Pharma IP Evergreening Strategies (i.e., Patent Extension) Using Nanotechnology

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No attorney-client relationship is being established by this presentation.

No client-confidential information is being disclosed. All information is publicly available.
Consider this...

- US Blockbuster drugs >$1 billion
  – (Lipitor® ~$11.7 billion 2010)

- $1.3 billion to develop a drug

- 5,000 compounds → 5 human testing
→ ... only one is approved

- 1-of-every-3 drugs approved recuperates development costs
### Top 10 Rx Drugs in 2014

Consensus sales forecasts for world's top 10 drugs in 2014 *

<table>
<thead>
<tr>
<th>Rank</th>
<th>Drug Name</th>
<th>Company</th>
<th>Sales Forecast</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Avastin (cancer)</td>
<td>Roche</td>
<td>$8.9 Bil.</td>
</tr>
<tr>
<td>2</td>
<td>Humira (arthritis)</td>
<td>Abbott</td>
<td>$8.5 Bil.</td>
</tr>
<tr>
<td>3</td>
<td>Enbrel (arthritis)</td>
<td>Pfizer/Amgen</td>
<td>$8.0 Bil.</td>
</tr>
<tr>
<td>4</td>
<td>Crestor (cholesterol)</td>
<td>AstraZeneca</td>
<td>$7.7 Bil.</td>
</tr>
<tr>
<td>5</td>
<td>Remicade (arthritis)</td>
<td>Merck/J&amp;J</td>
<td>$7.6 Bil.</td>
</tr>
<tr>
<td>6</td>
<td>Rituxan (cancer)</td>
<td>Roche</td>
<td>$7.4 Bil.</td>
</tr>
<tr>
<td>7</td>
<td>Lantus (diabetes)</td>
<td>Sanofi-Aventis</td>
<td>$7.1 Bil.</td>
</tr>
<tr>
<td>8</td>
<td>Advair (asthma/COPD)</td>
<td>GSK</td>
<td>$6.8 Bil.</td>
</tr>
<tr>
<td>9</td>
<td>Herceptin (cancer)</td>
<td>Roche</td>
<td>$6.4 Bil.</td>
</tr>
<tr>
<td>10</td>
<td>NovoLog (diabetes)</td>
<td>Novo Nordisk</td>
<td>$5.7 Bil.</td>
</tr>
</tbody>
</table>

*Source: Thompson-Reuters

Pfizer (Atorvastatin). Ranbaxy has a 6 month agreement to begin selling generic in Nov., 2011

Eli Lilly & Co. (Olanzapine). Antipsychotic drug for schizophrenia and bipolar disorder. $1 B sales in 2010.

J&J (Levofloxacin). Antibiotic commonly used to treat severe to life-threatening bacterial infections. $434 M sales in 2010. Hi-Tech Pharmacal obtained exclusive generic rights of oral solution for 6 mo.


Pfizer (Pantoprazole). Popular antacid.
Avg. 5-6 years of Patent Exclusivity
FDA Approval / Patent Exclusivity Timeline

Preclinical studies → FDA clinical trials + NDA

Patent Prosecution

Preclinical studies:
- Start
- 0 yrs
- 1.5yr
- 3yr
- 4.4yr

FDA clinical trials + NDA:
- Start FDA approval process
- 14yr
- 16yr
- 20yr

Patent Prosecution:
- File patent idea
- Publication of idea
- Patent issues (avg biotech)

Possible term extension and strategically extending market exclusivity

Market exclusivity for pioneer biotech company

Evergreening

Orange Book Listing

The Big Pharma Market

- Unpredictable and hazardous ...
- Unexpected side effects...
- New drugs with superior efficacy marginalize old drugs immediately and indefinitely.
Pharma IP Evergreening
Is Pharma IP Evergreening Simply Monopoly Extension?
Traditional Pharma: “Small Molecules”

Olanzapine —— 1 nm

NanoPharma: Nanoparticles of small molecules
Many ways to make medicine “nano”...
cool pic from nanoparticles.org
Nano is Great for Patenting!

- Unpredictable
- Unexpected Results
- New Formulations
- New Compositions
- Different/new dosage regimens

... and hopefully safer and more effective than traditional pharma
Recent Nanomedicine Patents

US8017156  Long-acting colloidal insulin formulation and its preparation  FLAMEL TECH

US8003127  Nanoparticulate corticosteroid and antihistamine formulations methods of making, and methods of administering thereof  Elan Pharma International Limited

US7998477  Spherical protein particles and methods for making and using them  Althea Technologies, Inc.

US7910577  Injectable nanoparticulate olanzapine formulations  Elan Pharma International Limited
US8017156 Long-acting colloidal insulin formulation and its preparation using at least one poly(Leu-block-Glu) in which the pH is between 5.8 and 7.0
Big Pharma’s Nanotech Patent Portfolios

- Elan – 44 "distinct patent families"
- Roche – 19
- Novartis – 18
- Abbott – 14
- Pfizer – 13
- Bristol-Meyers Squibb – 10
- AstraZeneca – 8
- Sanofi – 3
- GlaxoSmithKline – 0
nano orange book patents?

~6600 U.S. Patents listed in the FDA’s Orange Book

~2000 U.S. nanomedicine patents

To Date: About 40 nanotech patents listed in the Orange Book
nanoparticulate TriCor (fenofibrate)

U.S. Patents:
7,875,630
7,820,788
7,741,374
7,741,373
7,569,612
7,320,802
7,276,249
7,101,576
## Top 10 Rx Drugs in 2010

**Source**: Thompson-Reuters

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<tr>
<th>Rank</th>
<th>Drug</th>
<th>Manufacturer</th>
<th>Revenue (Bil.)</th>
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<tbody>
<tr>
<td>1.</td>
<td>Lipitor (cholesterol)</td>
<td>Pfizer</td>
<td>$11.7 Bil.</td>
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<td>2.</td>
<td>Plavix (anticlotting)</td>
<td>Sanofi/BMS</td>
<td>$9.6 Bil.</td>
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Nanomedicine Patenting by Big Pharma
Bristol Myers Squibb

7 Issued U.S. Nanomed Patents, e.g.,

- 7255875, Integrin Targeted Imaging Agents (using an emulsion of nanoparticles) [Not in Orange Book]

- 7115587, Aripiprazole complex formulation and method [In Orange Book]

- antipsychotic agent aripiprazole in the form of an inclusion complex in a β-cyclodextrin
Cyclodextrin
WO2008079834A2

PREPARATION OF PARAMAGNETIC NANOPARTICLES CONJUGATED TO LEUKOTRIENE B4 (LTB4) RECEPTOR ANTAGONISTS, AND THEIR USE AS MRI CONTRAST AGENTS FOR THE DETECTION OF INFECTION AND INFLAMMATION
Abbott: -Labs, -Cardiovascular, Diabetes Care, -Medical Optics

14 families of nanomed patents
4 issued patents, none in Orange Book

- Formulations comprising lipid-regulating agents
- Nanocrystals for use in topical cosmetic formulations and method of production thereof
- Nanoparticle-coated medical devices and formulations for treating vascular disease
- Therapeutic composition with enhanced endothelium targeting nanoshells on polymers
Magnetic Nanoparticle Therapies

Various compositions, methods, and devices are provided that use fluorescent nanoparticles, which can function as markers, indicators, and light sources.

The fluorescent nanoparticles can be formed from a fluorophore core surrounded by a biocompatible shell, such as a silica shell.
• 20 distinct nanomed patent families
  – Mainly UV protection agents and pigments (for sunscreens)
• 6 issued patents
• None listed in Orange Book
### Pfizer’s 5 Issued Nanotech Patents >2001

<table>
<thead>
<tr>
<th>US Pat No.</th>
<th>Title</th>
<th>Composition / Orange Book?</th>
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<th>Title</th>
<th>Composition / Orange Book?</th>
</tr>
</thead>
<tbody>
<tr>
<td>6852746</td>
<td>Crystalline drug form</td>
<td>6-[(2,2-diphenylethyl)amino… / No</td>
<td>6548555</td>
<td>Basic drug compositions with enhanced bioavailability</td>
<td>(general structures) / No</td>
</tr>
<tr>
<td>6548555</td>
<td>Basic drug compositions with enhanced bioavailability</td>
<td></td>
<td>6713461</td>
<td>Pharmaceutical complex</td>
<td>Eletriptan / No</td>
</tr>
<tr>
<td>6713461</td>
<td>Pharmaceutical complex</td>
<td></td>
<td>6632803</td>
<td>Pharmaceutical formulations containing voriconazole (with cyclodextrin, lyophilized)</td>
<td>Voriconazole (Vfend – antifungal) / Yes ($1 Bil) Lit!</td>
</tr>
<tr>
<td>6632803</td>
<td>Pharmaceutical formulations containing voriconazole (with cyclodextrin, lyophilized)</td>
<td></td>
<td>6232304</td>
<td>Inclusion complexes of aryl-heterocyclic salts (with cyclodextrin)</td>
<td>Ziprasidone (Geodon/Zeldox - antipsychotic) / Yes ($1 bil)</td>
</tr>
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Nanof ormulation “Evergreening” of Drugs Coming Off Patent in 2011

Atorvastatin - 15 new patents (Lipocine, Inc., NanoPax Pharma, Orbus Pharma, Flamma, Sp.A); nanoparticles and improved delivery

Olanzapine – 12 new patents (Elan Pharma – orange book, Acusphere, Skye Pharma, academia); mainly various nanoparticulate formulations

Levofloxacin – 15 new patents (Acusphere, Sonus Pharm., UNC, Revalesio Corp., Pari Pharma); mainly various nanoparticulate formulations

Methylphenidate – 5 new patents (i.e., solid lipid nanoparticles)

Pantoprazole – 6 new patents (i.e., cyclodextrin…)

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Future Nanomedicine IP Battlegrounds?

• Drug Delivery
  – Site-specific targeted drug-delivery systems (dendrimers, nanoshells, nanoparticles, nanoliposomes)

• Personalized Medicine
  – Pharmacogenetics, pharmacogenomics

• Expiration of Traditional Blockbuster Drug Patents improved with nanotech (Product-Line Extensions, Patent Evergreening)
Nanomedicine IP

many nanoparticle patents

several in the orange book

big pharma has few nanopharma patents

evergreening today’s blockbusters with nanotech → most likely future IP battles…

Pharmaceutical formulations containing voriconazole (with cyclodextrin, lyophilized)
Which phrase is more “PC”?

“IP Evergreening”

or

“Next Generation Pharma Technology”
Thank you.

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