New Approaches to a Major Public-Health Problem

Infectious Diseases

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Overview

The Burden Of Infectious Disease Is Large And May Grow

Our Pipeline Has Breadth And Depth To Address Key Issues
  • Resistance
  • Prevention
  • Leveraging Our Science For The Developing World

We Will Highlight Candidates Across A Broad Array Of Areas
  • HIV: Maraviroc, *UK-453,061
  • Hepatitis And Fibrotic Liver Disease: *PF-3,491,390
  • Antibiotics: Dalbavancin, *PF-3,709,270 (Sulopenem Prodrug)
  • Vaccines: *PowderMed Influenza Vaccine
  • Diseases Of The Developing World: Azithromycin/ Chloroquine For Malaria

*First-time Disclosure By Pfizer Today

Valid as of November 30, 2006
<table>
<thead>
<tr>
<th><strong>Infectious Diseases</strong></th>
<th><strong>Therapeutic Area Vision</strong></th>
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<tbody>
<tr>
<td><strong>20th Century</strong></td>
<td></td>
</tr>
<tr>
<td>◆ Kill The Bugs</td>
<td>◆ Protect The Patient</td>
</tr>
<tr>
<td>• Delayed Diagnosis</td>
<td>• Improve Host Immunity</td>
</tr>
<tr>
<td>• Best-Guess Treatment</td>
<td>• Emphasize Prevention</td>
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<tr>
<td>◆ Broad-spectrum Agents Drive</td>
<td>◆ Rapid Diagnostics spree</td>
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<tr>
<td>Resistance and Superinfections</td>
<td>• Immediate, Informed Treatment</td>
</tr>
<tr>
<td>◆ HIV Destroys Lives</td>
<td>◆ Targeted Spectrum</td>
</tr>
<tr>
<td>◆ Hepatitis C Virus (HCV) Treatment</td>
<td>• Precision Therapy</td>
</tr>
<tr>
<td>◆ Research Focused on Pathogen Targets</td>
<td>◆ HIV As A Chronic Livable Disease</td>
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<td></td>
<td>◆ HCV Cures With No Quality-Of-Life Penalty</td>
</tr>
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<td>◆ Research Platforms Leveraged Across Other Therapeutic Areas</td>
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### Infectious Diseases

**Leading Cause of Morbidity and Mortality Worldwide**

<table>
<thead>
<tr>
<th>Condition or Illness</th>
<th>2000 WW Burden</th>
<th>2020 WW Burden</th>
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<tbody>
<tr>
<td>1 Neuropsychiatric Condition</td>
<td>13%</td>
<td>15%</td>
</tr>
<tr>
<td>1 Cardiovascular Disease</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>3 Infectious/Parasitic Disease</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>3 Unintentional Injuries</td>
<td>9%</td>
<td>10%</td>
</tr>
<tr>
<td>5 HIV</td>
<td>21%</td>
<td>6%</td>
</tr>
<tr>
<td>5 Respiratory Infections</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>6 Nutritional Deficiencies</td>
<td>2%</td>
<td>1%</td>
</tr>
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Infectious Diseases Remain the Leading Cause of Morbidity and Mortality Worldwide; Drug-Resistance Exacerbates this Problem

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Infectious Diseases

Strategy

- Deliver Targeted Anti-Bacterials
- Invest in Partnerships for Diagnostics
- Produce Superior HIV and HCV Therapies
- Address Prevention Through a Novel and Superior Vaccine Platform

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Estimated Market Growth Over Next 10 Years: 50%

2006 WW Sales ($US B)
Total Sales = $66.5 B

- Community AB, $24.3
- Hospital AB, $10.6
- Anti-Fungals, $7.3
- HIV, $8.6
- Other AV, $7.5
- Vaccines, $8.1

Driven by Vaccines, Antivirals, And Hospital Anti-Infectives

Projected 2015 WW Sales ($US B)
Total Sales = $100.6 B

- Community AB, $28.5
- Hospital AB, $16.1
- Anti-Fungals, $8.0
- HIV, $14.2
- Other AV, $12.3
- Vaccines, $21.5

Source: For Treatment Categories, IMS MIDAS, Based On 2006 Sales And Pfizer Forecasts By Category; For Vaccines, Based On Third-party Analyses, Company Reports, And IMS Sales Data

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### Concept

<table>
<thead>
<tr>
<th>Concept</th>
<th>Description</th>
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</table>
| HIV Next-Generation ARV (NNRTI, CCR5) | First-Choice Anti-Retroviral Agent from Existing Class  
- Active in All Stages of Disease Due to High Functional Barrier to Resistance  
- Well-Tolerated, Convenient Regimen |
| HIV Next-Generation Novel Agent | First-Choice Novel Agent for all Stages of Disease  
- Profile Consistent with Long-Term Treatment |
| Hepatitis C Virus | Small-Molecule or Biologic Agent Superior to Either Current Standard of Care: Ribavirin or Pegylated Interferon  
- Improved Efficacy (Cure) and Safety/Toleration  
- Idun: Pan-Caspase Inhibitor for HCV-Induced Liver Fibrosis |
Current Medications in the Prevention of The Completion of HIV Infection

Entry Inhibitors
Maraviroc

Reverse Transcription Inhibitors
UK-453,061

Protease Inhibitors
Viracept

Hammer, S.M., NEJM 346 (26):2022 • Copyright©2002 Massachusetts Medical Society. All rights reserved.

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Before 1996 Host Factors Implicated Included HLA, CD4

- 1996 HIV-1 Entry Cofactor:
  - Seven-Transmembrane, G Protein-Coupled Receptor


- Resistance to HIV-1 Infection in Caucasian Individuals Bearing Mutant Alleles of the CCR-5 Chemokine Receptor Gene

Maraviroc
HIV Co-Receptor Entry Inhibitor

Selective, Reversible CCR5 (R5) Antagonist
First-In-Class, Active *in vitro* Versus R5-Tropic HIV-1, MDR HIV-1 But Not X4-Tropic Or R5x4-Tropic HIV-1
Cross-Clade Activity (~ 2 Nm Antiviral IC90)
Generally Well Tolerated

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Expected Claim: Use in Treatment-Experienced Patients
- Two Pivotal Studies Achieved 24-Week Readout
  - Data to be Presented at Retroviral Meeting (2/07)
  - U.S. Regulatory Filing on Track for December

Expected Claim: Use in Treatment-Naïve Patients
- Pivotal Study Enrolled, with Readout in Mid-2007
- Filing Mid-2007

Promising Safety Profile
- No Evidence of Hepatic Intolerance
- No Concern Regarding Neoplastic Disease
- No Evidence for Progression of HIV Disease in Dual-Tropic Patients
Maraviroc
Expanded Access Program (EAP)

- Purpose: Make Maraviroc Available to Patients With Limited or No Treatment Options Due to:
  - Resistance or Intolerance
  - Virologic Failures to Therapy

- Scope
  - Over 30 Countries
  - Extensive Use of Investigators Experienced with EAP
  - To Continue Until Maraviroc Approved for in that Country

- Design
  - Open-Label, Non-randomized (All Subjects Get Maraviroc Provided by Pfizer)
  - On Top of any Other Therapies Selected by Investigator

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UK-453,061
Next-Generation NNRTI for HIV

- \textit{In-vitro} Activity Against Common NNRTI Mutations
  - Multiple Mutations Required for Resistance

- Safe And Well Tolerated in Toxicology And Phase 1
  - No CNS Adverse Events as with Efavirenz
  - No Need to Boost with Ritonavir

- Antiviral Activity Demonstrated in Patients
  - Significant Viral-load Reductions Observed
    - With Qd and Bid Regimens
    - Study Ongoing to Explore Additional Dosing Options

- Potential Use Both in Anti-Retroviral-Naïve and Anti-Retroviral-Experienced Patients

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Approaches to Treating Hepatitis C Virus

HCV Infection and Replication

Cell Death

Pan-Caspase Inhibitor

Inflammatory Mediator Release

Fibrosis

Cirrhosis

Entry Inhibitors (Early Approaches)

Polymerase Inhibitor + (Other Early Approaches)

M. Peters. 2nd Int. Workshop on HIV & Hepatitis C Coinfection, San Francisco, 2005

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Chronic Liver Disease

- Hepatitis B
- Hepatitis C
- Alcohol
- NASH
- Others

Phenotypic Change in Stellate Cell
Abnormal Accumulation of Collagen, Scarring
Bridging of Collagen
Cirrhosis
Liver Failure
Hepatocellular Carcinoma
GI Hemorrhage

Inflammation
Apoptosis
Deposition of Collagen
Fibrosis

10 – 30 years

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PF-3,491,390
Pan-Caspase Inhibitor

- Pfizer Acquired PF-3,491,390 (IDN 6556) from Idun Pharmaceuticals in 2005

- Novel Mechanism and Therapeutic Approach
  - Oral Pan-caspase (Irreversible) Inhibitor Inhibits Apoptosis and Inflammation with Potential Utility in Hepatic Disease

- Potential Unprecedented Therapeutic Indications (High Unmet Medical Need) Include:
  - Treatment of Liver Fibrosis Associated with Hepatitis C Virus Infection
  - Treatment of Non-Alcoholic Steatohepatitis (NASH)