New Options for Prevention & Treatment of Invasive Fungal Infections

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Chief Medical Officer
Cidara Therapeutics, Inc.

HTIDE 2018, Venice
# Cidara Pipeline

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Discovery</th>
<th>Research/ in vitro</th>
<th>in vivo</th>
<th>IND-enabling</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rezafungin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rezafungin IV</td>
<td>Treatment (Candida)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rezafungin IV</td>
<td>Fungal prophylaxis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rezafungin Subcutaneous</td>
<td>Fungal Infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cloudbreak™ Immunotherapy Platform</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cloudbreak Antibody Drug Conjugates (ADC)</td>
<td>Gram (-) Viral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Infectious Disease Focus*  
*Hematology/Transplant Focus*  
*With NIH, 1Q19*
Rezafungin: a Novel, Second-Generation Echinocandin

• Prolongs PK
• Allows high exposures
• Eliminates toxic degradation products
• Enables multiple formulations

Structural modification yields improved chemical & biological properties

- Prolongs PK: once-weekly dosing in clinical studies
- Allows high exposures: improved efficacy and tissue distribution
- Eliminates toxic degradation products: improved safety
- Enables multiple formulations: intravenous and subcutaneous

James K et al, 2017.
# Current Antifungal Formulary: Unmet Needs

<table>
<thead>
<tr>
<th>Emerging Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacokinetics</td>
</tr>
<tr>
<td>Safety/Tolerability</td>
</tr>
<tr>
<td>Drug-drug Interactions</td>
</tr>
<tr>
<td>Dosing Flexibility</td>
</tr>
</tbody>
</table>
### Table: MIC and MEC Values

<table>
<thead>
<tr>
<th></th>
<th>Candida MIC&lt;sub&gt;90&lt;/sub&gt; (µg/mL)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Aspergillus MEC&lt;sub&gt;90&lt;/sub&gt; (µg/mL)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>albicans (n=655)</td>
<td>glabrata (n=321)</td>
</tr>
<tr>
<td>Rezafungin</td>
<td>0.06</td>
<td>0.125</td>
</tr>
<tr>
<td>Anidulafungin</td>
<td>0.03</td>
<td>0.125</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>0.03</td>
<td>0.25</td>
</tr>
</tbody>
</table>

CLSI broth microdilution methodology was employed for MIC/MEC determination (M27-A3, M38-A2).


<sup>b</sup>Collected internationally by JMI (2007-2011) and tested as part of a retrospective study (Pfaller et al, 2016).
Rezafungin Activity against *Candida auris*

<table>
<thead>
<tr>
<th>Rezafungin MIC (µg/mL)</th>
<th>0.03</th>
<th>0.0625</th>
<th>0.125</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of <em>C. auris</em> isolates</td>
<td>2</td>
<td>21</td>
<td>28</td>
<td>32</td>
<td>13</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Isolate</th>
<th><em>FKS1</em> mutation</th>
<th>Rezafungin</th>
<th>Anidulafungin</th>
<th>Caspofungin</th>
<th>Micafungin</th>
</tr>
</thead>
<tbody>
<tr>
<td>B11211</td>
<td>S639P</td>
<td>4</td>
<td>8</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>B11222</td>
<td>None</td>
<td>0.25</td>
<td>2</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>B11780</td>
<td>None</td>
<td>0.06</td>
<td>4</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>B11784</td>
<td>None</td>
<td>0.5</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>&gt;8</td>
</tr>
<tr>
<td>B11858</td>
<td>None</td>
<td>0.25</td>
<td>4</td>
<td>&gt;16</td>
<td>1</td>
</tr>
<tr>
<td>B12131</td>
<td>S639P</td>
<td>8</td>
<td>8</td>
<td>&gt;16</td>
<td>8</td>
</tr>
<tr>
<td>B12137</td>
<td>S639P</td>
<td>8</td>
<td>8</td>
<td>&gt;16</td>
<td>8</td>
</tr>
<tr>
<td>B12149</td>
<td>S639P</td>
<td>8</td>
<td>8</td>
<td>&gt;16</td>
<td>8</td>
</tr>
</tbody>
</table>

Rezafungin Potency against Azole-Resistant A. fumigatus

- Azole-resistant clinical isolates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rezafungin</th>
<th>Caspofungin</th>
<th>Micafungin</th>
<th>Posaconazole</th>
<th>Voriconazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azole-Resistant A. fumigatus isolates (n = 31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEC/MIC Range</td>
<td>≤0.015-2</td>
<td>≤0.015-&gt;8</td>
<td>≤0.015-4</td>
<td>0.5-&gt;16</td>
<td>0.12-&gt;16</td>
</tr>
<tr>
<td>MEC/MIC&lt;sub&gt;50&lt;/sub&gt;</td>
<td>0.06</td>
<td>0.06</td>
<td>≤0.015</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>MEC/MIC&lt;sub&gt;90&lt;/sub&gt;</td>
<td>0.12</td>
<td>0.06</td>
<td>0.06</td>
<td>4</td>
<td>&gt;16</td>
</tr>
<tr>
<td>GM MEC/MIC</td>
<td>0.043</td>
<td>0.058</td>
<td>0.023</td>
<td>1.91</td>
<td>3.27</td>
</tr>
</tbody>
</table>

Current Antifungal Formulary: Unmet Needs

Emerging Resistance

Pharmacokinetics

Safety/Tolerability

Drug-drug Interactions

Dosing Flexibility
Echinocandin Efficacy Driven by Shape of Exposure Curve

Rezafungin
- Concentration-dependent killing
- Long half-life
- Safety supports front-loaded dosing

N = 5 Mice/Group
1 Week
Same Weekly Exposure / Group

**Echinocandin Efficacy Driven by Shape of Exposure Curve**

**Rezafungin**

- **Once-weekly dosing demonstrated greater fungal killing than divided doses**
- **Higher degree of fungal killing achieved with the same amount of weekly exposure**

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**Diagram:**

- **Vehicle:**
- **Daily:**
- **Twice weekly:**
- **Single dose:**

**Change in Log$_{10}$ CFU at 168h**

- **Less disease**
- **More disease**

Penetration & Accumulation at Site of Infection
Rezafungin versus Micafungin

Drug distribution in liver after single dose RZF 20 mg/kg determined by MALDI MS imaging

Fungi location stained by GMS

- 6- to 8-fold higher exposure at site of infection for RZF
- Multidose micafungin did not reach tissue drug levels achieved with single dose RZF

Extensive and Sustained ELF Distribution

Rezafungin versus Micafungin

- RZF concentrations in the mouse after 3 days remained >20-fold higher than the MEC$_{90}$ for A. fumigatus and A. flavus (0.015 µg/mL)
  - in plasma: 3 µg/mL
  - in ELF: 4 µg/mL

- Reasonable to expect comparable plasma/ELF concentrations to be maintained after 1 week in humans (based on RZF plasma half-life of 133 h in human vs. 21 h in mouse)

Sandison T et al, 2018 (HTIDE)
Current Antifungal Formulary: Unmet Needs

Emerging Resistance

Pharmacokinetics

**Safety/Tolerability**

Drug-drug Interactions

Dosing Flexibility
Rezafungin IV Comparative Liver Histology

- Rezafungin
  - Normal Plasma Liver Enzymes
  - Normal Liver Histology
  - *Portal Tracts

- Anidulafungin
  - Plasma Liver Enzymes Elevated
  - Hepatocellular Necrosis

2-week Rat Hepatotoxicity Screening Study

20-min IV Infusion via Tail Vein at Comparable Plasma Exposures

Emerging Resistance

Pharmacokinetics

Safety/Tolerability

Drug-drug Interactions

Dosing Flexibility
Phase 1 Drug-Drug Interaction (DDI) Study

Phase 1, single center, randomized, comparative trial in 26 subjects dosed for 3 weeks with substrate drugs and then repeated substrate drugs with Rezafungin x 3 weeks

Designed and conducted in accordance with FDA feedback and relevant guidance

Objective: assess the effect of Rezafungin on the PK of multiple drugs

- **Tacrolimus**: CYP 3A isozyme and P-glycoprotein (P-gp) drug transporter
- **Repaglinide**: CYP2C8 and OATP substrate
- **Metformin**: OCT-1 and OCT-2 substrate and MATE1 and MATE2K substrate
- **Rosuvastatin**: BCRP and OATP substrate
- **Pitavastatin**: OATP substrate
- **Caffeine**: CYP1A2 sensitive index substrate
- **Efavirenz**: CYP2B6 substrate
- **Midazolam**: CYP3A4 sensitive index substrate
- **Digoxin**: PK transporter-mediated interaction (P-gp substrate)
# Phase 1 DDI Study Results

<table>
<thead>
<tr>
<th>Drug</th>
<th>Possible Mechanism(s)</th>
<th>Observations</th>
<th>Suggested Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrolimus</td>
<td>CYP3A4, P-gp</td>
<td>↔C&lt;sub&gt;max&lt;/sub&gt; ↓AUC ~15%</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>CYP2C8, OATP</td>
<td>↔C&lt;sub&gt;max&lt;/sub&gt; ↑AUC ~15%</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Metformin</td>
<td>OCT, MATEs</td>
<td>↔C&lt;sub&gt;max&lt;/sub&gt; ↔AUC</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>BCRP, OATP</td>
<td>↑C&lt;sub&gt;max&lt;/sub&gt; ~12% ↑AUC ~15%</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>OATP</td>
<td>↔C&lt;sub&gt;max&lt;/sub&gt; ↔AUC</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Caffeine</td>
<td>CYP1A2</td>
<td>↔C&lt;sub&gt;max&lt;/sub&gt; ↔AUC</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>CYP2B6</td>
<td>↔C&lt;sub&gt;max&lt;/sub&gt; ↔AUC</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Midazolam</td>
<td>CYP3A</td>
<td>↔C&lt;sub&gt;max&lt;/sub&gt; ↔AUC</td>
<td>No change in dose</td>
</tr>
<tr>
<td>Digoxin</td>
<td>CYP2B6</td>
<td>↑AUC ~10 (0-inf), ~15% (0-t)</td>
<td>No change in dose</td>
</tr>
</tbody>
</table>

Current Antifungal Formulary: Unmet Needs

- Emerging Resistance
- Pharmacokinetics
- Safety/Tolerability
- Drug-drug Interactions
- Dosing Flexibility
**Human Dosing Regimen Model**

**Distributions of Weekly AUC:**
MIC Ratios Following Rezafungin Dosing Regimens

The likelihood that drug levels are sufficient to cover MICs for *Candida* pathogen.

**Target**

The likelihood that drug levels are sufficient to cover MICs for *Candida* pathogen.
Future: Possible subcutaneous dosing, unique to RZF (IV dosing currently planned in phase 3 BMT trial)

PK profile in cynomolgus monkeys
sustained exposures, 10 days

Facilitates administration for outpatient and prophylaxis patients

First in man study with SC formulation in 1Q19
A randomized, double-blind, multicenter, Phase 2 trial of rezafungin in patients with candidemia and/or invasive candidiasis designed to:

- Establish safety and tolerability in patients
- Establish efficacy (clinical and mycological) across timepoints
- Establish efficacy vs caspofungin
- Establish dosing regimen for Phase 3
Phase 2 Trial Design

STRIVE Part A

Analysis Populations:
- Intent-to-treat (ITT): all randomized subjects
- Safety: all subjects who received any amount of study drug
- Microbiological Intent-to-treat (mITT): all subjects in safety population who had documented *Candida* infection
Demographics and Baseline Characteristics

**STRIVE Part A**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rezafungin 400 mg/400 mg (QWk) N= 35</th>
<th>Rezafungin 400 mg/200 mg (QWk) N= 36</th>
<th>Caspofungin 70 mg/50 mg (QD) N= 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean ± SD [Range]</td>
<td>57 ± 15.9 years [24, 88]</td>
<td>57 ± 14.3 years [26, 84]</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Candidemia</td>
<td>32 (91.4)</td>
<td>31 (86.1)</td>
</tr>
<tr>
<td>IC</td>
<td>3 (8.6)</td>
<td>5 (13.9)</td>
<td>3 (8.3)</td>
</tr>
<tr>
<td>Child-Pugh score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;7</td>
<td>12 (34.3)</td>
<td>10 (27.8)</td>
</tr>
<tr>
<td></td>
<td>7-9</td>
<td>15 (42.9)</td>
<td>16 (44.4)</td>
</tr>
<tr>
<td></td>
<td>10-15</td>
<td>0</td>
<td>2 (5.6)</td>
</tr>
<tr>
<td>APACHE II score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0-9</td>
<td>12 (34.3)</td>
<td>9 (25.0)</td>
</tr>
<tr>
<td></td>
<td>10-19</td>
<td>16 (45.7)</td>
<td>18 (50.0)</td>
</tr>
<tr>
<td></td>
<td>≥20</td>
<td>6 (17.1)</td>
<td>8 (22.2)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Numbers of subjects with scores not calculated/missing are not shown.
### Summary of Results

**STRIVE Part A**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Response D14</td>
<td>73%</td>
<td>79%</td>
<td>69%</td>
</tr>
<tr>
<td>Invasive Candidiasis Patients</td>
<td>50%</td>
<td>50%</td>
<td>1/2</td>
</tr>
<tr>
<td>Response - High APACHE II Score Patients</td>
<td>60%</td>
<td>58%</td>
<td>80%</td>
</tr>
<tr>
<td>Investigator Assessment D14</td>
<td>78%</td>
<td>71%</td>
<td>86%</td>
</tr>
<tr>
<td>All Cause Mortality D30</td>
<td>15%</td>
<td>3%</td>
<td>11%</td>
</tr>
</tbody>
</table>

*Excluding Indeterminate Response (inability to assess outcome due to missing data point(s))

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**400/200/(200)mg QWk**

Dose selected for P3

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- Rezafungin 400mg/400mg QWk
- Rezafungin 400mg/200mg QWk
- Caspofungin 70mg/50mg QD
Non-*albicans* species comprised ~54% of baseline isolates. *Other comprised 1 isolate each of C. guilliermondii, C. intermedia, C. krusei, and C. rugosa.
PI Clinical Response by *Candida* Species (Day 14)

*STRIVE Part A- mITT Population*

- **Group 1:** RZF 400 mg/400mg QWk (N=33)
- **Group 2:** RZF 400 mg/200 mg QWk (N=31)
- **Group 3:** CAS 70 mg/50 mg QD (N=28)

Not shown: 100% responses against Other isolates in Group 1 (*C. dubliniensis*, n=3; *C. guilliermondii* and *C. rugosa*, n=1 each) and in Group 3 (*C. intermedia* and *C. krusei*, n=1 each)
**Most Frequent (≥10%) Adverse Events**

**STRIVE Part A- Safety Population**

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Rezafungin 400 mg/400 mg (QWk) N= 35</th>
<th>Rezafungin 400 mg/200 mg (QWk) N= 36</th>
<th>Combined Rezafungin Groups N=71</th>
<th>Caspofungin 70 mg/50 mg (QD) N= 33</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypokalemia</td>
<td>5 (14.3)</td>
<td>7 (19.4)</td>
<td>12 (16.9)</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3 (8.6)</td>
<td>7 (19.4)</td>
<td>10 (14.1)</td>
<td>8 (24.2)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (5.7)</td>
<td>6 (16.7)</td>
<td>8 (11.3)</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Anemia</td>
<td>4 (11.4)</td>
<td>4 (11.1)</td>
<td>8 (11.3)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Edema/swelling peripheral</td>
<td>5 (14.3)</td>
<td>2 (5.6)</td>
<td>7 (9.9)</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (5.7)</td>
<td>4 (11.1)</td>
<td>6 (8.5)</td>
<td>5 (15.2)</td>
</tr>
</tbody>
</table>

- No concerning AE trends observed; RZF appears to be safe and well-tolerated
Rezafungin Treatment Trials

**Phase 2**

- STRIVE Part A met objectives of establishing clinical safety and efficacy and determining dosing for Phase 3 (400 mg/200 mg)
- Part B ongoing

**Phase 3**

- Enrollment underway for the ReSTORE Ph 3 treatment trial, similar to STRIVE in design except
  - 1° endpoints: Day 14 global response (EMA), Day 30 all-cause mortality (FDA)
  - More severe patient population expected: ~ 25% IC (~10% STRIVE Part A)
Prophylaxis
Current Prophylaxis Approach Requires Multiple Drugs
Regimens exacerbate clinical complexity and risk of complications

Comprehensive antifungal prophylaxis requires **one or more azole agents** plus an anti-PCP agent post-engraftment

SOC for *Candida* and *Aspergillus*

- **Fluconazole**
- **Posaconazole or voriconazole**

SOC for *Pneumocystis* (PCP)

- **Anti-PCP: TMP/SMX, dapsone, atovaquone**

Risk of IFI

- **High**
  - *Candida*
  - *Aspergillus*
  - *Pneumocystis*

- **Low**
  - *Pneumocystis*
  - *Candida*

Day: -10 to 100

Pre-engraftment

Post-engraftment

HSCT: hematopoietic stem cell transplantation; TMP/SMX: Trimethoprim/sulfamethoxazole (co-trimoxazole, Bactrim).
RZF: Potential for a Simplified Single-drug Paradigm

- Enhanced safety profile over polyenes, azoles, and TMP-SMX
- No DDI or myelosuppression
- Prolonged half-life allows for once-weekly dosing (IV or SC)
- Unique PK profile may help treat or prevent of resistant pathogens
Echinocandins Initially Discovered as Treatment for PCP

- First-gen echinocandins show varying levels of treatment efficacy
  - Micafungin: diminished activity at lower doses
  - Caspofungin: ‘successful’ as monotherapy and in combination with TMP-SMX

- Echinocandins may have larger role in PCP prevention
  - Increasing resistance to TMP-SMX
  - Nephrotoxicity, rashes and risk of myelosuppression preclude use pre-engraftment and leads to frequent discontinuation post-engraftment
  - Tolerability of TMP-SMX alternatives (dapsone, atovaquone, pentamidine) even worse, and breakthrough common
  - Rezafungin is faster acting than TMP-SMX and very active against BD glucan which is the main proponent for inflammation and symptoms

RZF Prophylactic Efficacy in Disseminated Aspergillosis
Versus Amphotericin B

STUDY DESIGN

6 mice per arm
Controls: Amphotericin B control 3 mg/kg; one hour after infection
9 reza groups at 5, 10 and 20 mg/kg as prophylaxis was dosed once at Day -5, -3 or -1 before infection
All animals immunosuppressed
Day 0, infected with A. fumigatus

10 mg/kg = human dose of 200mg
20 mg/kg = human dose of 400mg
Mice clear CD101 2-3 fold faster than humans.
RZF Prophylactic Efficacy in Pulmonary Aspergillosis Model
Versus Micafungin and Posaconazole

RZF 20 mg/kg showed higher survival versus micafungin 5 mg/kg or posaconazole 2 mg/kg suggesting an advantage for RZF weekly at human equivalent doses

STUDY DESIGN

6 neutropenic mice per arm

Single dose of test agent one day prior to A. fumigatus challenge (~$10^5$ CFU/mouse, intranasally) on Day 0

Survival evaluated up to 10 days post-infection

Ong et al, 2018 (ECCMID).
RZF Prophylactic Efficacy in Neutropenic Pneumocystis Model
Versus TMP/SMX - Study #1

STUDY DESIGN

10 mice per arm

Infected with *P. murina* by intranasal inoculation

Immunosuppression with dexamethasone throughout study

CD101 was administered at the same time the mice were infected

Quantification of PCP from lung

‘Prophylaxis with CD101, which blocked cyst/asci formation, offers a new means to prevent PCP’

20 mg/kg/1x/wk ≈ human dose of 400 mg
10 mg/kg/1x/wk ≈ human dose of 200 mg
2 mg/kg/1x/wk ≈ human dose of 40 mg
RZF Prophylactic Efficacy in Neutropenic Pneumocystis Model
Versus TMP/SMX and Caspo - Study #2

STUDY DESIGN

10 mice per arm

Infected with *P. murina* by intranasal inoculation

Immunosuppression with dexamethasone throughout study

RZF was administered at the same time the mice were infected

Quantification of PCP from lung

Log₁₀ mean counts after 42 days of study drug administration.

**Nuclei Counts**

**Asci Counts**
Phase 3 Antifungal Prophylaxis Trial in BMT Patients

**Rezafungin Arm** (n~300)

- Week 1
  - Rezafungin
  - Azole placebo
  - Bactrim placebo

- Day 1

**Comparator Arm** (n~150)

- Week 1
  - Rezafungin Placebo
  - Azole*
  - Bactrim

  *Fluconazole to start in all patients. Posaconazole optional in patients who develop GVHD per label.

Adaptive design: interim analysis @ 50% enrollment for futility/sample size (for FDA non-inferiority endpoint)
Approximately 20 sites globally, with planned initiation Q1-2019. Size and timing pending additional regulatory input
Summary


- Antifungal pipeline includes mostly early-stage candidates in development for treatment.

- Rezafungin is a novel echinocandin in Phase 3, demonstrating:
  - Safety and DDI profile of the echinocandin class, sparing myelosuppression, TDM, hep & ren tox, non-compliance, and complications related to managing/avoiding DDIs.
  - Enhanced PK allowing once-weekly, high-exposure, front-loaded dosing and greater tissue penetration.
  - Potent activity against *Candida*, *Aspergillus*, and *Pneumocystis*, including resistant azole-resistant isolates and *Candida auris*.

- Potential for earlier hospital discharge and outpatient use; SC administration.