To Develop a Breakthrough Therapy for Radical Cure of Fungal Infections

EliV5 Vision and Mission Statement

Potent: Active against drug sensitive and resistant strains
Safe: No toxicity in mammals
Radical cure: Eliminate infection with no recrudescence

Pulmonary aspergillosis
TEAM

Choukri Ben Mamoun
Founder
Yale

Marwan Azar, MD
Yale, Consultant

Yulia Surovsteva, PhD
Yale / Biology

Joy Chiu
Yale / Biology

William Hungerford
Yale / Chemistry

Peter Gareiss, PhD
Yale / Biology
Problem & Opportunity

High
Medium
Very High
Low

>150 million with serious fungal diseases
>1.6 million deaths globally
~100,000 deaths in the US

Candida auris
GLOBAL ANTIFUNGAL MARKET

>$12B IN 2018  ➔ $19.3B by 2023

- **Azoles**: 42%
- **Echinochandins**: 33%
- **Polyenes**: 9%
- **Allyamines**: 6%
- **Pyrimdines**: 4%
- **Others**: 6%

**Fungal Disease**

<table>
<thead>
<tr>
<th>Fungal Disease</th>
<th>Estimated Cases/year</th>
<th>Estimated Mortality Rates (% of infected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptococcus infections</td>
<td>&gt; 1,000,000</td>
<td>20 – 70%</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>&gt;400,000</td>
<td>10 - 75%</td>
</tr>
<tr>
<td>Aspergilosis</td>
<td>&gt;200,000</td>
<td>30 – 95%</td>
</tr>
<tr>
<td>Pneumocystis Pneumonia</td>
<td>&gt;400,000</td>
<td>20 – 80%</td>
</tr>
<tr>
<td>Mucormycosis</td>
<td>&gt;11,000</td>
<td>30 - 90%</td>
</tr>
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</table>

www.marketresearchfuture.com; www.grandviewresearch.com
Pantothenate phosphorylation (PanK): An essential step in Coenzyme A biosynthesis in fungi

Pantothenate phosphorylation (PanK):
An essential step in Coenzyme A biosynthesis in fungi.
TARGET PURIFICATION AND ASSAY OPTIMIZATION

### Kinase Assay

**No inhibitor**

- ATP → ADP
- Pantothenate → 4'-Phosphopantothenate
- ATP + Kinase Glo™ → light

**With inhibitor**

- ATP → ADP
- Pantothenate → 4'-Phosphopantothenate
- ATP + Kinase Glo™ → light

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**Graph**

- Percent ATP consumed
- Enz concentration (log2 scale)

### Assay Details

- S. cer CàB1
- A. fum N-His
- A. fum C-His
- C. auris N-His
- C. auris C-His
- C. alb N-His
- C. alb C-His
- H. cap N-His
- H. cap C-His
## AfPanK Inhibitor Screening and SAR Metrics

<table>
<thead>
<tr>
<th>HTS, Metrics &amp; Go / No-Go Criteria</th>
<th>Results</th>
</tr>
</thead>
</table>
| **Compounds Tested in Primary HTS**  
Avg Z' : Avg %ATP Consumption                                                                       | 156,593  
0.63 : 50.3% |
| Average Hit ID Threshold Inhibition (Mean + 6 SD)                                                  | 44%     |
| # Hits Primary Screen : Hit Rate                                                                  | 377 : 0.28% |
| # Hits Confirmed, n=3, without Assay Interference                                                 | 268/377 |
| # Hits Passing Medicinal Chemistry Triage                                                         | 76/268  |
| # Primary Screen Hits with a) IC$_{50}$ A.fum $< 100$ µM, b) $> 10x$ Selectivity over Human PanK3 Enzyme, and c) LD$_{50}$ HeLa Cytotoxicity $> 50$ µM from Reorder or Resynthesis | 22/76   |
| **Chemotypes for Fungal PanK Inhibitors**                                                         | 12      |
| **Analogs of the 12 Chemotypes Tested for AfPanK Inhibition**                                     | 415     |
| **Primary Chemotype: PTZs**                                                                     |         |
| # Analogs Tested                                                                                  | 82      |
| # PTZ1-12                                                                                         | 12      |
| # PTZ 13-33                                                                                       | 21      |
| $IC_{50}$ AfPanK 600 nM - 30 µM                                                                  |         |
| $IC_{50}$ AfPanK $< 100$ µM                                                                     |         |
TECHNOLOGY & PRODUCTS
STRENGTHS

Lead Properties
- Highly selective
- Excellent safety profile
- Novel compounds (IP: competitive advantage)

<table>
<thead>
<tr>
<th>Compound</th>
<th>EC&lt;sub&gt;50&lt;/sub&gt; (µM)</th>
<th>LD&lt;sub&gt;50&lt;/sub&gt; (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aspergillus PanK</td>
<td>Human PanK3</td>
</tr>
<tr>
<td>YU281445</td>
<td>0.6</td>
<td>&gt;100</td>
</tr>
<tr>
<td>YU182690</td>
<td>1.3</td>
<td>Inactive</td>
</tr>
<tr>
<td>YU254361</td>
<td>2.2</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>
First fungal PanK crystal structure solved:

A new path toward FPanK structure-based drug optimization and design
**BLAVATNIK $300K: USE OF FUNDS**

**Structure-based drug optimization**
- Co-crystallization & Medicinal Chemistry
- SI > 100: AfPanK EC$_{50}$ <100 nM vs HuPanK >10 µM
- No toxicity >50 µM
- Permeability: >1 x 10$^{-6}$ cm/sec
- Microsomal & hepatocyte stability: >20 min t$_{1/2}$
- hERG inhibition: >30 µM

**In vitro efficacy & Pharmacology**
- IC$_{50}$ < 100 nM (S and R strains)
- In vitro TI >100
- PK: t1/2 >2h

**In vivo efficacy**
- Radical cure

**Clinical Candidate**
SUMMARY

ELIV5 TECHNOLOGY AND COMPETITIVE ADVANTAGE

- Novel inhibitors
- Novel mode of action
- Novel strategy for radical cure
- Competitive advantage (IP to 2039)

- Blavatnik Funding $300,000
- Milestone: Identify lead clinical candidates
- Goal: Therapy for radical cure
STRATEGIC PLANNING

Pre-clinical

2017 | 2018 | 2019

Clinical

2020 | 2021 | 2022 | 2023 | 2024

Launch

2025 | 2026 | 2027

PITCH
$438,870

STTR+SBIR
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Private funding

Blavatnik

Strategic partner/Joint Venture

Acquisition / IPO
<table>
<thead>
<tr>
<th>Primary objective (Hospital focus)</th>
<th>Potential future applications</th>
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<tr>
<td>Candidiasis and Aspergillosis</td>
<td>Topical (spinoff licensing)</td>
</tr>
<tr>
<td>IV (priority) with oral stepdown</td>
<td>Athlete’s Foot</td>
</tr>
</tbody>
</table>