

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

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# 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.**

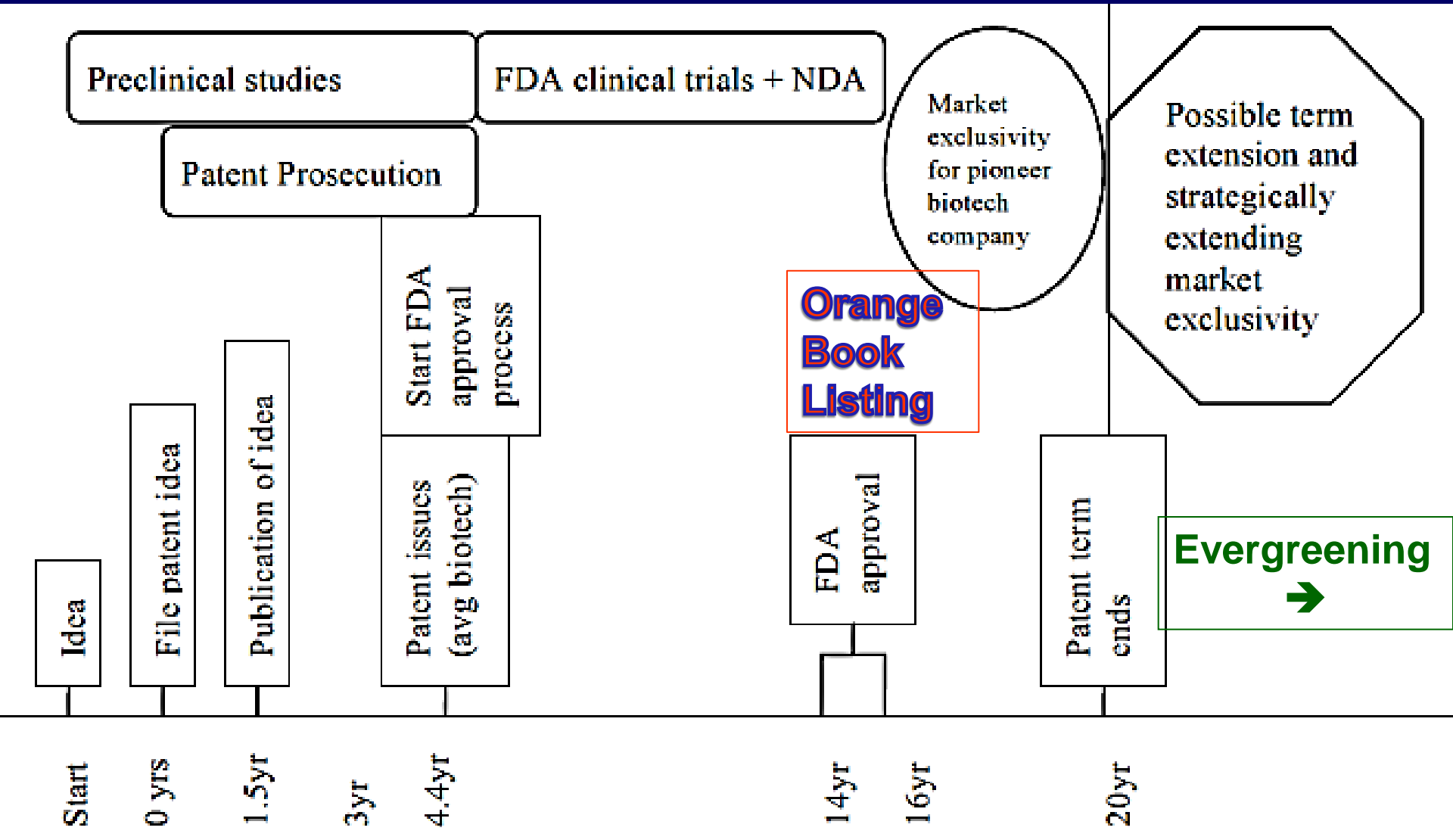


**Pfizer (Pantoprazole). Popular antacid.**

# 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 ?

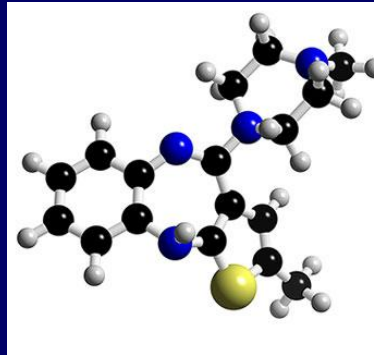


CONTROVERSY

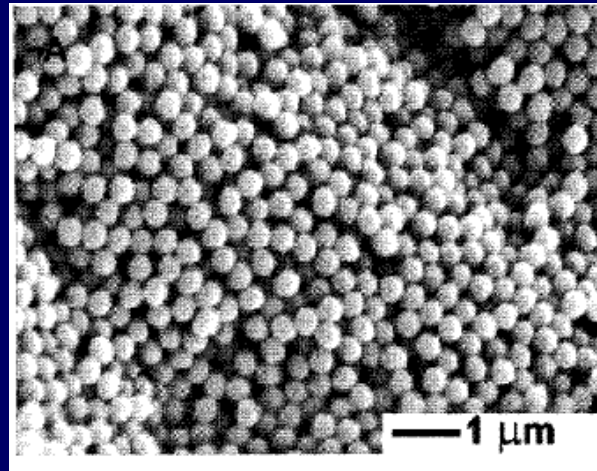
# Traditional Pharma: “Small Molecules”

**Olanzapine**

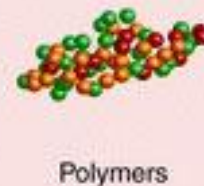
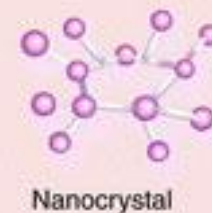
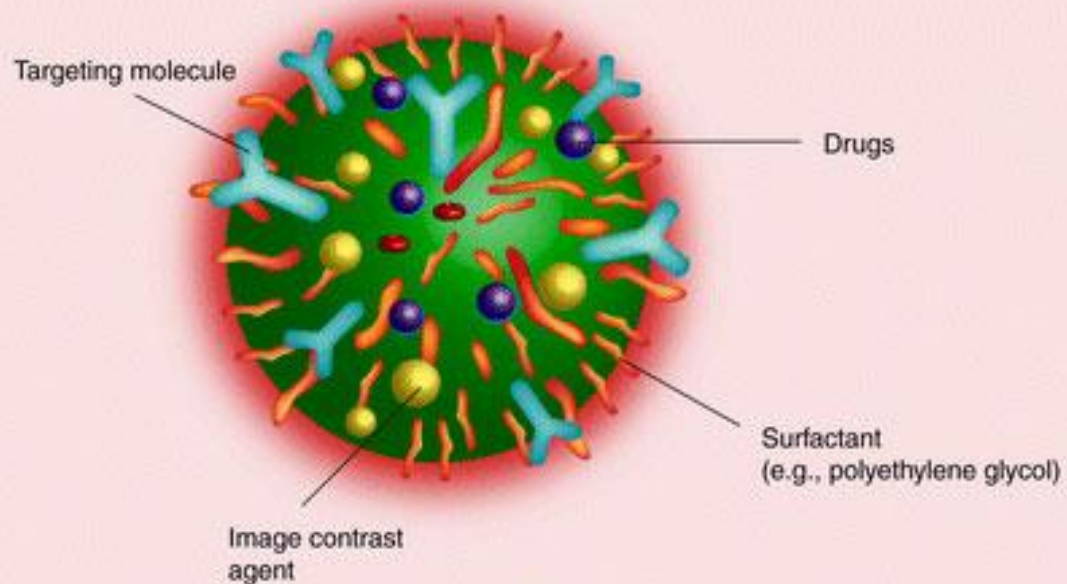
—— 1 nm



**NanoPharma: Nanoparticles of small molecules**

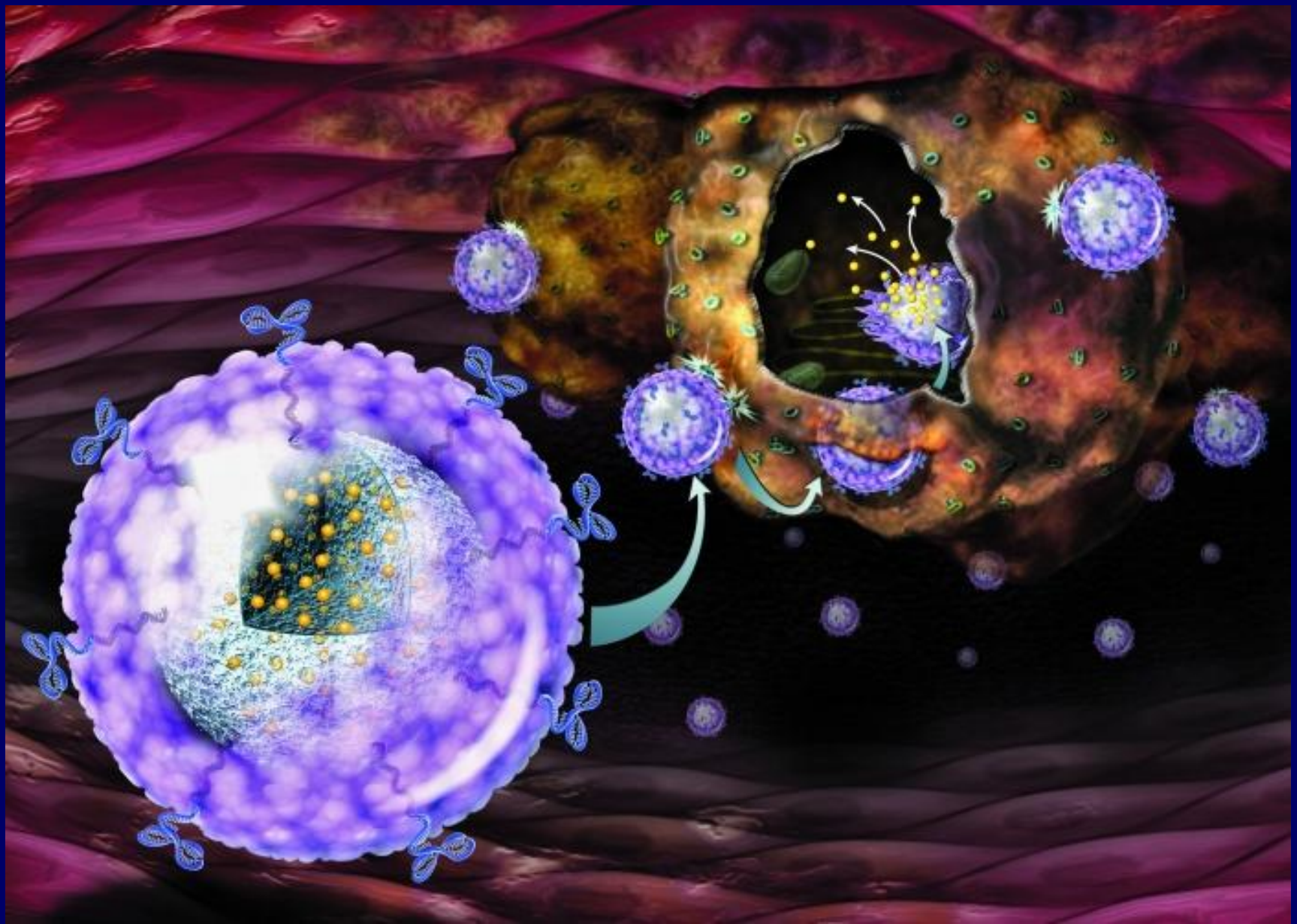


# Many ways to make medicine “nano”...





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

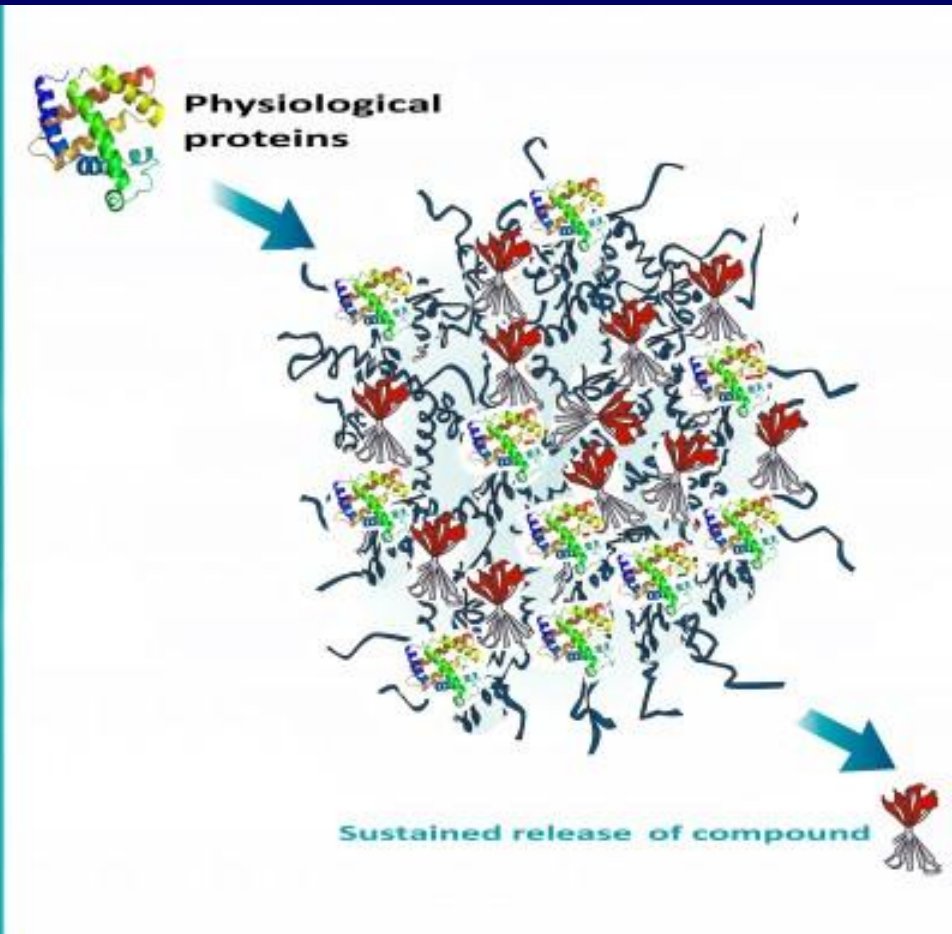
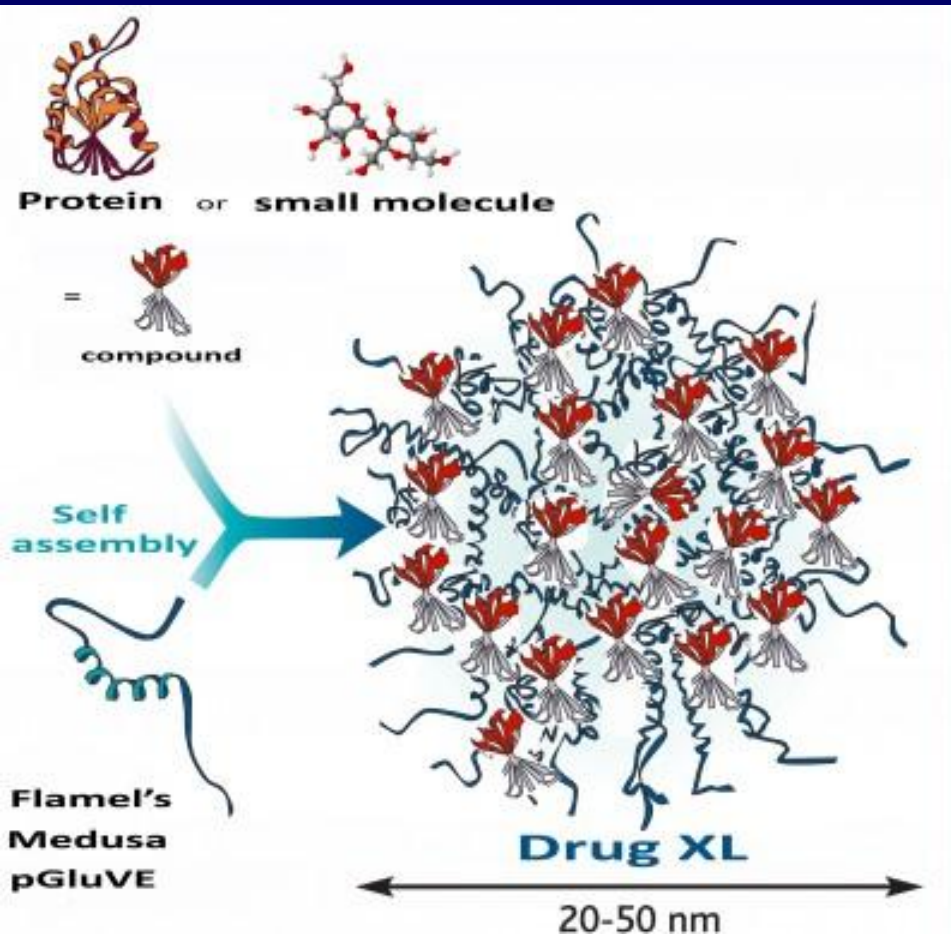
**US8003127 Nanoparticulate corticosteroid and antihistamine formulations methods of making, and methods of administering thereof** Elan Pharma International Limited

**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

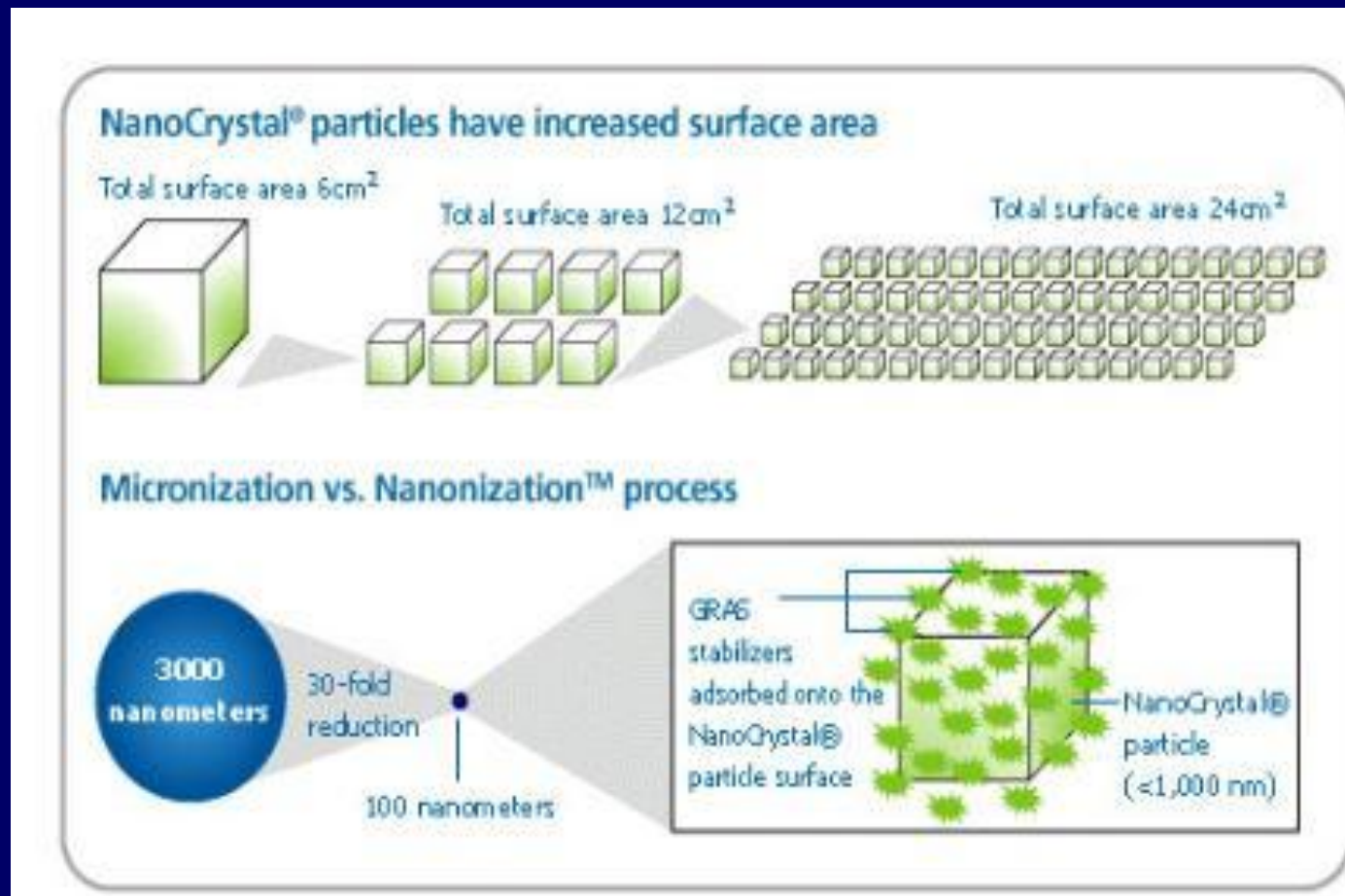
7,741,373

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 (anticlotting)	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

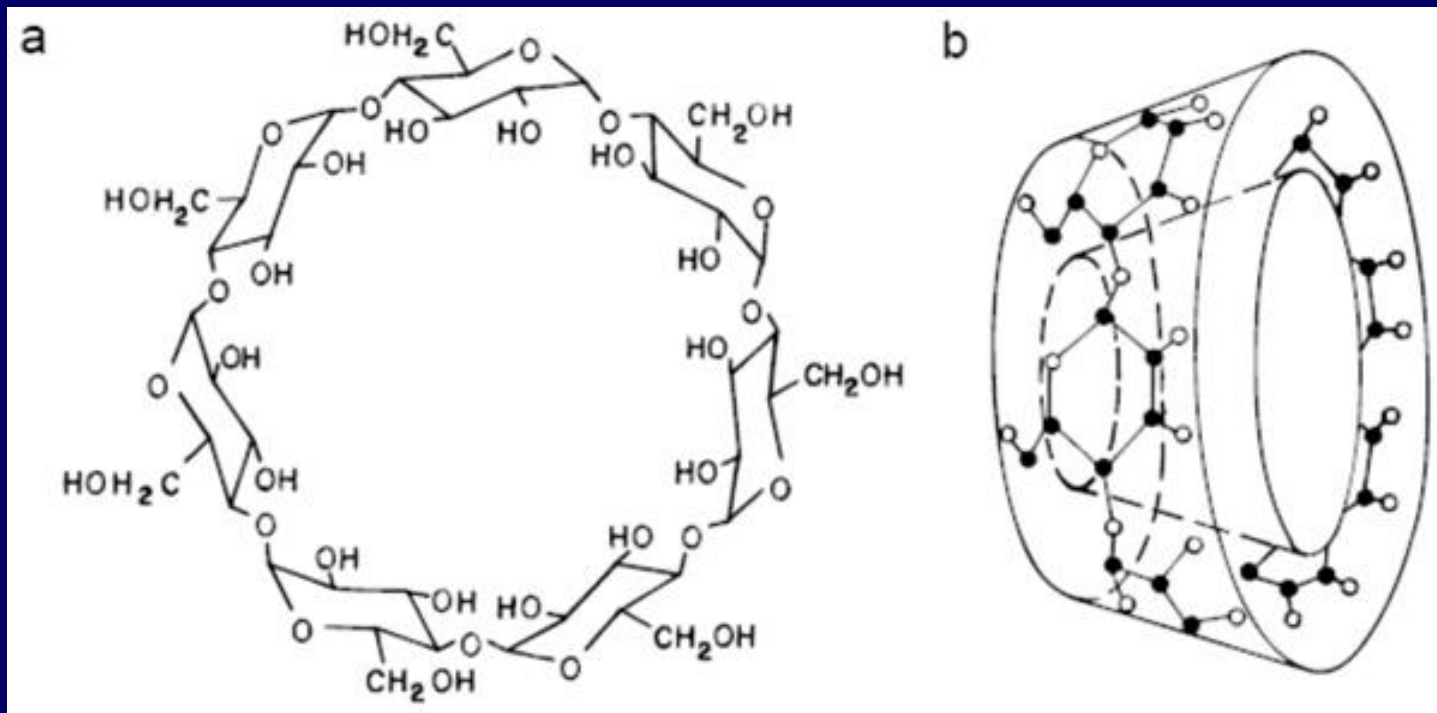


# Bristol Myers Squibb

- 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  $\beta$ -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... / <b>No</b>
6548555	Basic drug compositions with enhanced bioavailability	(general structures) / <b>No</b>
6713461	Pharmaceutical complex	Eletriptan / <b>No</b>
6632803	Pharmaceutical formulations containing voriconazole (with cyclodextrin, lyophilized)	Voriconazole (Vfend – antifungal) / <b>Yes (\$1 Bil) Lit!</b>
6232304	Inclusion complexes of aryl-heterocyclic salts (with cyclodextrin)	Ziprasidone (Geodon/Zeldox - antipsychotic) / <b>Yes (\$1 bil)</b>

# 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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