Outline

• Background on Vertex Pharmaceuticals
• Vertex drug discovery collaboration with Cystic Fibrosis Foundation
• Why is Vertex interested in Huntington’s disease?
• Vertex collaboration with CHDI on Huntington’s disease
Vertex Pharmaceuticals Incorporated

Small molecule drugs for serious diseases

- Founded in 1989
- 1200+ employees
- 4 R&D sites with stand-alone drug discovery capabilities
  - Cambridge, MA, USA
  - San Diego, CA, USA
  - Milton Park, UK
  - Coralville, IA, USA

Cambridge, MA
Immune Mediated Inflammatory Diseases
Anti-infectives
Cancer
Biochemistry
Clinical Development
Pharmaceutical Development & Operations

San Diego, CA
Ion channels and Receptors
Cystic Fibrosis & Neurodegenerative Diseases
HTS Screening and Automation

Milton Park, UK
X-ray Crystallography
Immune Mediated Inflammatory Diseases
Cancer

Coralville, IA
Tuberculosis
Anti-microbials
Clinical Virology

www.vrtx.com
Vertex Drug Pipeline

Vertex may be “Goldilocks” partner in Huntington’s disease

- Not too big to ignore HD due to market size
- Not too small to fully develop drugs on our own
Highly successful collaboration with Cystic Fibrosis Foundation

• Collaboration between Vertex and the Cystic Fibrosis Foundation to discover drugs targeting the molecular defect in CF
• Collaboration began in 1998 with high throughput screen; by 2007 Vertex had two compounds in clinical trials
  – May 2008: VX-770 showed clinical efficacy in CF patients
  – Demonstrated proof-of-concept for correcting the molecular defect in CF with a drug → showed that VX-770 is acting on the intended target and is providing a clinical benefit
• Establishing new paradigm for industry: non-profit organization collaboration in drug discovery

www.cff.org  www.vrtx.com
Intervene early with disease-modifying approaches in CF

Reducing Loss of Lung Function by 1%/yr Could Double Life Span

Graph showing the relationship between patient age, loss in lung function, and disability levels.

Key points:
- Reduction in loss of lung function by 1%/yr can double life span.
- Lines indicate different rates of lung function loss: 2%, 1.5%, 1%.
- Disability levels are marked at 20, 40, 60, and 80% predicted lung function.
- Lung function decreases over time, with lung transplant and serious disability markers.

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www.cff.org  www.vrtx.com
## Similarities between CF and HD

<table>
<thead>
<tr>
<th></th>
<th>Cystic fibrosis</th>
<th>Huntington’s disease</th>
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</thead>
<tbody>
<tr>
<td>Inherited disease</td>
<td>Yes (single gene)</td>
<td>Yes (single gene)</td>
</tr>
<tr>
<td>Unmet medical need</td>
<td>High</td>
<td>High</td>
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<tr>
<td>Disease modifying therapies possible</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Patient size</td>
<td>30,000 in US</td>
<td>30,000 in US</td>
</tr>
<tr>
<td>Vol health org and advocacy base</td>
<td>Strong</td>
<td>Strong</td>
</tr>
</tbody>
</table>

- **CF**: Cystic Fibrosis
- **HD**: Huntington’s Disease
Why is Vertex interested in Huntington’s disease?

• High unmet medical need
• Maturing scientific understanding of the disease
• Readily identified and motivated patient base
• Possibility for smart clinical trials
• Vertex has expertise in developing drugs to fix broken proteins (CF)
• Replicate successful CF collaborative network model in HD
Vertex-CHDI collaboration in HD

- Vertex and CHDI research collaboration initiated in April 2008
- Focused on two scientific approaches to potential therapeutics for HD
  - Protein folding: repairing mutant huntingtin
  - Stem cells: repairing nerve cell loss in HD
- Phased exploration makes sense for both CHDI and Vertex
  - Initially two years, could be extended upon positive results
- CHDI and other organizations bring a network of researchers, clinicians and patients
Vertex and HD

• Entry into neurodegenerative diseases via CHDI collaboration
• Vertex brings strong expertise in cellular assays and protein folding
• Commitment to translating scientific breakthroughs into improved patient care