The safety and single-dose pharmacokinetics of CD101 IV: results from a phase 1, dose-escalation study

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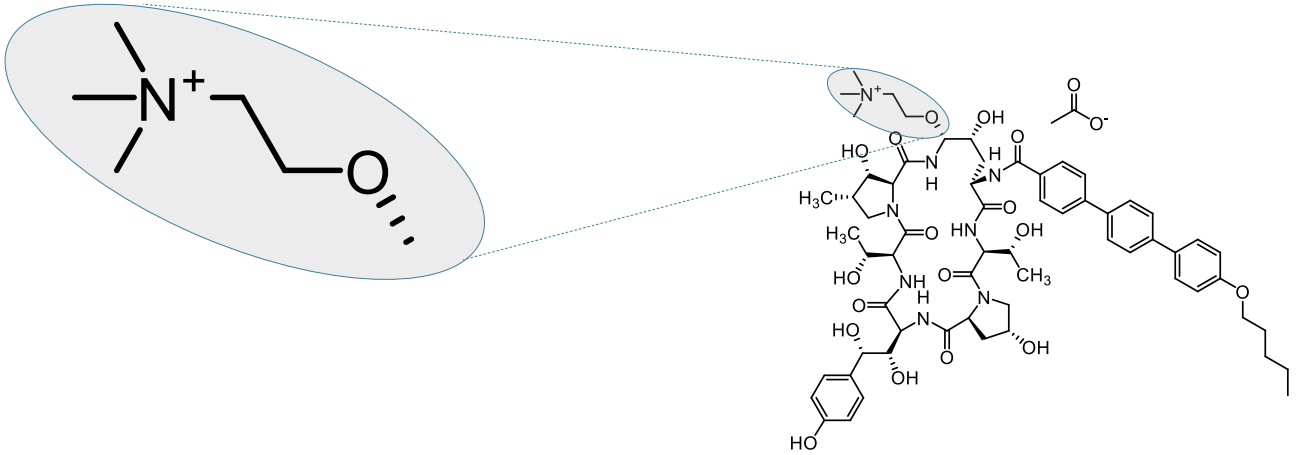
Disclosures

- Dirk Thye, MD, is an employee and shareholder of Cidara Therapeutics, Inc.

CD101 – A novel echinocandin



Structural modification yields unique chemical & biological properties

- Prolongs PK: enables weekly dosing, convenient inpatient and outpatient use
- Allows high, front-loaded drug exposures
- Eliminates toxic intermediates: improved safety & dose range
- Enables injectable and topical formulations

CD101 - potent against *Candida* and *Aspergillus*

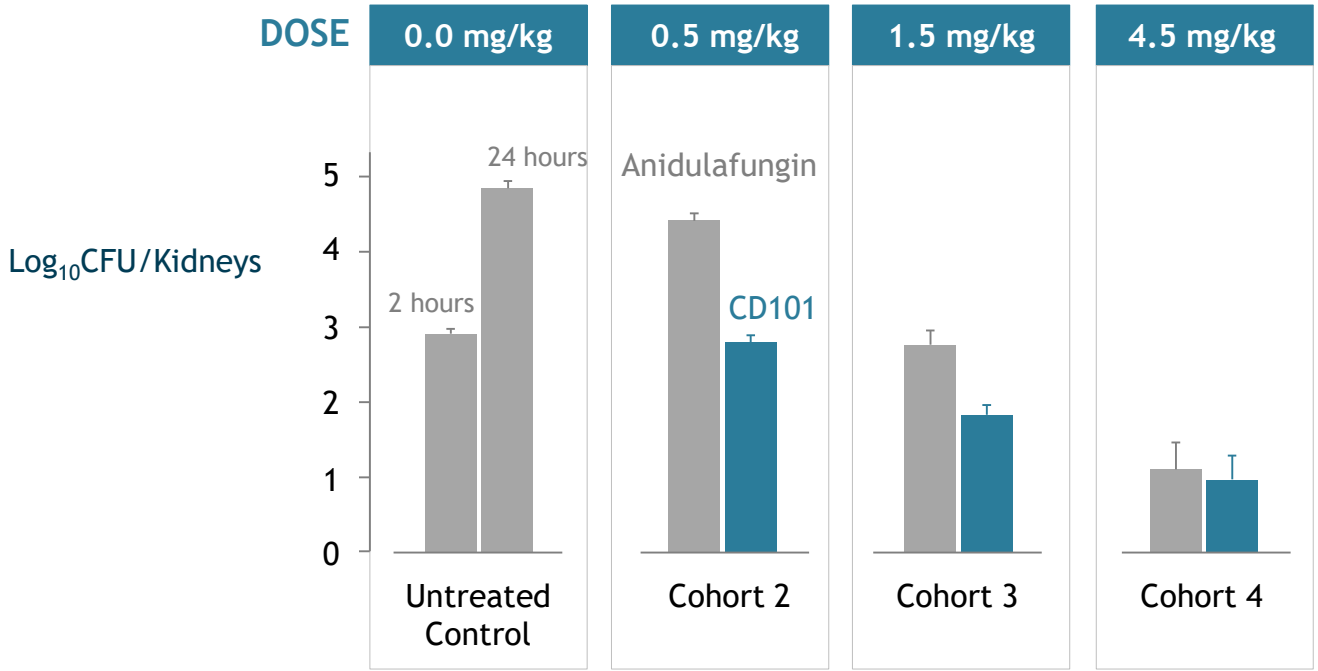
CD101, anidulafungin and caspofungin tested against a panel including azole- & echinocandin-resistant strains

	Candida MIC_{90} (µg/mL)					*Aspergillus* MEC_{90} (µg/mL)*			
	albicans (n=351)	*glabrata* (n=200)	*tropicalis* (n=151)	*krusei* (n=116)	parapsilosis (n=192)	*fumigatus* (n=20)	*terreus* (n=19)	*niger* (n=16)	*flavus* (n=12)
CD101	**0.06**	**0.06**	**0.03**	**0.03**	**2**	**0.015**	**0.015**	**0.03**	**≤0.008**
Anidulafungin	0.03	0.12	0.03	0.03	2	0.015	0.015	<0.008	≤0.008
Caspofungin	0.12	0.25	0.25	0.5	1	0.03	0.12	0.12	0.06

*CLSI methodology was employed for MIC/MEC determination, MECs vs *Aspergillus* were determined for CD101, anidulafungin and caspofungin.
Combined JMI and Micromyx US and international surveillance studies, ICAAC 2014 & 2015

CD101 – efficacy in *Candida* animal model

CFU in kidneys of mice 24 hours after infection with *C. albicans* and treatment with anidulafungin or CD101



Phase 1 single ascending dose study design

Number of subjects by dose

Dose	50 mg	100 mg	200 mg	400 mg	TOTALS
CD101 IV	6	6	6	6	24
Placebo	2	2	2	2	8
					32

- 1º objective: safety, tolerability and pharmacokinetics
- Safety assessments included AEs, ECGs, hematology, chemistry labs, urinalysis, vital signs, physical exam
- Subjects followed for 21 days after dosing

Phase 1 single ascending dose adverse events

Dose	CD101				Placebo
	50 mg	100 mg	200 mg	400 mg	
Subjects w/ AEs	3 of 6	0 of 6	3 of 6	1 of 6	5 of 8

- No serious AEs
- No severe AEs
- No dose-response effects in AE
- No withdrawals due to AEs
- No clinically significant vital sign, physical exam or ECG abnormalities
- No clinically significant laboratory abnormalities (hematology, chemistry, LFTs)

Single ascending dose lab summary- hematology

Dose	CD101				Placebo
	50 mg	100 mg*	200 mg	400 mg	
Hematology, n (%)					
Normal	78 (87)	80 (99)	89 (99)	88 (98)	115 (96)
Abnormal- not CS	12 (13)	2 (2)	1 (1)	2 (2)	5 (4)
Abnormal- CS	0	0	0	0	0

***1** subject in 100mg group had only 2 blood draws due to early departure for family reasons.
CS= clinically significant.

- **Hematology**: white blood cell count, hemoglobin, platelets
- 5 blood draws for each subject (Days 2, 4, 7, 14, 21) following dosing of study drug

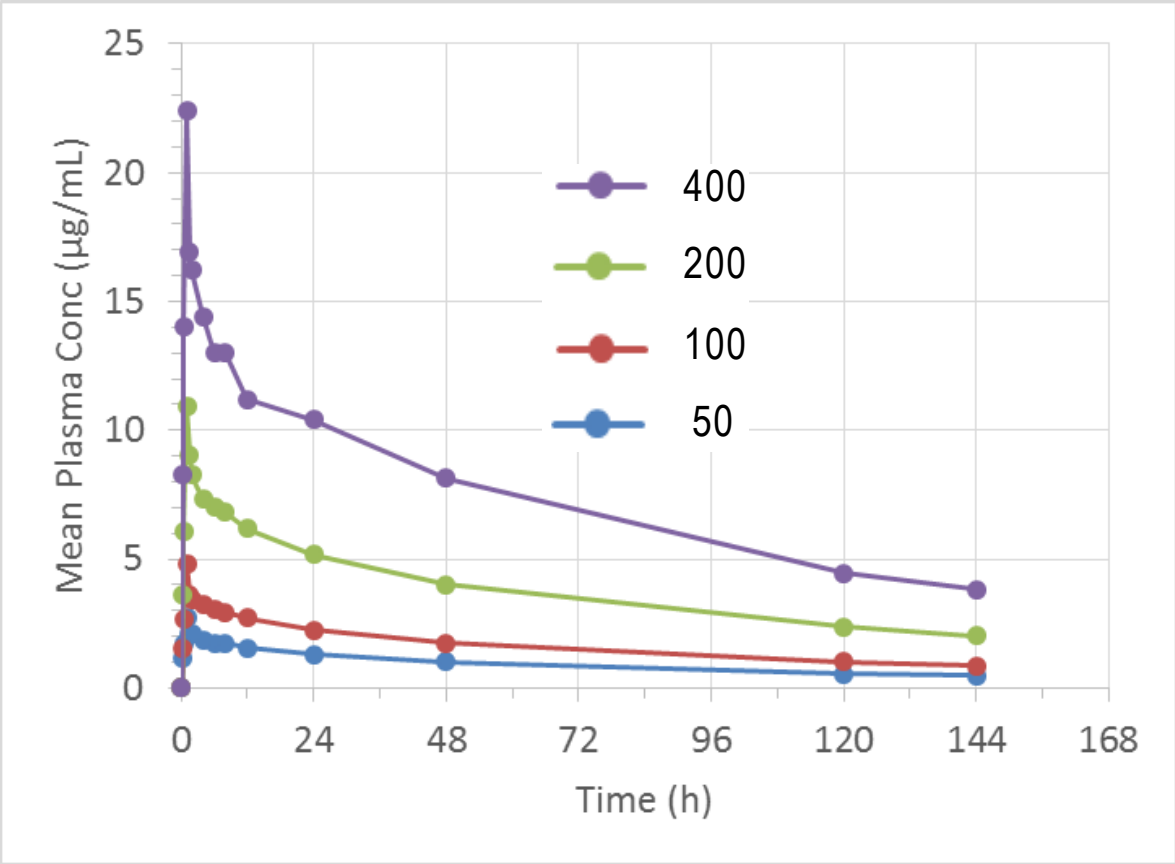
Single ascending dose lab summary- chemistries

Dose	CD101				Placebo
	50 mg	100 mg*	200 mg	400 mg	
Chemistries, n (%)					
Normal	461(96)	432(100)	465(97)	475(99)	619(96.5)
Abnormal- not CS	19(4)	0	16(3)	5(1)	18(3)
Abnormal- CS	0	0	0	0	2(0.5)‡

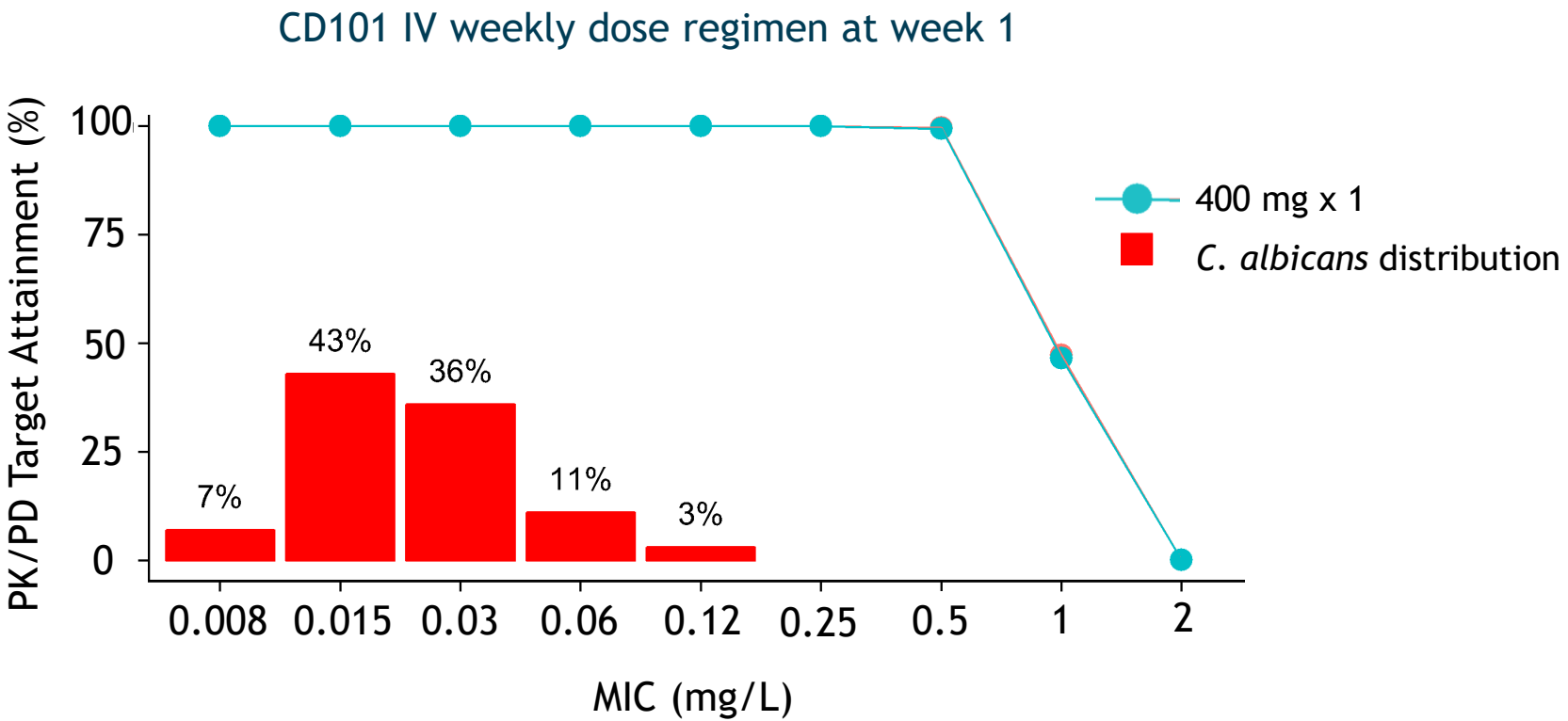
*1 subject in 100mg group had only 2 blood draws due to early departure for family reasons.
‡All clinically significant abnormal labs were in the placebo group: 1 hypocalcemia and 1 hyperglycemia
CS= clinically significant.

- **Chemistries**: calcium, chloride, bicarbonate, potassium, albumin, bun, creatinine, glucose, alkaline phosphatase, AST, ALT, total bilirubin, direct bilirubin, protein, sodium
- 5 blood draws for each subject (Days 2, 4, 7, 14, 21) following dosing of study drug

Dose proportional pharmacokinetics



Predicted PK/PD target attainment by MIC against Candida



CD101 IV single dose summary

- CD101 IV is safe and well-tolerated at single doses up to 400mg
  - No SAEs, severe AEs, or dose-response relationships for any AE
  - No clinically significant laboratory abnormalities
  - Pharmacokinetics linear across dose range
  - 400mg single dose results in 90% PTA at MIC=0.5 mg/L
- CD101 IV is being developed as a once weekly treatment and prevention regimen for invasive fungal infections for inpatients and outpatients
- CD101 IV Phase 2 candidemia trial anticipated to initiate 2Q16 in North America and Europe