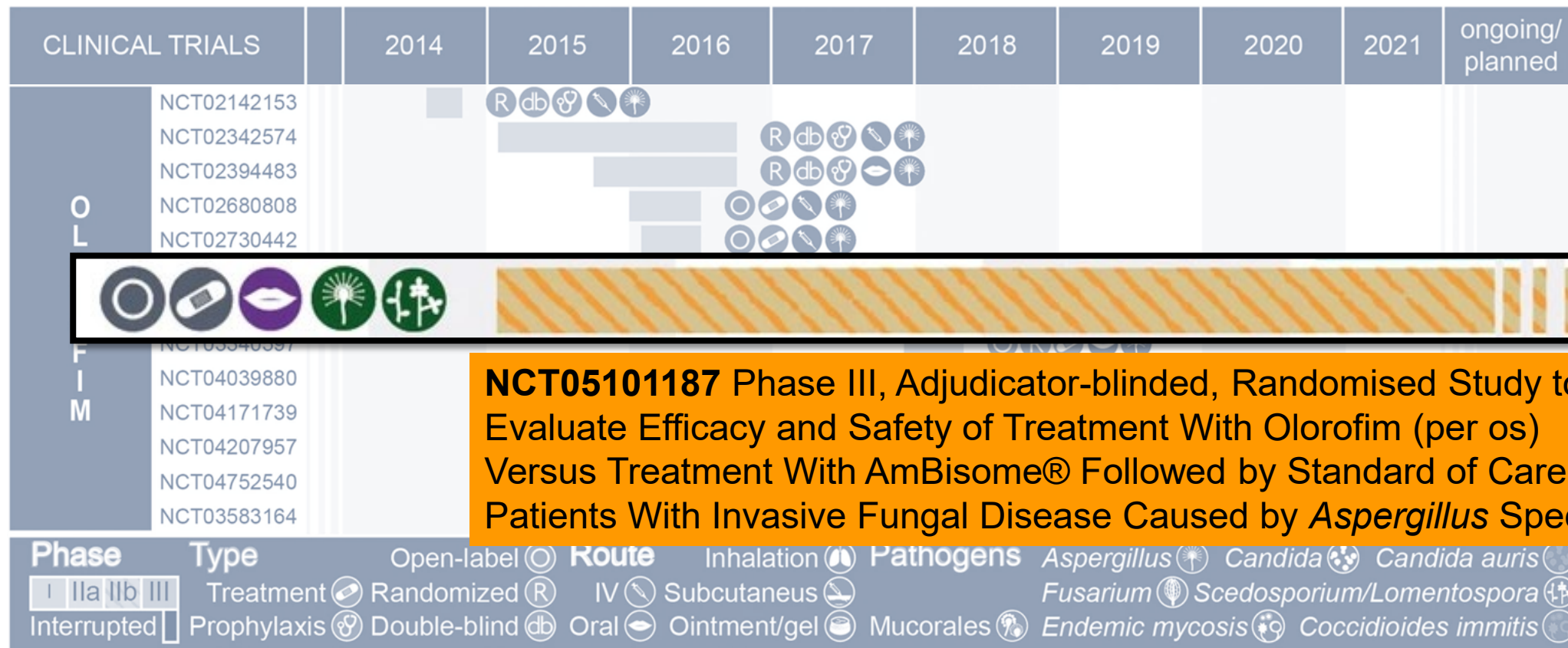


F2G and Shionogi Present Full Data Set from Pivotal Phase 2b Study at Trends in Medical Mycology (TIMM) 2023 Demonstrating Positive Therapeutic Responses in Patients with Invasive Fungal Infections Treated with Oral Olorofim

TIMM 10/2023: Data from 203 patients

Open-label, single-arm, phase 2b FORMULA-OLS / Study 32

- Patients with limited/no treatment options for proven IFI or probable IPA
- *Aspergillus* spp. (101, including 22 cases with azole-resistant strains), *Lomentospora prolificans* (26), *Scedosporium* spp. (22), *Coccidioides* spp. (41), *Scopulariopsis* spp. (6)
- Overall success rate at d42 was 28.7% (IA: 34.7%)
- Overall success in IFI other than coccidioidomycosis (n = 161) was 36.0% at d42
- All-cause mortality at d42 and d84 was 11.4% and 15.8%, resp. (IA: 17.8% and 25.7%)
- Changes in liver biochemistry at least possibly related to olorofim in 9.9%, managed by dose reduction/pause and by permanent discontinuation in 2.5%
- Mild gastrointestinal intolerance to olorofim noted in 9.9%



FORMULA
-OLS

NCT05101187 Phase III, Adjudicator-blinded, Randomised Study to Evaluate Efficacy and Safety of Treatment With Olorofim (per os) Versus Treatment With AmBisome® Followed by Standard of Care in Patients With Invasive Fungal Disease Caused by *Aspergillus* Species

OASIS

Phase: I | IIa | IIb | III | Interrupted

Type: Treatment | Prophylaxis



Open-label | Randomized | Double-blind

Route: IV | Oral

Inhalation | Subcutaneous | Ointment/gel

Pathogens: *Aspergillus* | *Candida* | *Candida auris* | *Fusarium* | *Scedosporium/Lomentospora* | *Mucorales* | *Endemic mycosis* | *Coccidioides immitis*



 Advantages	 Limitations
<p>Oral formulation (and IV and inhaled)</p> <p>Activity against various <i>Aspergillus</i> spp. including azole-resistant strains and difficult to treat cryptic species</p> <p>Broad tissue distribution including CNS and kidneys</p>	<p>No broad-spectrum antifungal with no activity against <i>Mucorales</i> or yeasts</p> <p>Metabolized by cytochrome P450, potential interactions, liver toxicity</p> <p>Role for therapeutic drug monitoring?</p>



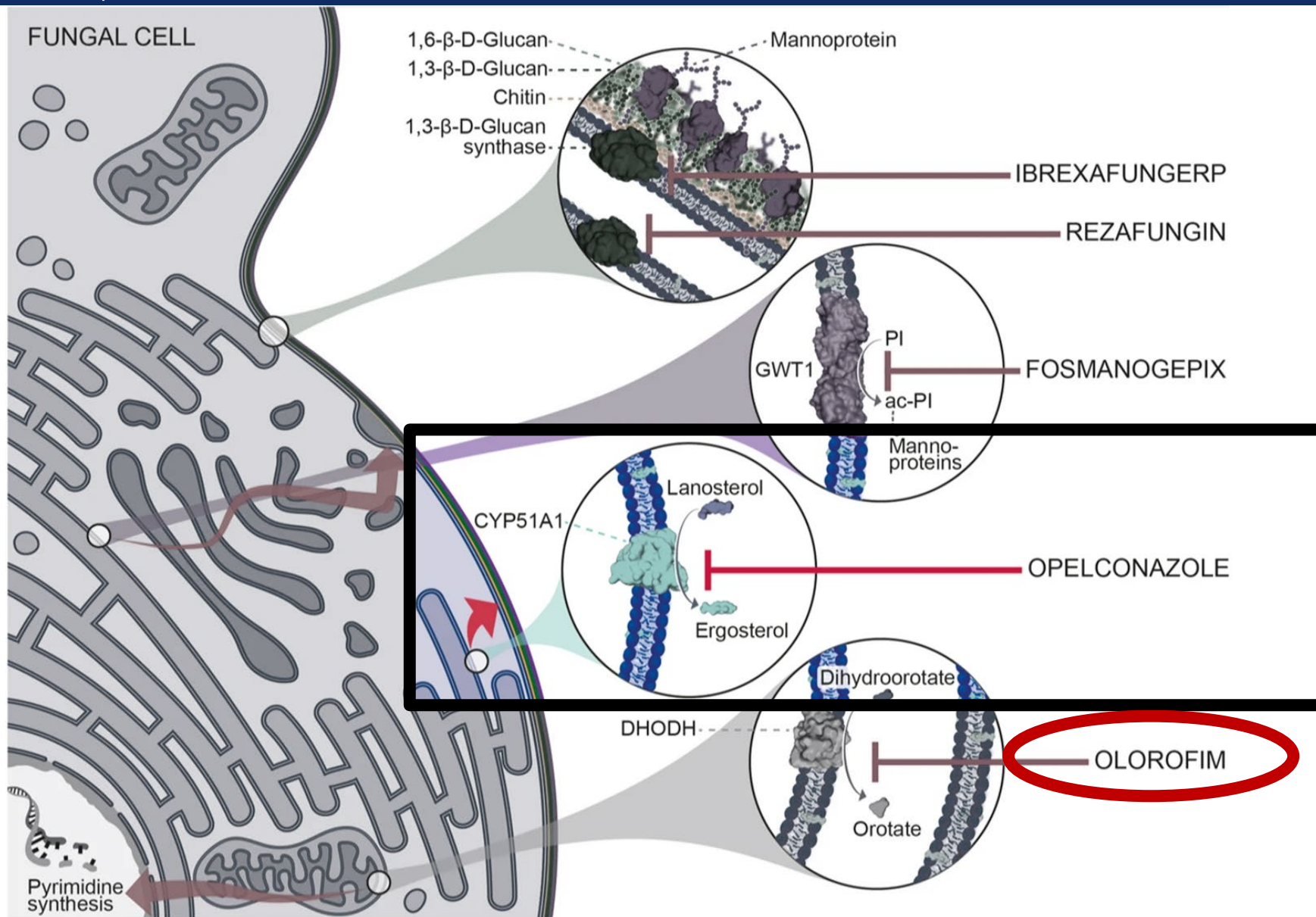
Future Roles: Difficult-to-treat and refractory mold infections




- **Class:** Triazole



Opelconazole (PC945; Pulmocide)



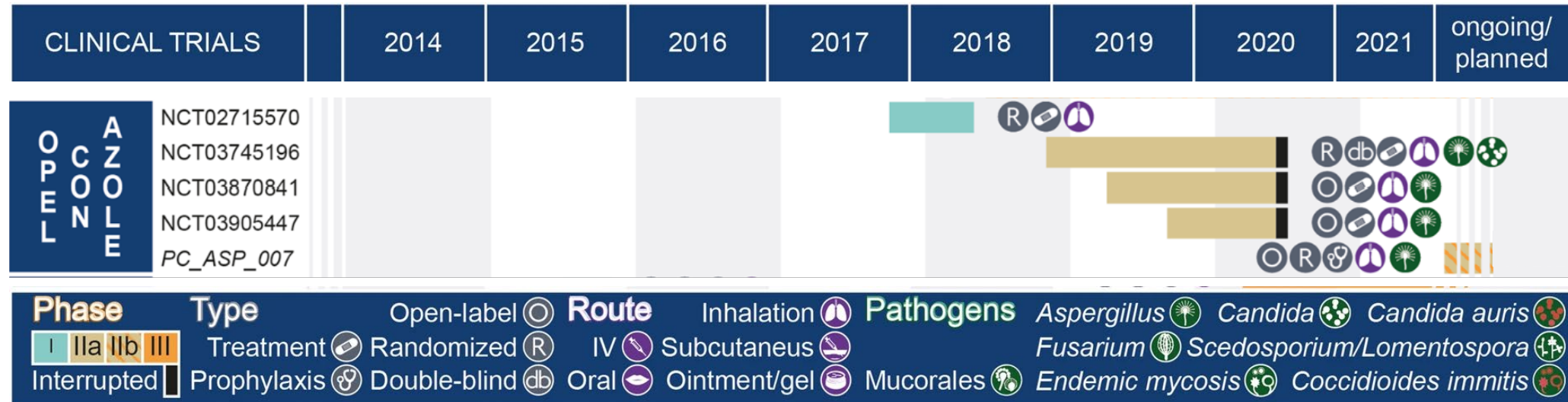


- **Class:** Orotomide
- **Mechanism of Action:** Inhibition of lanosterol demethylase, targets ergosterol synthesis
- **Form of Application:** Inhaled 

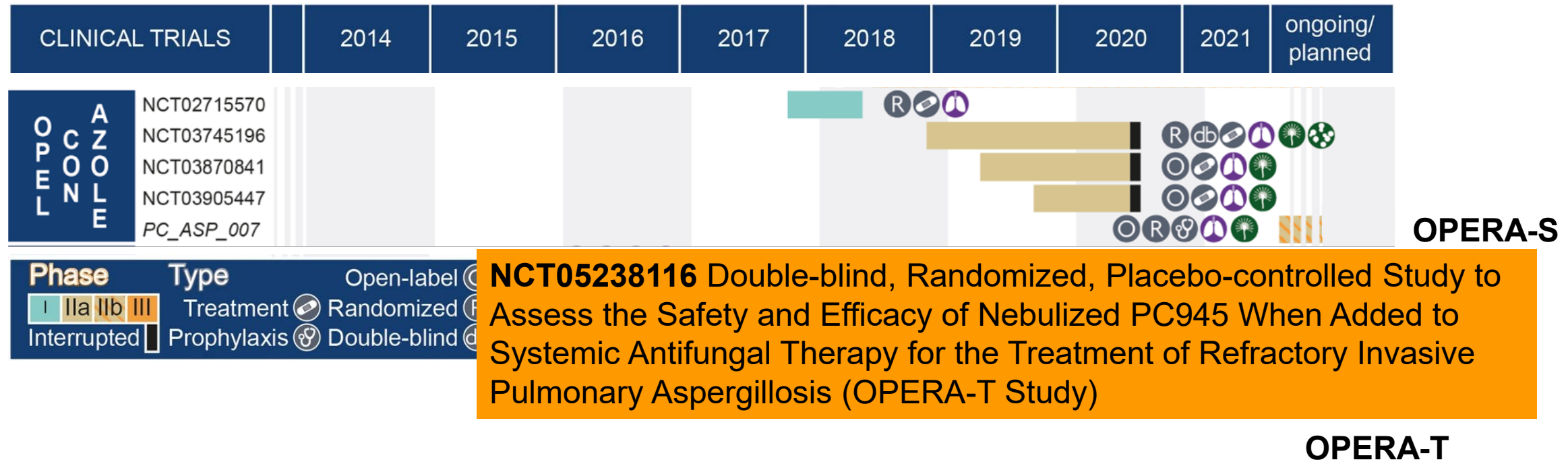


Opelconazole (PC945; Pulmocide)


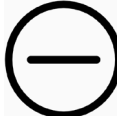
→		<i>Aspergillus calidoustus</i>			<i>Candida albicans</i>		
		<i>Aspergillus fumigatus</i>			<i>Candida auris</i>		
		Azole-resistant <i>A. fumigatus</i>			<i>Candida dubliniensis</i>		
		<i>Aspergillus flavus</i>			<i>Candida glabrata</i>		
		<i>Aspergillus lentulus</i>			<i>Candida krusei</i>		
		<i>Aspergillus nidulans</i>			<i>Candida lusitaniae</i>		
		<i>Aspergillus niger</i>			<i>Candida parapsilosis</i>		
		<i>Aspergillus terreus</i>			<i>Candida tropicalis</i>		
		<i>Aspergillus tubingensis</i>					
			<i>Cunninghamella</i>			<i>Cryptococcus gattii</i>	
		<i>Lichtheimia</i>			<i>Cryptococcus neoformans</i>		
		<i>Mucor</i>					
			<i>Rhizopus</i>			<i>Trichosporon asahii</i>	
					<i>Exophiala dermatitidis</i>		
					<i>Malassezia furfur</i>		
			<i>Fusarium spp.</i>				
			<i>Alternaria alternata</i>			<i>Pneumocystis jirovecii</i>	
		<i>Cladosporium spp.</i>					
	<i>Paecilomyces variotii</i>				<i>Blastomyces dermatitidis</i>		
	<i>Purpureocillium lilacinum</i>			<i>Coccidioides immitis</i>			
	<i>Scopulariopsis spp.</i>			<i>Histoplasma capsulatum</i>			
	<i>Rasamsonia spp.</i>			<i>Fonsecaea pedrosoi</i>			
				<i>Madurella mycetomatis</i>			
		<i>Scedosporium spp.</i>		<i>Talaromyces marneffeii</i>			
	<i>Lomentospora prolificans</i>			<i>Phialophora verrucosa</i>			



OPERA-S





 Advantages	 Limitations
<p>Broad activity against <i>Aspergillus</i> spp.</p> <p>High local concentrations while avoiding systemic adverse effects and drug interactions</p> <p>Synergism with systemically applied azoles</p> <p>Sustained lung retention due to lipophilia and micronized drug particles</p>	<p>No systemic activity</p>



Future Roles: IPA in non-neutropenic patients, e.g. COVID-19, combination therapy for IPA in immunocompromised hosts, prophylaxis e.g. in ALL or lung transplant, ABPA, CPA



Brief Communication

= KINOPROL®

The novel agrochemical fungicide ipflufenquin drives cross-resistance to olorofim in the human pathogen *Aspergillus fumigatus*.

Norman van Rhijn, Isabelle Storer, Mike Birch, Jason Oliver, Michael Bottery, and 1 more

This is a preprint; it has not been peer reviewed by a journal.

<https://doi.org/10.21203/rs.3.rs-2621591/v1>

Nelesh Govender @neleshg · 5. Mai
Recipe for future resistance!

- 1 Novel human antifungal medicine: olorofim Environmental fungicides w/ same mechanism of action registered/in the pipeline: ipflufenquin, tetflupyrolimet
- 2 Novel human antifungal med: fosmanogepix Environmental fungicide, same MOA: aminopyrifen

Regular Article

shares mode of action with fosmanogepix

Aminopyrifen, a novel 2-aminonicotinate fungicide with a unique effect and broad-spectrum activity against plant pathogenic fungi

Masahiro Hatamoto,^{1,*} Ryo Aizawa,² Kogomi Koda¹ and Toshiki Fukuchi¹

¹ Biological Section Research Department, AGRO-KANESHO Co., Ltd., 9511-4, Yuki Ibaraki 307-0001, Japan

² Chemical Synthesis Section Research Department, AGRO-KANESHO Co., Ltd., Tokorozawa, Saitama 359-0024, Japan

(Received December 21, 2020; Accepted March 22, 2021)

WIRED BACKCHANNEL BUSINESS CULTURE GEAR MORE SIGN IN SUBSCRIBE

MARYN MCKENNA SCIENCE MAY 3, 2023 8:00 AM

A Critical New Drug Is Coming—Unless Agriculture Gets There First

Two long-awaited fungus killers are about to roll out. But if one is widely deployed first, it might breed resistance and make the other useless.



Brief Communication

The novel
drives cross
pathogen A

Norman van Rhijn, Isabell

This is a preprint; it has

<https://doi.org/10.21203/rs>

Regular Article

Aminopyrifen, a
effect and broad

Masahiro Hatamoto,^{1,*} R

¹ Biological Section Research Departme

² Chemical Synthesis Section Research D

(Received December 21, 2020; Accepted March 22, 2021)

nature microbiology

Brief Communication

Aspergillus fumigatus strains that evolve resistance to the agrochemical fungicide ipflufenquin in vitro are also resistant to olorofim

Norman van Rhijn¹, Isabelle S. R. Storer¹, Mike Birch², Jason D. Oliver²,
Michael J. Bottery¹ & Michael J. Bromley¹✉

Received: 23 February 2023

Accepted: 31 October 2023

Utsunomiya, Saitama 359-0024, Japan

<https://doi.org/10.1038/s41564-023-01542->



Environmental fungicides
baseline: ipflufenquin,

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ing—Unless

to there First

Two long-awaited fungus killers are about to roll out. But if one is widely deployed first, it might breed resistance and make the other useless.



Fungi scope

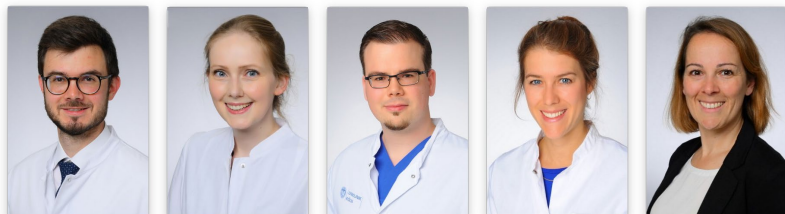
Global Fungal Infection Registry
ISHAM and ECMM Working Group
www.fungiscope.net

 @RosanneSprute

 rosanne.sprute@uk-koeln.de

Prof. Oliver A Cornely MD, FACP, FIDSA, FAAM, FECMM

Chair, Translational Research, CECAD Cluster of Excellence
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Rosanne Sprute
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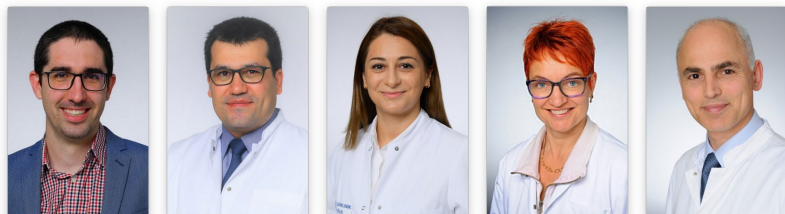
Therapeutic Drug Monitoring

Dr Carsten Müller MD

...and many others!

Coordinating Physicians and Quality Control Team Cologne

Dr Philipp Köhler MD, FECMM
Dr Jon Salmanton-García PhD



Jon Salmanton-García
Postdoctoral Researcher

Ertan Sal
Research Associate

Laman Rahimli
Research Associate

Birgid Schömig-Markiefka
Clinical Pathologist

Khosro Hekmat
Clinical Surgeon