

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

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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 *

1. Avastin (cancer)	Roche	\$8.9 Bil.
2. Humira (arthritis)	Abbott	\$8.5 Bil.
3. Enbrel (arthritis)	Pfizer/Amgen	\$8.0 Bil.
4. Crestor (cholesterol)	AstraZeneca	\$7.7 Bil.
5. Remicade (arthritis)	Merck/J&J	\$7.6 Bil.
6. Rituxan (cancer)	Roche	\$7.4 Bil.
7. Lantus (diabetes)	Sanofi-Aventis	\$7.1 Bil.
8. Advair (asthma/COPD)	GSK	\$6.8 Bil.
9. Herceptin (cancer)	Roche	\$6.4 Bil.
10. NovoLog (diabetes)	Novo Nordisk	\$5.7 Bil.

*Source : Thompson-Reuters

Top 5 U.S. Drug Patent Expirations in 2011



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.



J&J (Methylphenidate). Drug for attention-deficit disorder. \$ 362 M in sales in 2010.

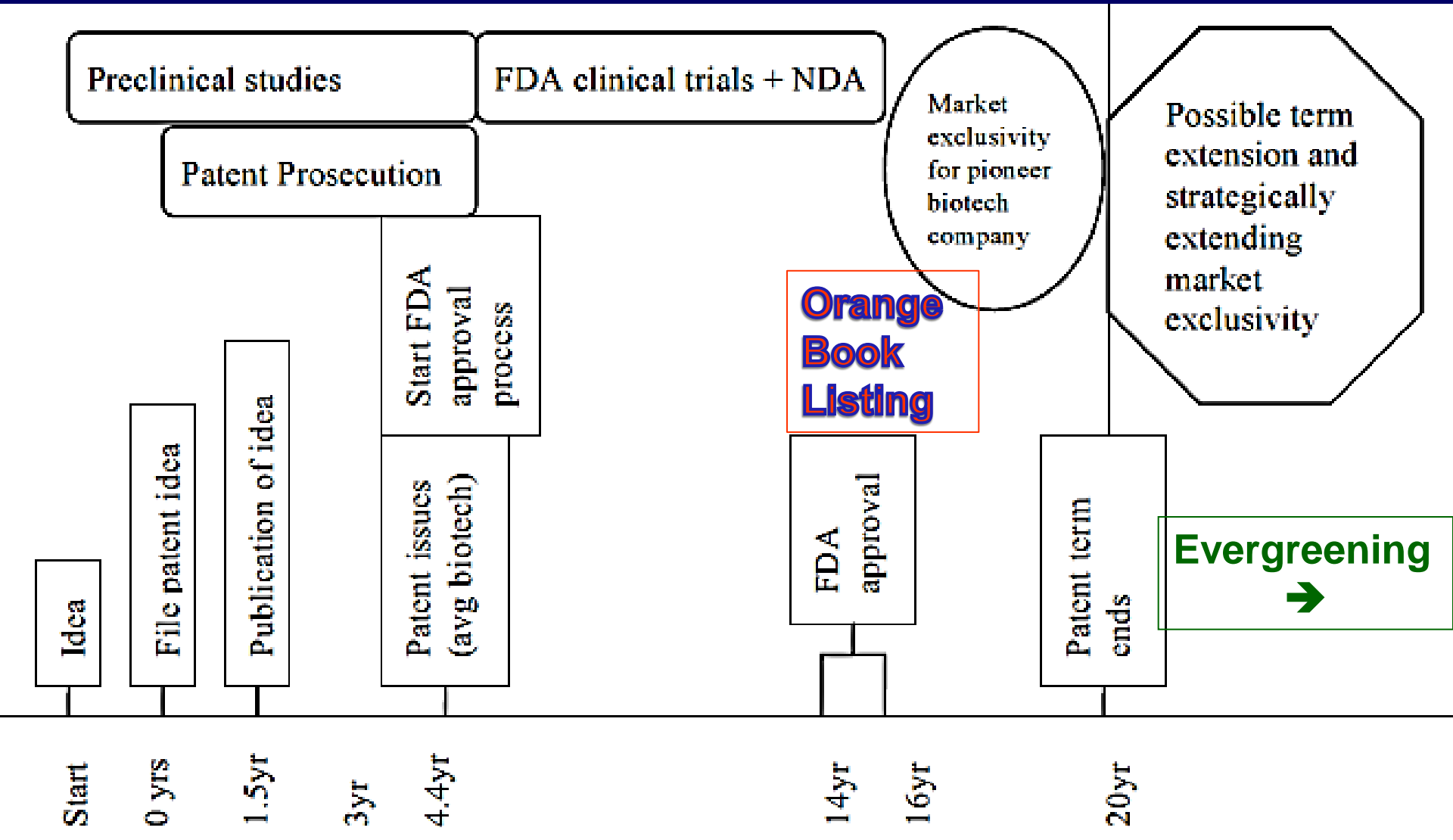


Pfizer (Pantoprazole). Popular antacid.

Avg. 5-6 years of Patent Exclusivity



FDA Approval / Patent Exclusivity Timeline



The Big Pharma Market



- Unpredictable and hazardous ...
- Unexpected side effects...
- New drugs with superior efficacy marginalize old drugs immediately and indefinitely.

Pharma IP Evergreening



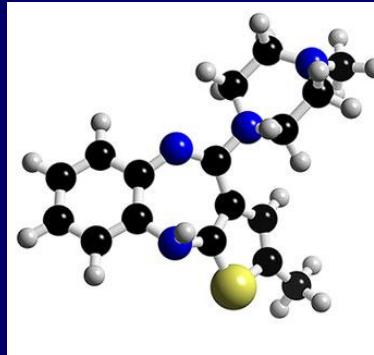
Is Pharma IP Evergreening Simply Monopoly Extension ?



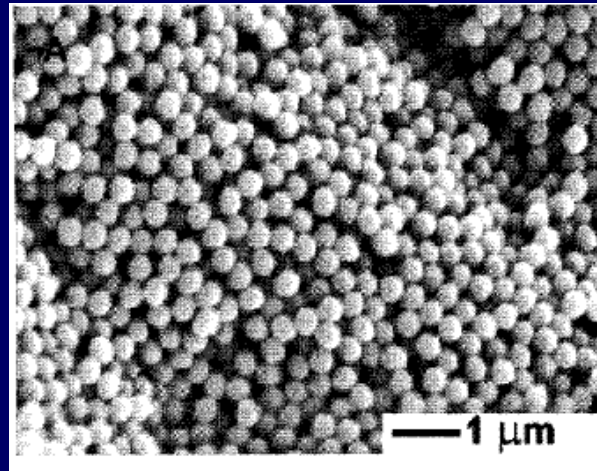
CONTROVERSY

Traditional Pharma: “Small Molecules”

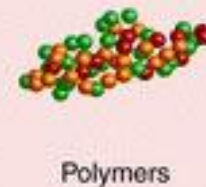
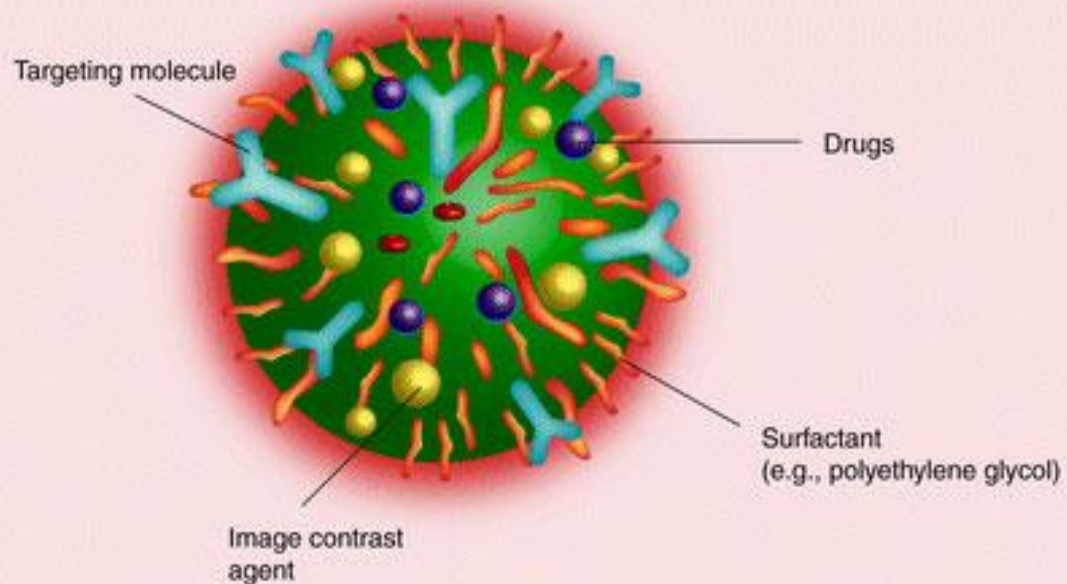
Olanzapine
—— 1 nm



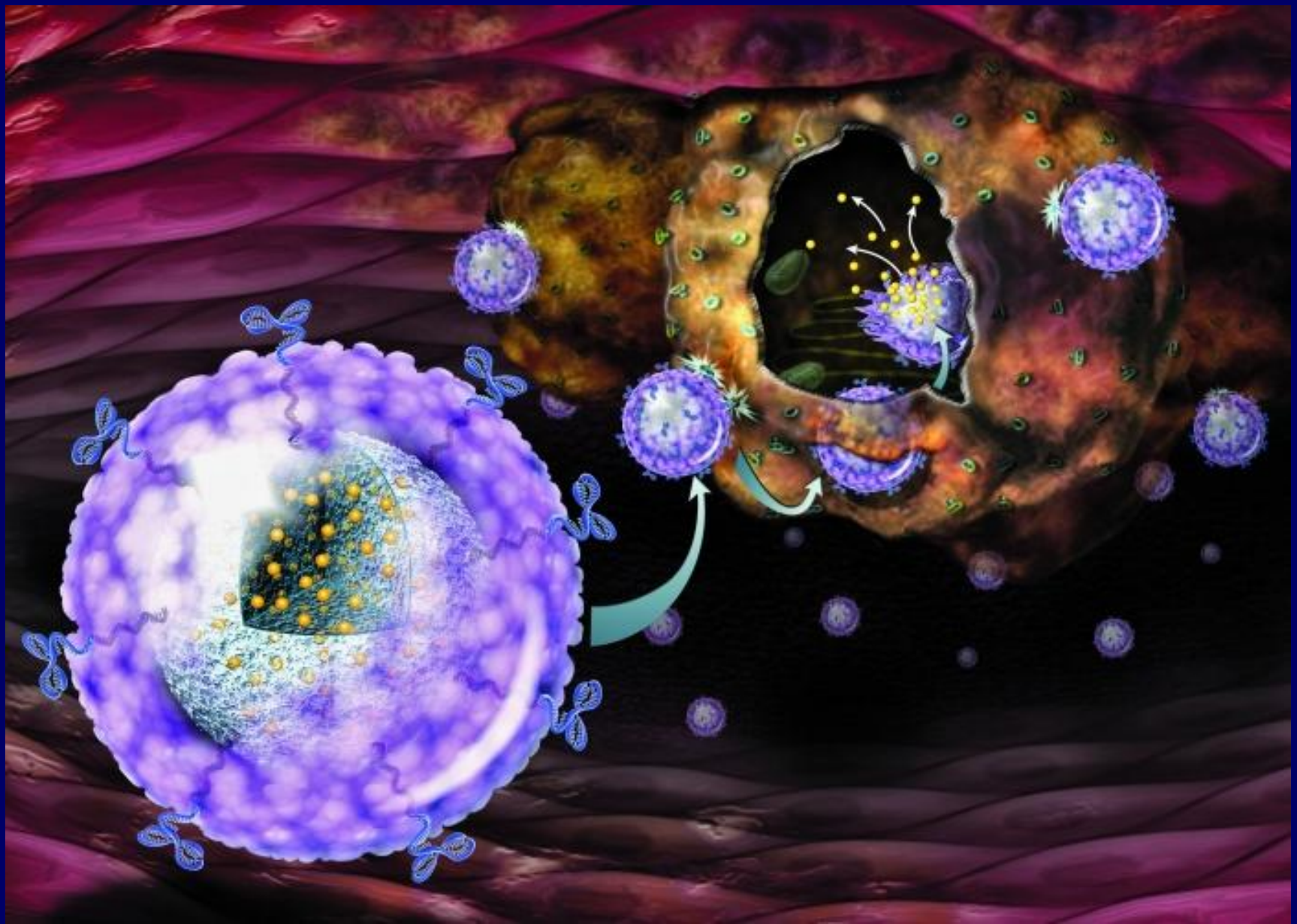
NanoPharma: Nanoparticles of small molecules



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

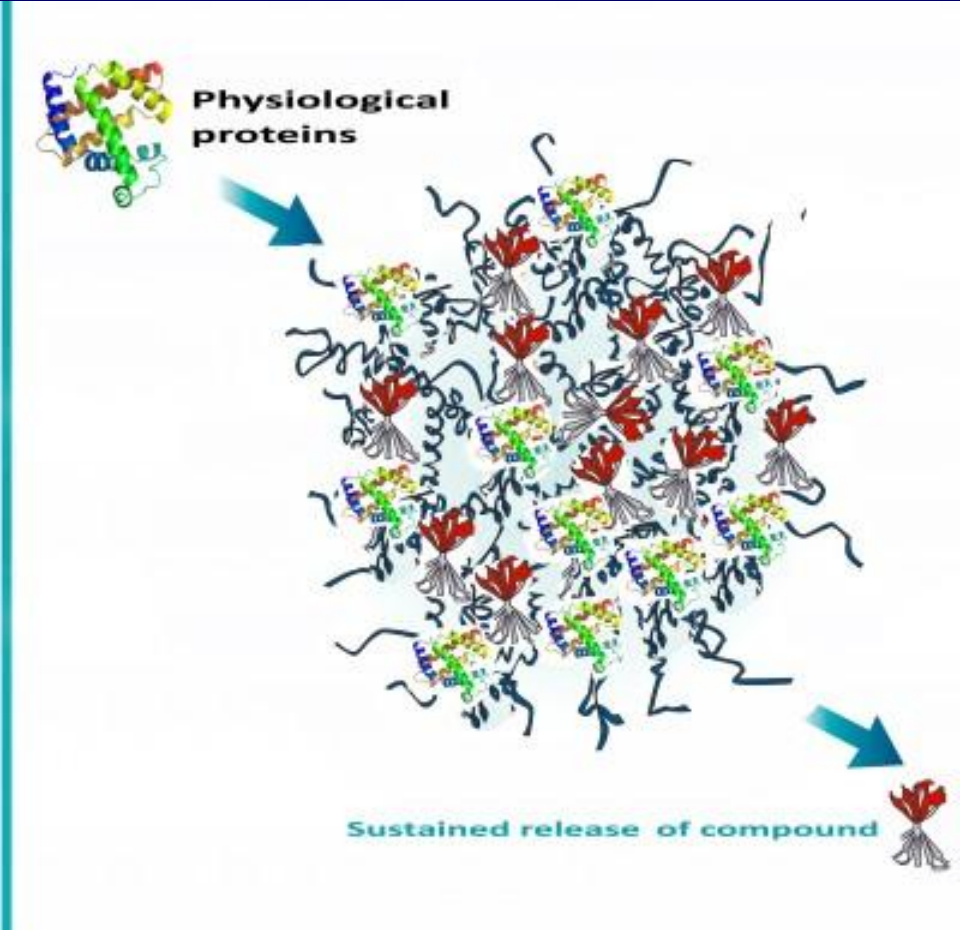
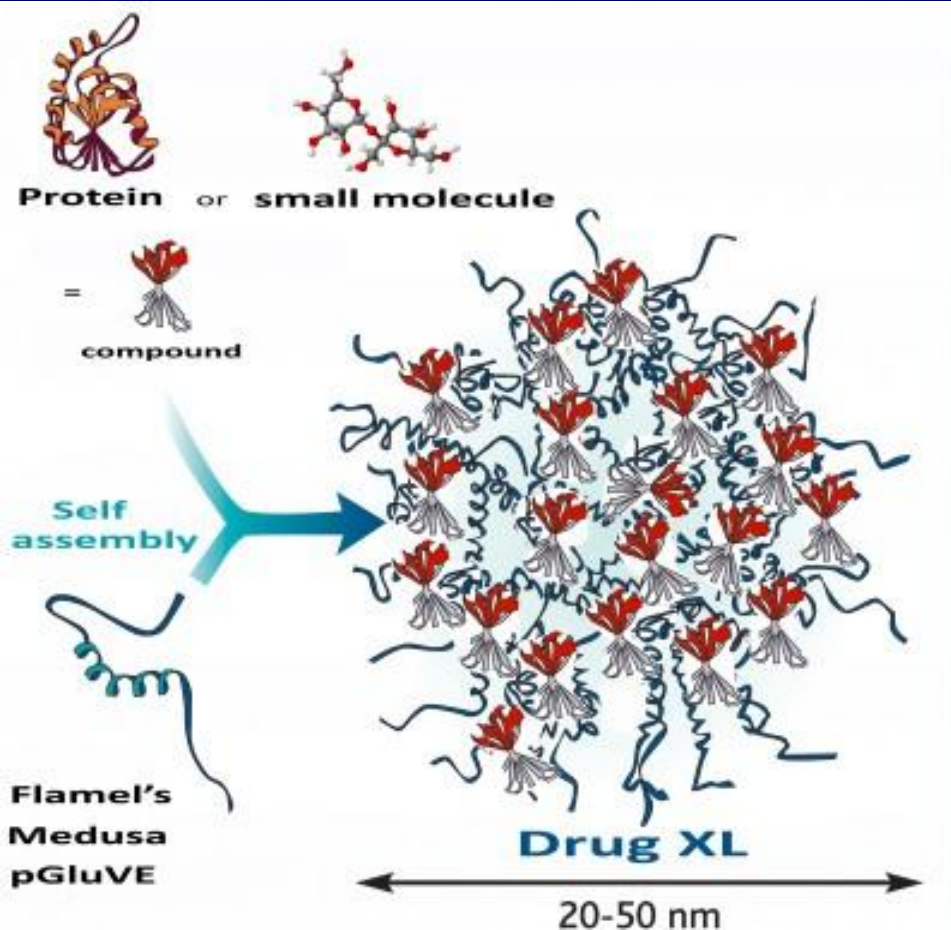
US8017156 Long-acting colloidal insulin formulation and its preparation FLAMEL TECH

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**



nano orange book patents

nanoparticulate TriCor (fenofibrate)

U.S. Patents:

7,875,630

7,820,788

7,741,374

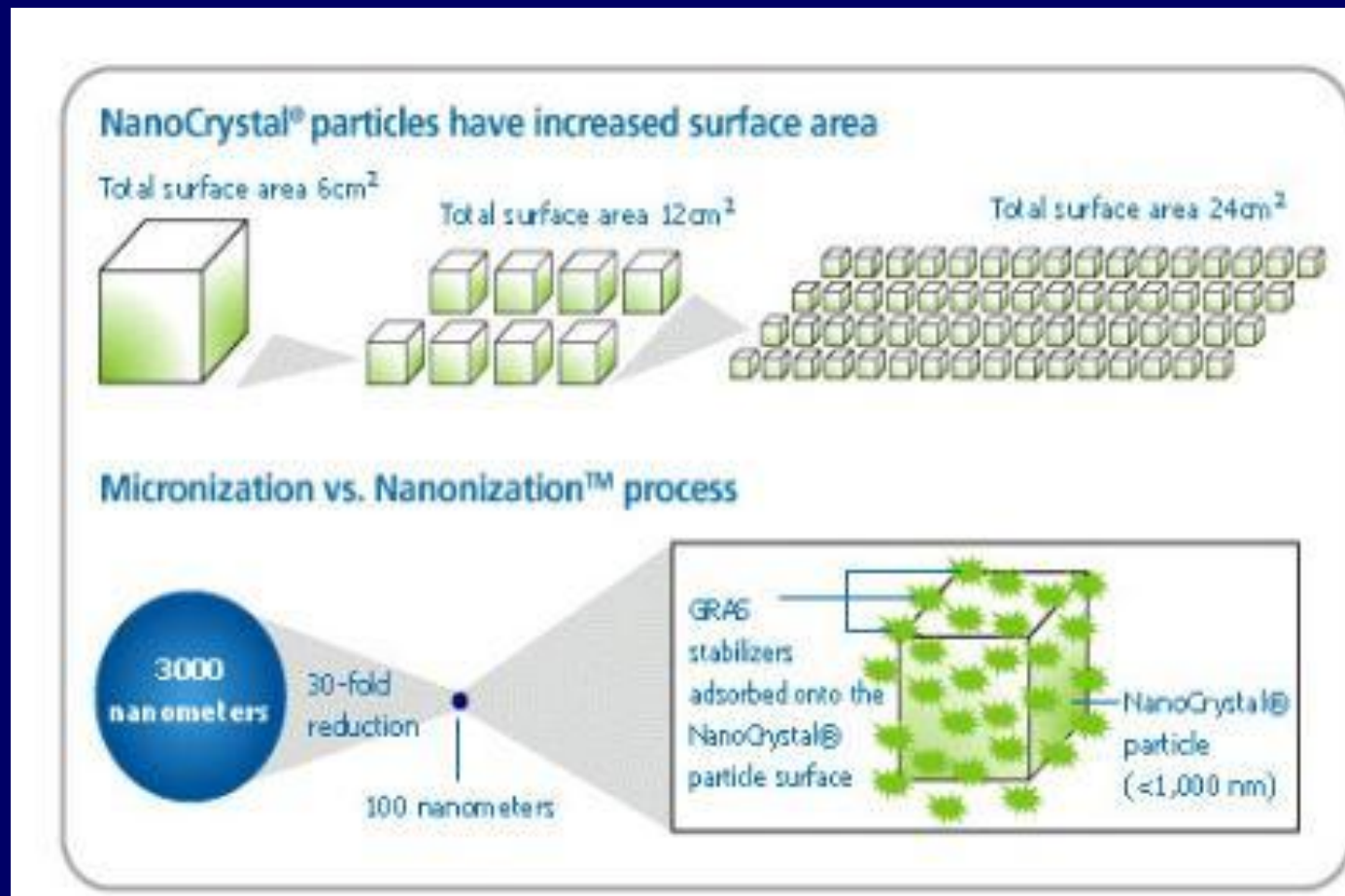
7,741,373

7,569,612

7,320,802

7,276,249

7,101,576



Top 10 Rx Drugs in 2010

Source : Thompson-Reuters

1. Lipitor (cholesterol)	Pfizer	\$11.7 Bil.
2. Plavix (anticoagulation)	Sanofi/BMS	\$9.6 Bil.
3. Advair (asthma/COPD)	GSK	\$9.0 Bil.
4. Remicade (arthritis)	Merck/J&J	\$7.4 Bil.
5. Enbrel (arthritis)	Pfizer/Amgen	\$7.1 Bil.
6. Humira (arthritis)	Abbott	\$6.8 Bil.
7. Avastin (cancer)	Roche	\$6.7 Bil.
8. Rituxan (cancer)	Roche	\$6.1 Bil.
9. Diovan (hypertension)	Novartis	\$6.0 Bil.
10. Crestor (cholesterol)	AstraZeneca	\$5.8 Bil.

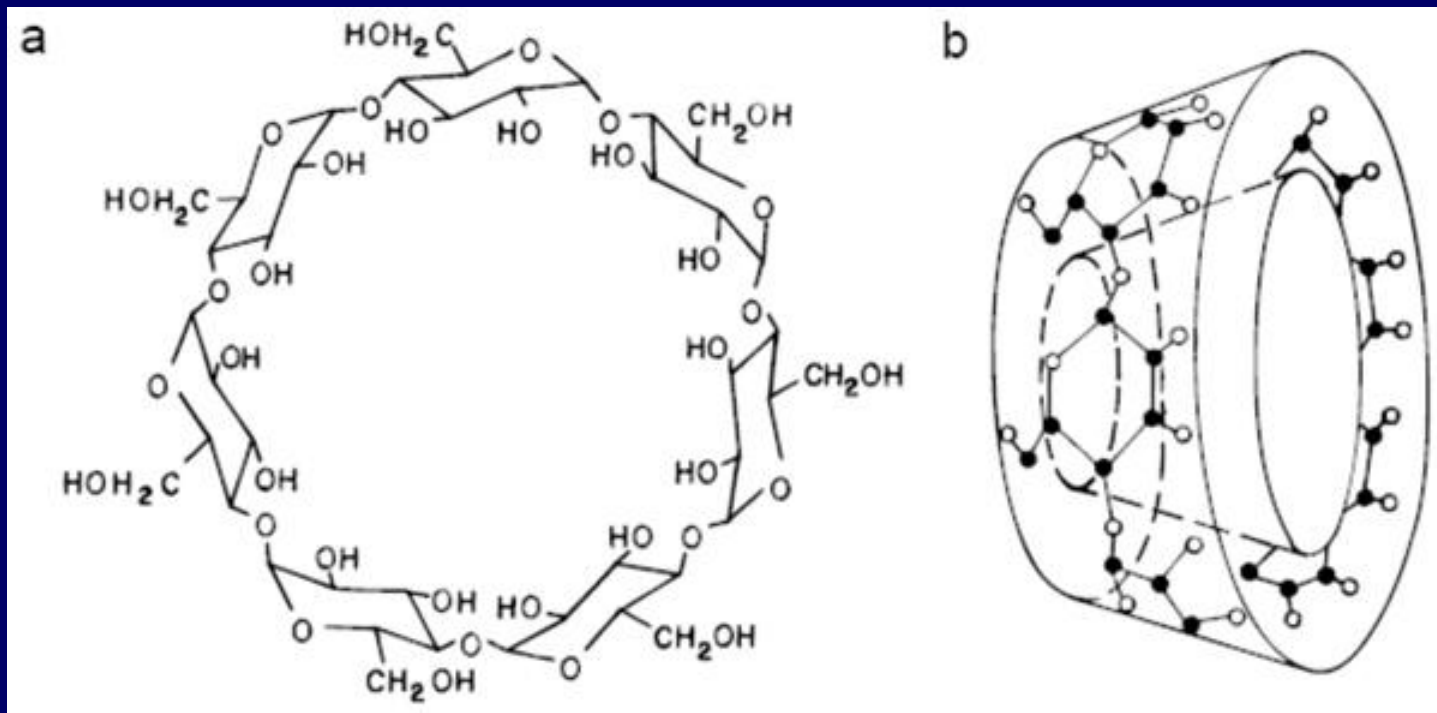
Nanomedicine Patenting by Big Pharma



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**



US20080255403A1

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

<u>US Pat No.</u>	<u>Title</u>	<u>Composition / Orange Book?</u>
6852746	Crystalline drug form	6-[(2,2-diphenylethyl)amino... / No
6548555	Basic drug compositions with enhanced bioavailability	(general structures) / No
6713461	Pharmaceutical complex	Eletriptan / No
6632803	Pharmaceutical formulations containing voriconazole (with cyclodextrin, lyophilized)	Voriconazole (Vfend – antifungal) / Yes (\$1 Bil) Lit!
6232304	Inclusion complexes of aryl-heterocyclic salts (with cyclodextrin)	Ziprasidone (Geodon/Zeldox - antipsychotic) / Yes (\$1 bil)

Nanoformulation “**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...)

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...

Current Nanomed Patent Litigation:

***Pfizer v. Vfend* U.S. Pat. No. 6632803**

**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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