Ensuring Access to Innovative Therapies: Discovery to Approved Product

September 28, 2012
Access to Innovative Therapies

- Discovery: Identifying the commercial need for novel compounds
- Developing & registering a marketable novel product
- Case example: Improvest
- Conclusion – the innovation paradox
The business of pioneer pharmaceutical companies is to **identify medical needs** that can be treated with novel compounds.

...then **develop novel products** from those compounds and demonstrate safety, efficacy, and product quality for the intended uses.

Return on R&D investment depends on:
- Novelty
- “Patentability”
- Value in the marketplace
Commercial Need for Novel Compounds

Identifying Medical Needs

• What are the drivers for discovery of novel agents?
  – User needs (convenience, compliance, cures, cost)
  – Resistance to existing therapies
  – Regulatory framework
  – Consumer acceptance
• Predict the market’s needs 8–12 years ahead!
AH Substrate Being Expanded to Include Novel Compounds

• Substantial decrease in human health antibiotics programs
  • Human health more focused on chronic use drugs / conditions
  • Less available substrate for leveraging

• Where can animal health antibiotics programs look for new substrate?
  – Traditional Small Molecules
    • Novel Antibacterial Classes
    • Re-exploration of older generations of existing classes
  – Novel Substrate
    • Antimicrobial peptides
    • Bacteriophages
    • Probiotics
Getting Novel Compounds to the Marketplace

Developing Novel Products

• Commercial accessibility of novel compounds depends on
  – Successful new molecule discovery
  – Advancement of the drug candidate through clinical development
  – Formulation and chemistry
  – Validation of a commercial-scale manufacturing process
  – Efficient regulatory review and final approval by the regulatory agency
  – Timely access to the market to meet the needs, by expedient market launch
Human and Animal Health R&D Processes

Product Profile  
Target ID  
Lead ID  
Candidate ID  
Preclinical Data  
Phase I  
Phase II  
Phase III  
Approval

First in Man Studies  
(Requires IND or Equivalent)  
12–15 years  
0.5–1.0B Euros

Human Health Discovery

First Target Animal Studies  
(Does not require INAD)

Product Profile  
Target ID  
Lead ID  
Candidate ID  
Preclinical Data  
Clinical Development  
Approval

Animal Health Discovery

12–15 years  
0.5–1.0B Euros

8–12 years  
80–100M Euros
Getting Novel Compounds to the Marketplace: The Discovery Process

Begins with a Target Profile

- Label Claim (treatment of X disease caused by X organisms)
- Market differentiators (single dose, oral, etc.)
  - Requires knowledge of current and future market conditions
- Market value

Key Points

- Investment is made at risk
- Timeline for process is 8–12 years
Getting Novel Compounds to the Marketplace: The Discovery Process

Preclinical Development Programs Identify Candidate Compounds

- Desirable efficacy including optimal ADME and PK parameters
- Favourable Animal Safety
- Demonstrable Human Food Safety
- Convenience of delivery system
- Positive Cost: Benefit ratio for the end-user
Getting Novel Compounds to the Marketplace: The Development Process

• Proof of efficacy: often not the rate-limiting step

• Greatest determining factors:
  – animal safety
  – method of delivery
  – economics

• Innovation can complicate PK / PD interpretation, may require new models

• Food animal compounds –
  – Complexity increases for food safety assessment
  – this increases development time and cost
Getting Novel Compounds to the Marketplace: Manufacturing

- Ability to manufacture the product at sufficient scale is key to the commercial viability of the product
- COG calculations are critical to moving ahead
- GMP requirements and manufacturing facility restrictions can block the transition to full-scale production
- Oversight may vary by regulatory jurisdiction, making it difficult to align globally in GMP vs. non-GMP environments
Getting Novel Compounds to the Marketplace: Regulatory

- Novel Anti-infectives Must Meet the Regulatory Requirements of Traditional Small Molecules
## Getting Novel Compounds to the Marketplace: Regulatory

<table>
<thead>
<tr>
<th>Drug Substance</th>
<th>Drug Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ General Information</td>
<td>✓ Pharmaceutical Development</td>
</tr>
<tr>
<td>✓ Nomenclature</td>
<td>✓ Method of Manufacture</td>
</tr>
<tr>
<td>✓ Chemical Structure</td>
<td>✓ Manufacturer(s)</td>
</tr>
<tr>
<td>✓ Physicochemical Properties</td>
<td>✓ Formulae</td>
</tr>
<tr>
<td>✓ Method of Manufacture</td>
<td>✓ Quantitative formula</td>
</tr>
<tr>
<td>✓ Structure Elucidation and Confirmation</td>
<td>✓ Batch formula</td>
</tr>
<tr>
<td>✓ Impurities</td>
<td>✓ Manufacturing Process</td>
</tr>
<tr>
<td>✓ Control of the Drug Substance</td>
<td>✓ Process Validation</td>
</tr>
<tr>
<td>✓ Reference Standards</td>
<td>✓ Control of Excipients</td>
</tr>
<tr>
<td>✓ Packaging</td>
<td>✓ Control of the drug product</td>
</tr>
<tr>
<td>✓ Stability</td>
<td>✓ Packaging</td>
</tr>
<tr>
<td></td>
<td>✓ Stability</td>
</tr>
<tr>
<td></td>
<td>Accelerated &amp; Long Term Studies</td>
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<tr>
<td></td>
<td>Proposed storage &amp; shelf life</td>
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<table>
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<tr>
<th>Efficacy</th>
<th>Animal Safety</th>
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<tr>
<td>✓ Microbiology</td>
<td>Laboratory Animal Studies</td>
</tr>
<tr>
<td>✓ Laboratory <em>in-vitro</em></td>
<td>✓ Acute Toxicity</td>
</tr>
<tr>
<td>✓ Animal Model Efficacy</td>
<td>✓ Sub-chronic Toxicity</td>
</tr>
<tr>
<td>✓ Clinical Pharmacology</td>
<td>✓ Chronic Toxicity</td>
</tr>
<tr>
<td>✓ Pharmacokinetics</td>
<td>✓ Irritation</td>
</tr>
<tr>
<td>✓ Bioavailability</td>
<td>✓ Reproduction &amp; Teratogenicity</td>
</tr>
<tr>
<td>✓ Pharmacodynamics</td>
<td>Target Animal Safety Studies</td>
</tr>
<tr>
<td>✓ Dose determination</td>
<td>✓ Margin-of-Safety</td>
</tr>
<tr>
<td></td>
<td>✓ Proposed Conditions of Use</td>
</tr>
<tr>
<td></td>
<td>✓ Tissue Irritation</td>
</tr>
<tr>
<td></td>
<td>✓ Reproductive Function</td>
</tr>
<tr>
<td></td>
<td>✓ Clinical Safety</td>
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<tr>
<td>✓ Dose confirmation</td>
<td>✓ Pharmacovigilance Data</td>
</tr>
<tr>
<td>pivotal</td>
<td></td>
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## Getting Novel Compounds to the Marketplace: Regulatory

### Human Food Safety
- Laboratory Animal Studies
  - Acute, sub-chronic, chronic toxicity
  - Carcinogenicity, teratogenicity
  - Multigeneration reproductive
  - Genotoxicity
  - Pharmacological
    - Immunotoxicity, Neurotoxicity
- Pharmacokinetics & Metabolism
- Residue detection & depletion
- NOEL & ADI
- MRL & withdrawal period

### Microbial Safety
- Resistance mechanism
- Transfer of resistance genes
- Cross-resistance
- Co-resistance
- Resistance development
- Animal Gut Effect
- Human Gut Effect
- Impact on Human Medicine
Getting Novel Compounds to the Marketplace

**Intellectual Property Protection**

- Patent lifecycle is critical to return on R&D investment
- Maximization of IP protection hinges on efficient development, predictable regulatory review, and expedient access to the market
Conclusion: The Innovation Paradox

• Antibiotics are the only product category where increased use theoretically promotes more rapid obsolescence.
• Contrary to popular belief, veterinarians don’t have that many options for treating diseases.
• Responsibly developing new antibiotics and alternatives to antimicrobials is important to both human and animal health and the regulatory pathway needs to remain predictable, transparent and science based.
• Otherwise, Industry will invest R&D in other areas with the consequence that veterinarians will have even fewer treatment options available in the future – compromising our one health.
Thank You!