What the New Bio/Pharma Business Model Means for CMOs and CROs

Jim Miller
Interphex
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Agenda

Outline

- 2011 review
- New bio/pharma business model
- Key challenges and opportunities
- Final thoughts

Key points

- Strengthening market
- New pharma priorities
- Pharma still investing in manufacturing facilities
- New pharma manufacturing needs and technologies
- Preferred provider model favors larger suppliers
2011 review

Contract services market improved

- Most of contract services industry enjoyed more growth in 2011
- Discovery services providers in Asia grew most rapidly
- API manufacturers hurt by Swiss Franc strength
  - Many private API manufacturers did well

Sources: PharmSource Advantage database and revenue estimates; public reports
Dose CMO overview

NME approvals up, outsourced NMEs down

- High % of older APIs in 2011
  - 505(3) b filings
  - Branded generics, new forms

- Only 33% of injectable NMEs outsourced
  - 2006-2010 avg. = 51%

- 24 CMOs got approvals:
  - Patheon 7
  - DSM 3
  - Catalent 2

NDA Approvals by FDA

- Number above bar is number of NME approvals.
- Source: FDA data, PharmSource analysis
2011 review

R&D spending continues to climb

- Segments other than global bio/pharma spending more
- CMOs and CROs report rapid growth but not evenly
  - Phase 2/3 projects growing as early stage companies resurrect shelved projects
  - Preclinical/Phase 1 lags due to lack of financial support
- Global bio/pharma outsourcing more, esp. small molecule-related
Total VC up but early stage support weak

- Total venture capital has improved but established companies favored
- VCs favor companies with later phase candidates
  - Many were shelved in 2008 when funding was difficult
- Earliest stage companies are having a difficult time
- Likely to be less VC in future as investors back away
Bio/Pharma adapts to new environment

New industry environment
- Loss of blockbusters
- Price and volume resistance
- Low R&D productivity

<table>
<thead>
<tr>
<th>New growth opportunities</th>
<th>Reduce R&amp;D Risk</th>
<th>Manage Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biologics</td>
<td>Kill it early</td>
<td>Fewer therapeu</td>
</tr>
<tr>
<td>Niche products</td>
<td>POC focus</td>
<td>tic areas</td>
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<tr>
<td>Emerging markets</td>
<td>In-licensing</td>
<td>Greater outsou</td>
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<td></td>
<td>Partnering</td>
<td>cing</td>
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</table>
Challenges facing CR&D industry

Impact of price/volume pressure on bio/pharma

- EU & US debt /cost crises
  - Lower drug prices/ margins
  - Smaller volumes
  - Lack of bank capital (EU)

- Margin squeeze hits costs
  - Reduced R&D and marketing
  - Pressure to reduce cost of goods (CGS)
  - More outsourcing if cost-effective

- Bio/pharma companies must preserve branded model
Global pharma trends

**Outsourcing depends on value of know-how**

<table>
<thead>
<tr>
<th>Specialized Know-how</th>
<th>Foundational Know-how</th>
<th>Mature Know-how</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Occasional need</td>
<td>• Core to strategy</td>
<td>• Widely-available</td>
</tr>
<tr>
<td>• Costly to build/maintain</td>
<td>• Knowledge-generating</td>
<td>• Routine</td>
</tr>
<tr>
<td>• Materials engineering</td>
<td>• Biomanufacturing</td>
<td>• Slow evolution</td>
</tr>
<tr>
<td>• Cytotoxics</td>
<td>• Methods development</td>
<td>• Sm. mole API</td>
</tr>
<tr>
<td>• Genetic mouse breeding</td>
<td>• Injectable formulations</td>
<td>• Solid dose</td>
</tr>
<tr>
<td></td>
<td>• Protocol design</td>
<td>• Raw materials testing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Trial monitoring</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Propensity to outsource</th>
<th>High</th>
<th>Low</th>
<th>High</th>
</tr>
</thead>
</table>
Challenges facing CMO industry

Bio/pharma investing in growth targets

- Companies invest where there is growth
  - Large molecule API/dose
  - Vaccines
  - Emerging markets

- More countries granting tax-favored status to bio/pharma
  - UK
  - Ireland
  - Hungary
  - Singapore
  - Switzerland
Challenges facing CMO industry

Many projects recently announced or completed

<table>
<thead>
<tr>
<th>Company</th>
<th>Facility</th>
<th>Details</th>
<th>Country</th>
<th>Investment</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSK</td>
<td>Dose</td>
<td>Expansion</td>
<td>Ireland</td>
<td>$ 60</td>
</tr>
<tr>
<td>Merck</td>
<td>Dose</td>
<td>new vaccine facility</td>
<td>Ireland</td>
<td>$ 270</td>
</tr>
<tr>
<td>Novartis</td>
<td>Dose</td>
<td>new facility</td>
<td>Russia</td>
<td>?</td>
</tr>
<tr>
<td>Roche</td>
<td>Dose</td>
<td>clinical supplies</td>
<td>Switzerland</td>
<td>$ 270</td>
</tr>
<tr>
<td>GSK</td>
<td>Dose</td>
<td>facility expansion</td>
<td>UK</td>
<td>$ 60</td>
</tr>
<tr>
<td>Genzyme</td>
<td>Dose-inject</td>
<td>Injectables</td>
<td>Ireland</td>
<td>$ 208</td>
</tr>
<tr>
<td>Novartis</td>
<td>Dose-solid</td>
<td>OTCs</td>
<td>Switzerland</td>
<td>$ 42</td>
</tr>
<tr>
<td>BI</td>
<td>Dose-solid</td>
<td>Hipo solid</td>
<td>USA</td>
<td>$ 50</td>
</tr>
<tr>
<td>Roche</td>
<td>Dose-solid</td>
<td>clinical supplies</td>
<td>USA</td>
<td>?</td>
</tr>
<tr>
<td>Watson</td>
<td>Dose-specialty</td>
<td>patches and gels</td>
<td>USA</td>
<td>$ 44</td>
</tr>
</tbody>
</table>
## Challenges facing CMO industry

### Tax incentives are difficult hurdle for CMOs

<table>
<thead>
<tr>
<th></th>
<th>Base Case</th>
<th>Tax Incentive</th>
<th>CGS Savings</th>
</tr>
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<tbody>
<tr>
<td>Revenue</td>
<td>$100</td>
<td>$100</td>
<td>$100</td>
</tr>
<tr>
<td>CGS</td>
<td>20</td>
<td>20</td>
<td><strong>14</strong></td>
</tr>
<tr>
<td>R&amp;D</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>SG&amp;A</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>EBT</td>
<td>30</td>
<td>30</td>
<td>36</td>
</tr>
<tr>
<td>Tax rate</td>
<td>25%</td>
<td><strong>10%</strong></td>
<td>25%</td>
</tr>
<tr>
<td><strong>Net income</strong></td>
<td><strong>$22.5</strong></td>
<td><strong>$27.0</strong></td>
<td><strong>$27.0</strong></td>
</tr>
</tbody>
</table>

- Matching tax breaks requires big CGS savings
- Manufacturing costs must drop 30% to match tax savings
Challenges facing CMO industry

Global Pharma has complex manufacturing calculus

**Basic requirements**
- Unit cost
- Security of supply
- Technology
- Cost flexibility
- IP protection

**Financial impacts**
- Tax implications
- Government subsidies
- Exchange rate exposure

**Restructuring costs**
- Severance arrangements
- Disposal of old facilities

**Commercial demands**
- Local market portfolio
- Local market approvals
- Local market brand

CMO model addresses only basic requirements
Challenges facing CMO industry

Lower unit volumes a threat

- Lower volume products
  - Niche products
  - Orphan drugs
  - Branded generics
  - Emerging markets

- Inventory management
  - Lower inventories to free cash for deals

- Long-term challenge
  - Smaller CMOs compete for commercial work
  - Traditional CMO cost structure a liability
    - Large scale, large batch campaigning model
  - New technologies may change in-vs-out calculus

CMO industry will face new cost pressures and increased competition
Challenges facing CMO industry

New technologies challenge CMOs

- **API manufacture**
  - Microreactors
  - Improving cell culture and fermentation yields
  - Bioreactors in a bag

- **Dose manufacture**
  - Disposable contact parts
  - Continuous processing
  - Automation
  - Pre-processed inputs (e.g., SCF syringes)

- **Lower capital costs**
  - Smaller facilities
  - Simpler HVAC
  - Smaller equipment

- **Lower operating costs**
  - Lower facility operating costs
  - Less direct and indirect labor
  - Faster line changeovers

- **Less working capital**
  - More inventory turns

CMO industry will face added competition from in-house manufacture even from smaller companies
Global pharma trends

Outsourcing favors preferred providers

- 80+% of outsourced clinical work going to preferred suppliers
- Previous experience, size and price drive choice of preferred provider
- Integrated service model winning out over functional services model

<table>
<thead>
<tr>
<th>Pharma</th>
<th>Preferred Clinical CRO Providers</th>
</tr>
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<tbody>
<tr>
<td>Sanofi</td>
<td>Covance</td>
</tr>
<tr>
<td>Lilly</td>
<td>Covance, Quintiles, Icon, i3, Parexel</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Icon, Parexel</td>
</tr>
<tr>
<td>GSK</td>
<td>PPD, Parexel</td>
</tr>
<tr>
<td>BMS</td>
<td>Icon, Parexel</td>
</tr>
<tr>
<td>Eisai</td>
<td>PPD</td>
</tr>
<tr>
<td>Otsuka</td>
<td>Covance</td>
</tr>
<tr>
<td>Elan</td>
<td>PPD</td>
</tr>
<tr>
<td>Takeda</td>
<td>Covance, Quintiles</td>
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Challenges and trends facing CR&D industry

**Integrated models for early development**

<table>
<thead>
<tr>
<th>Business Model</th>
<th>Services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully integrated development</td>
<td>Aptuit, Wuxi, AMRI</td>
</tr>
<tr>
<td>Integrated CMC</td>
<td></td>
</tr>
<tr>
<td>Integrated chemistry</td>
<td></td>
</tr>
<tr>
<td>Integrated dose</td>
<td></td>
</tr>
<tr>
<td>Niche/specialty provider</td>
<td></td>
</tr>
</tbody>
</table>

A strategic response to supplier consolidation and quick to clinic/quick to fail
Dose CMO overview

API/Dose one-stop CMOs emerging

- **Small molecule**
  - Siegfried
  - AMRI
  - Cambrex
  - DSM

- **Large molecule**
  - Rentschler
  - BI
  - Laureate
  - Cook Pharmica

**Rationale**
- Differentiate by offering customers single supplier
  - Reduce supply chain complexity
  - Reduce sourcing expense
- Capture more of spend

**Will it be successful?**
- Some traction in large molecule segment
- Will global bio/pharma buy it?

Potential threat to dose-only CMOs
Global pharma trends
Preferred deals force CROs to consolidate

Clinical CRO Market
$14 B Spend

- Q 14%
- CVD 10%
- Inc 7%
- PPD 10%
- INC 5%
- inVentiv 6%
- Others 40%

- Major acquisitions build size
  - INC+Kendle = $750 M
  - inVentiv + PharmaNet +i3 = $900 M
  - But integration could be a distraction

- Market leaders build on scale
  - CVD: Data mining to make clinical site selection more efficient
Dose CMO overview

Consolidation underway, faces major hurdles

Consolidation events
- Ben Venue exit
- Nextpharma BE bankruptcy
- Patheon
  - Exits semisolids
  - Exits PR site
- CPL closed Buffalo site
- Osny absorbed by Cenexi
- Akrimax failure
- A few market leaders have differentiated themselves
  - Examples: Vetter, DPT

Consolidation drivers
- EU debt crisis
- Global pharma sourcing
- Return on capital focus

Consolidation barriers
- Low entry barriers
- High exit barriers
- Cost of moving products
- Weak differentiation
- Marginal CMO profitability
- Lack of capital

CMO consolidation could be messy, and threaten drug supply
Final thoughts

- Industry undergoing slow consolidation
- External environment will pressure CMOs
- New manufacturing requirements and technologies are the greatest threats, not India and China

- Success strategies
  - Strong, reliable operating performance
  - Innovative business models