VL-2397: A Novel Approach to Treat Life-Threatening Invasive Fungal Infections

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Safe Harbor Statement

This presentation contains forward-looking statements that are subject to risks and uncertainties that could cause actual results to differ materially from those set forth in the forward-looking statements, including risks related to whether any product candidates will be shown to be safe and efficacious in clinical trials and the other risks set forth in the company’s Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Actual results may differ materially from those projected. These forward-looking statements represent the company’s judgment as of the date of this presentation. The company disclaims, however, any intent or obligation to update these forward-looking statements.
Vical at a Glance

- Small biotechnology company based in San Diego, CA
- Platform of DNA delivery technologies
- Core competency in vaccines and infectious diseases
  - ASP0113 vaccine in pivotal Phase 3 study for prevention of CMV reactivation in transplant patients
  - VCL-HB01 vaccine in Phase 2 study for treatment of HSV-2
  - VL-2397 antifungal planned for Phase 2 study in invasive aspergillosis
- Strategic partnerships with Astellas
# VL-2397 for Invasive Fungal Infections

| PRODUCT CANDIDATE | Antifungal compound with a novel mechanism of action  
In-licensed from Astellas |
|-------------------|----------------------------------------------------------|
| TARGET INDICATIONS | Treatment of invasive aspergillosis (IA)  
Treatment of infections caused by other pathogenic fungi |
| DEVELOPMENT STATUS | QIDP, orphan & Fast Track designations for treatment of IA  
Potential for Limited Use Indication in IA based on successful outcome of a single Phase 2 trial  
Phase 1 trial in healthy volunteers completed  
Phase 2 trial in IA planned to start in 4Q 2017 |
Invasive Aspergillosis

- More than 200,000 diagnoses annually worldwide\(^1\)
  - Predominantly occurs in immunocompromised patients

- Limitations of current antifungals
  - 20% all-cause mortality at 6 weeks\(^2\)
  - Drug-drug interactions
  - Toxicities, intolerance
  - Lack of coverage against resistant strains

- Only 1 new therapy class introduced in past 30 years

\(^1\) Brown, Sci Transl Med, 2012
\(^2\) Maertens, Lancet, 2016
VL-2397 Characteristics

- Resembles the siderophore ferrichrome
- Isolated from fungus *Acremonium persicinum*
  - Produced by fungal fermentation
  - Amino acid sequence: Phe-Leu-Asn-Orn-Orn-Orn • (Al+3)
- Aluminum (Al3+) chelation by hydroximated ornithines is required for antifungal activity
# In Vitro Antifungal Activity

## Susceptible fungal pathogens (MIC ≤ 2)

<table>
<thead>
<tr>
<th>Fungal Species</th>
<th>Affected Patient Populations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspergillus species</strong></td>
<td><em>A. fumigatus, A. terreus, A. flavus, A. nidulans</em></td>
</tr>
<tr>
<td></td>
<td>Immunosuppressed, older patients</td>
</tr>
<tr>
<td><strong>Candida species</strong></td>
<td><em>C. glabrata, C. kefyr</em></td>
</tr>
<tr>
<td></td>
<td>UTI, intra-abdominal infections, MDR infections</td>
</tr>
<tr>
<td><strong>Other yeast species</strong></td>
<td><em>Cryptococcus neoformans</em></td>
</tr>
<tr>
<td></td>
<td>HIV, Africa, South East Asia</td>
</tr>
<tr>
<td></td>
<td><em>Trichosporon asahii</em></td>
</tr>
<tr>
<td></td>
<td>Immunocompromised</td>
</tr>
</tbody>
</table>

Assayed in inactivated human serum-containing media

MIC, minimal inhibitory concentration
VL-2397 Novel Mechanism of Action

- VL-2397 represents a potentially new class of antifungal agents
- Active transport into *A. fumigatus* occurs via Sit1
  - Mammalian cells lack Sit1 transporter
- Activity results from effect on an intracellular target

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Adapted from Denning *Science* 2015

VL-2397 Antifungal
Rapid Activity Against *Aspergillus*
Including Drug-Resistant Isolates

Rapid Onset of Antifungal Activity

Activity vs. Azole-Resistant *Aspergillus*

MIC: minimal inhibitory concentration
VRCZ: Voriconazole

Nakamura, ICAAC, 2014

VL-2397 Antifungal
Phase 1 Summary

- Seven single-ascending dose cohorts, three 7-day multiple-ascending dose cohorts, one 28-day cohort
  - Total enrollment 96 healthy subjects-ages 18 to 55
- VL-2397 appeared to be safe and well-tolerated
  - Safety review committee did not identify any overall concerns with the safety profile
- Predictable PK
  - Minimal inter-subject variability
  - No apparent accumulation of VL-2397 was observed
- Data support advancement to Phase 2 in IA patients
Planning for Phase 2 in IA

- **Potential expedited development pathway**
  - Intensive interaction with FDA under QIDP designation
  - VL-2397 will be eligible for Limited Use Indication approval assuming a successful outcome of a single Phase 2 trial
    - The trial must be carried out in accordance with a protocol and statistical analysis plan consistent with the Agency's advice
    - Final determination whether the drug is approvable will be made by FDA after review of all relevant data

- **Collaboration with the Mycoses Study Group Education and Research Consortium (MSGERC)**
  - Trial design and protocol input

- **Planned initiation in 4Q 2017**
Phase 2 Overview

- Global, multicenter, randomized, open-label study
- N=200 adults with AML, ALL or allo HCT recipients
- 2:1 randomization VL-2397 to active comparator
  - Comparator: Physician’s choice of voriconazole, isavuconazole or liposomal amphotericin B
- 6 weeks of antifungal treatment
  - 4 weeks of VL-2397 followed by 2 weeks of comparator
- Primary endpoint: All-cause mortality at 4 weeks
  - Key secondary endpoint: ACM at 6 weeks
- Noninferiority design
VL-2397 Summary

- First-in-class antifungal with novel MOA
- Extensive nonclinical data support rapid antifungal effect against azole-sensitive and resistant strains
- Favorable safety and PK profiles in Phase 1 trial support advancement to Phase 2 trial in IA patients
- Phase 2 trial in IA planned for initiation in 4Q 2017
  - Potential for Limited Use Indication approval
  - Collaboration with MSGERC