Technology Transfer & Disruptive Innovation at NIH: The Case of Taxus Express™

Steven M. Ferguson
Director, Division of Technology Development & Transfer
NIH Office of Technology Transfer
HHS Email: sf8h@nih.gov
Technology Source: National Institutes of Health

Basic Biomedical Research in Support of the Public Health

- Funding
- Training
- Basic Research
- Clinical Trials
- Inventions
- Policies
NIH Licensing: Transfer of Commercial Rights To Technology From Research Program

• Annual budget of $28 billion (2005)
• 8% of funding for intramural research
• 6,000 intramural scientists / 2,000 projects
• 212,000 extramural scientists / 46,000 grants
• Basic & clinical research discoveries
• Partners commercialize into products
How Could Just One Technology From the NIH Portfolio Be Disruptive?

- 400+ invention disclosures per year
- 2300 total pending/issued patents
- 1650+ active licenses (276 executed FY04)
- $56.3 million in royalties collected FY04
- >$456 million in royalties collected FY93-FY04
- 231 active CRADAs (1500 to date)
- ~200 products developed to date (20 vaccines and therapeutics)
How Could Something So Small Be Disruptive?
Cardiovascular Disease (circa 1996)

- Stents (as part of balloon angioplasty) have revolutionaryized atherosclerosis treatment.
- Johnson & Johnson controls the stent market in the U.S. and Europe.
- But 30% or more cases form scar tissue that recloses arteries (restenosis).
- Incremental design changes in stents fail to solve the problem.
That Was Then, This Is Now (2005)

• “Most successful new medical product in history” launched by NIH licensee & corporate partners.
• >$2.6B estimated for first full year sales in U.S. and Europe.
• Johnson & Johnson no longer market leader in stents.
• What happened?
Disruptive Innovation – Drug-Eluting Stents (DES)
Disruptive Innovation – Drug-Eluting Stents (DES)

Paclitaxel Coating
Why Would DES Be Considered Disruptive?

• Combination drug/devices uncommon approach.
• Double regulatory issues / double risk.
• NIH licensee (Angiotech) small innovative Canadian firm.
• Disruptive Partnering Strategy: Angiotech unsuccessful with Market Leader (J&J) but partners with multiple Market Trailers, including Boston Scientific.
Industry

Expertise
Chemistry & Biology

Solutions
Small Molecules, Drugs, Biologics

Corporate Competency
Target Identification, Molecular Design, ADME, Animal & Human Testing, Marketing

FDA
Drugs: Slow/Expensive

Risk
High Risk: 1/10 Succeed

User
INTERNISTS & GP's

MEDICAL DEVICES/SURGERY

Engineering

Solutions
Structural, Mechanical, Electrical, Radioactivity

Corporate Competency
Mechanical & Electrical Engineering, Clinical, Marketing

FDA
Devices: Faster/Cheaper

Risk
Low Risk: 9/10 Succeed

User
SURGEONS & INTERVENTIONALISTS
Small Molecule Therapeutics

Solving Structural Problems with Therapeutics “Beyond Engineering”

Interventional Technologies

Using Devices to Deliver Drugs “Beyond Systemics”

Chemistry & Biology

Small Molecule Drugs, Biologics

Target Identification, Molecular Design, ADME, Animal & Human Testing, Marketing

Drugs: Slow/Expensive

High Risk: 1/10 Succeed

PHARMACEUTICALS

ANPI OPPORTUNITY

MEDICAL DEVICES/SURGERY

Engineering

Structural, Mechanical Electrical, Radioactivity

Mechanical & Electrical Engineering, Clinical, Marketing

Devices: Faster/Cheaper

Low Risk: 9/10 Succeed

SURGEONS & INTERVENTIONALISTS

INTERNISTS & GP’S
Why Would DES Be Disruptive At NIH?

• Research came from National Institute of Aging (not typically focused on cardiovascular disease).
• Royalty income provides a sharp increase in NIA research budget.
• Royalty income not disruptive to inventors due to cap (unlike university paclitaxel synthesis).
• Licensing Issues: Revisit standard license contract language for drug/device combos.
• Change in standard of healthcare.
Why Would DES Be Disruptive At Angiotech?

• Expected success but not market domination!
• Cash makes acquisition strategies possible. Three subsidiaries!!
• Able to extend product concept to product platform to corporate mission (“Knowledgy”)
• Additional partnerships & product extensions based upon DES concepts.
AGM Financial Review
Q2:05 Guidance

- Q1:05 TAXUS Revenue Summary: Total $686MM; U.S. $494MM; EU/ROW $192MM
- U.S. Market Share holding steady at approximately 60%+

<table>
<thead>
<tr>
<th>Quarter</th>
<th>TAXUS</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q104A</td>
<td>$4.1</td>
<td>$7.8</td>
<td>$11.9</td>
</tr>
<tr>
<td>Q204A</td>
<td>$10.0</td>
<td>$3.4</td>
<td>$13.4</td>
</tr>
<tr>
<td>Q304A</td>
<td>$40.4</td>
<td>$3.9</td>
<td>$44.3</td>
</tr>
<tr>
<td>Q404A</td>
<td>$43.8</td>
<td>$3.5</td>
<td>$47.3</td>
</tr>
<tr>
<td>Q105A</td>
<td>$50.0</td>
<td>$3.4</td>
<td>$53.4</td>
</tr>
<tr>
<td>Q205E</td>
<td>$49.0</td>
<td>$3.0</td>
<td>$52-54</td>
</tr>
</tbody>
</table>

$US in Millions
Expectations: Why Were We So Wrong?

(from Angiotech Annual Meeting)

<table>
<thead>
<tr>
<th>WW DES Model</th>
<th>2004</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>WW Revenue ($MM))</td>
<td>3.658</td>
<td>4.621</td>
</tr>
<tr>
<td>Market Share</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSC</td>
<td>22%</td>
<td>22%</td>
</tr>
<tr>
<td>Guidant</td>
<td>13%</td>
<td>25%</td>
</tr>
<tr>
<td>JNJ</td>
<td>61%</td>
<td>43%</td>
</tr>
<tr>
<td>Medtronic</td>
<td>1%</td>
<td>5%</td>
</tr>
<tr>
<td>Other</td>
<td>3%</td>
<td>5%</td>
</tr>
</tbody>
</table>


What Occurred... (2005 Analyst Reports)

<table>
<thead>
<tr>
<th>WW DES Model</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>WW Revenue ($MM))</td>
<td>3,900</td>
<td>5,506</td>
<td>5,817</td>
<td>5,968</td>
</tr>
<tr>
<td>Market Share</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSC</td>
<td>53%</td>
<td>53%</td>
<td>46%</td>
<td>43%</td>
</tr>
<tr>
<td>Guidant</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>JNJ</td>
<td>46%</td>
<td>44%</td>
<td>48%</td>
<td>47%</td>
</tr>
<tr>
<td>Medtronic</td>
<td>0%</td>
<td>2%</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Abbott</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Source: see above left (January to March, 2005)
Additional Paclitaxel Eluting Technology Applications Now In Development

• Use in actual bypass surgery (Angiotech with CABG Medical).
• Treatment of emphysema (Angiotech with Broncus Technologies).
• Peripheral stents and wraps (Angiotech with Cook, Inc.)
CABG Medical
The Holly Grail System for Bypass Surgery

Implanted Vessel Connector

The Holly Grail System

Holly GRAFT™ Vessel Connector
Drug Eluting Graft

Below is a magnified version of the Holly Graft System vessel connector.
Normal XRay

Emphysema XRay

Over expanded
Flattened diaphragm
Clinical & Regulatory Summary

- Treated 80 patients to date
- Over 25 patients implanted with paclitaxel-eluting stents
  - Duration of airway bypass seems to improve
    - Leveraging proven paclitaxel technology
  - Apparent improvement at 1, 3 and 6 months:
    - Symptoms
    - Quality of Life
    - PFT’s
- Currently treating patients outside the U.S.
- Planning to start U.S. pivotal study in 1H06
Zilver® Paclitaxel-Eluting Peripheral Stent (Partnered with Cook Inc.)

- First drug-eluting stent to be used outside the heart
- Proof-of-concept with success in treating CAD
- U.S. Trial Initiated
  - 60 patients, 10 sites
  - Objective: safety and efficacy in peripheral vascular disease above-the-knee in the femoropopliteal artery
  - Pilot study enrollment completion expected by end of 2005
  - Pivotal study enrollment completion by end of 2006
  - Trial expansion upon further FDA review
Vascular Wrap: European Pivotal Clinical Trial

The study is designed to address the need of surgeon, to prevent or reduce the incidence of stenosis in synthetic peripheral bypass grafts.

Initiated: September, 2003
Enrolment: Complete, 108 pts
Double-blind: Randomization after anastomosis complete
Randomized: 2:1 Wrap vs Standard of Care
Multi-center: 13 (Expanded to 17)
Primary Endpoint: Safety
Secondary Endpoint: Binary Restenosis
                    (Duplex Measurements)
                    Clinical restenosis, limb salvage
Conclusions Regarding Disruptive Innovation

• Disruptive Innovation brings changes to both marketplace as well as technology developer & provider.

• Disruptive Innovation appears to support notion that true innovation is increasingly driven by smaller firms – see for example …
Older NIH “Homerun” Licensed Products (All From Large Firms)

- Abbott HIVAB (AIDS Test Kit)
- BMS Videx (ddI)
- BMS Taxol (paclitaxel)
- Schering Fludara (fludarabine)
- GlaxoSKB Havrix (hepatitis A)
- Roche Hivid (ddC)
More Recent Product Approvals (All From Small Firms At The Time)

- Angiotech: Taxus (paclitaxel-eluting stents)
- Genzyme: Thyrogen (rTSH)
- Isis: Vitravene (antisense CMV)
- Medimmune: Synagis (RSV mab)
- Millennium: Velcade (myeloma drug)
- Biogen Idec: Zevalin (NHL I$_{131}$ mab)
- Amgen: Kepivance (KGF)
Sources Of Information On NIH Licensing And Technologies

- NIH Technology Transfer – ott.od.nih.gov
- NIH CRISP Database - nih.gov/grants
- Global TechnoScan – globaltechnoscan.com
- Pharmalicensing - pharmalicensing.com
- Technology Exchange - techex.com
- University Ventures - uventures.com
- Pharma-transfer - pharma-transfer.com
- Knowledge Express - keonline.com