Transforming Drug Discovery

Innovative Platforms

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Valid as of November 30, 2006
From a Linear Process

More, Better, Faster

To a Parallel Process

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Drug Discovery at Scale

- PDE-1b – ADHD
- PDE-2 – Bone Healing, Cognition, Inflammatory Pain
- PDE-4 – COPD, Asthma
- PDE-4B – Cognition
- PDE-5 – Erectile Dysfunction, Hypertension
- PDE-7B – Neuropathic Pain, Schizophrenia
- PDE-8B – Diabetes
- PDE-9 – Diabetes, Cognition
- PDE-10A – Schizophrenia, Diabetes, Obesity

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The Kinome
A Substantial Drug-Discovery Opportunity

- 30,000-40,000 Human Genes
- 3,000-4,000 Druggable Targets
- 518 Kinases In Genome
- 17 Major Kinase Groups, 134 Kinase Families
- 214 Kinases Implicated in Disease

Manning et al., Science 298: 1912, 2002

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# Early Success at Pfizer

![Pfizer Logo](image)

<table>
<thead>
<tr>
<th>Name</th>
<th>Target</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tarceva*</td>
<td>EGFR</td>
<td>Launched 2004</td>
</tr>
<tr>
<td>Sutent</td>
<td>Multi Tyr Kinase</td>
<td>Launched 2006</td>
</tr>
<tr>
<td>Axitinib</td>
<td>Multi Tyr Kinase</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>

*Discovered at Pfizer, owned by OSI/Genentech

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A Dazzling Kinase Portfolio

56 Kinase Programs Across 9 Therapeutic Areas

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Pfizer Leads in Number of Kinase Patents
20% from Jubilant Database Published to 2005

Kinase Targeted Library (KTL)
Kinase Co-Crystal Structure DB

Kinase Selectivity Panel (KSS)
Integrated Knowledge Platform (K2B)

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A New Era of Kinase Inhibitors

- Janus Kinase 3 (JAK 3)
- c-Met
CP-690,550 Shows Potential Across Many Diseases

- Human Genetics Implicated JAK 3 as Target for Immune-System Disorders
- CP-690,550 Shown to be Effective in Organ Transplant
- Rheumatoid Arthritis is an Autoimmune Disorder Hence our Desire to Test in this Indication
**c-Met Inhibitors**

*Offer a New Treatment for Cancer*

- **c-Met Dysregulation**
  - Gene Amplification
  - Extracellular
    - R988C
  - Intracellular
    - T1010I
    - H1094R
    - Y1230C
    - M1250T
  - Kinase
    - R988C
    - T1010I

- **Altered Tumor-Cell Growth**
  - Tumor Angiogenesis
  - Tumor Invasion and Metastasis

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PF-2,341,066
Significantly Reduces Tumor Burden in Mice

Tumor Volume (mm³)

Control

PF-2341066

Time (days)

0 10 20 30 40 50 60

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Leading Kinase Collaborations

- Academic Institutions - e.g. Lauffenberger and Sorger, MIT, Kinase Pathway Analysis; I. Hunter, MIT, Novel Technology for Kinase-cmpd Analysis
- Biotech Companies - e.g. Caliper, Biosource, Novel Kinase Screening Technologies
- Kinase Drug Pfnder program e.g. J. Blenis-Harvard, S6K; J. Liao-B&W Hospital, Rho Kinase; Dr. Tsichlis-Tufts, Cot; L. Rameh-BBRI, PI5P4K

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