

# The Drug Industry:

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## *Pharmaceuticals and Biopharmaceuticals*

*Presenter*

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## Disclosure



- Prof. Poitras is a professor of Finance at Simon Fraser University in Vancouver, BC, Canada. He currently has a nominal common stock position in Pfizer and, in the past, has been a shareholder of Amgen.
  - Information in this presentation has been prepared from publicly available sources and is provided solely for educational purposes.
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# Agenda

- **Industry Analysis**

- Industry Structure, Market Leaders, Regulatory Bodies, Current Industry-wide Issues and Future Trends

- **Pfizer**

- Blockbusters going off patent

- **Amgen**

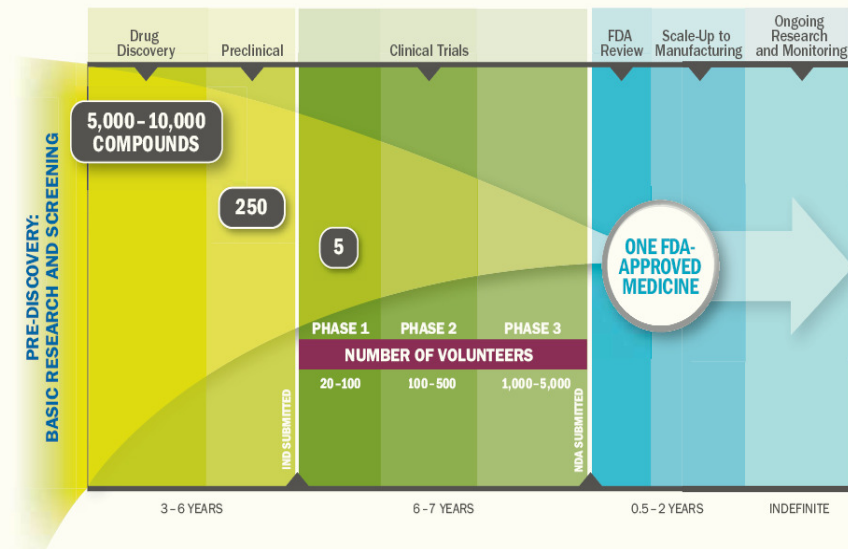
- Large Biotech vs. Big Cap Pharma

- **Onconova Therapeutics**

- Stage III setback implications for Startups
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# Current Industry Landscape

Figure 11: The Research and Development Process



- The 2013 *10-K* filing (p.7) for Pfizer observes about the biopharmaceutical industry (Figure from PhRMA, 2013 *Profile*):
- “Drug discovery and development is time-consuming, expensive and unpredictable ... out of 5,000-10,000 screened compounds, only 250 enter preclinical testing, five enter human clinical trials and one is approved by the FDA. The process from early discovery or design to development to regulatory approval can take more than 10 years. Drug candidates can fail at any stage of the process, and candidates may not receive regulatory approval even after many years of research.”

Increasing financial pressures leads to conflict with traditional 'patient centered' medical ethics and objectives

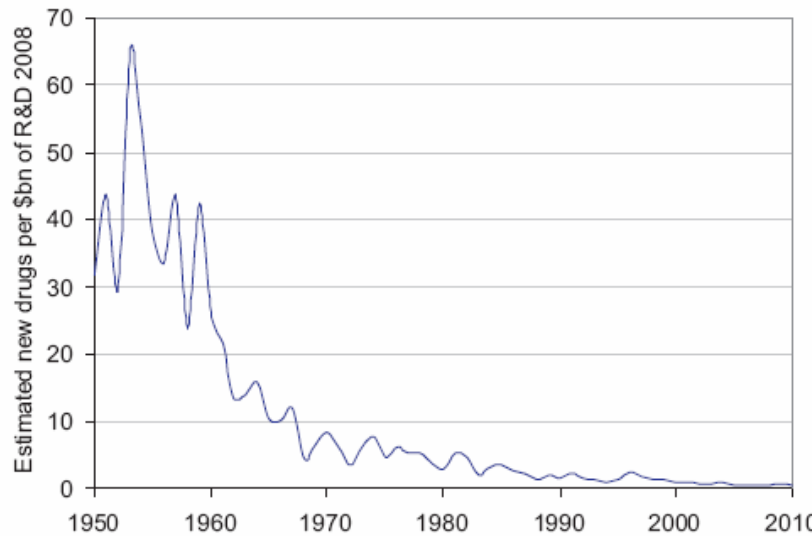


Figure 10: Biopharmaceutical Companies Continue to Invest Strongly in R&D



## ■ Serious Decline of R&D productivity

Sources: Gleadle et al. *Critical Perspectives in Accounting* (2014, p.69) using data from Scannell et al., *Nature: Review of Drug Discovery*, v11, n3.; Figure 10 from PhRMA, *Profile*

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# What Drug Industry?

- Different Sectors
    - Prescription Pharmaceutical
    - Prescription Biotechnology products
    - Established (off patent) biopharmaceuticals/pharmaceuticals
    - OTC Consumer Products
      - Commercial 'economics' differs across sectors
      - Current 'Big Cap' Pharma companies in most or all sectors
  
  - Difference between Biotech and Pharma
    - Variation in Definition
      - Industry Trade Association, the Pharmaceutical Research and Manufacturers of America (PhRMA), combines reference to pharmaceutical and biotechnology products as "biopharmaceuticals"
  
  - Different numbers and Types of Firms
    - Increasing prevalence of small firms in initial stage 'research'
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# Pharmaceuticals and Biotechnology

The 'Drug' Industry can be defined with reference to the regulatory framework. While 'drugs' and 'biologics' are distinguished for regulatory purposes (BLA vs. NDA), there is a blurring line between the commercial activities of biotech and pharmaceutical firms

Johnson & Johnson is **globally**: the sixth-largest consumer health company; the largest medical devices and diagnostics company; the fifth-largest biologics company; and, the eighth-largest pharmaceuticals company

Slides from HMS Webinar, *FDA: Historical Perspective and Overview*, Mar. 13, 2014, B-Elective. Rankings for J&J from company website.

## What is a drug?

- ❑ Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals
- ❑ Articles (other than food) intended to affect the structure or any function of the body of man or other animals
- ❑ Small, chemically-synthesized

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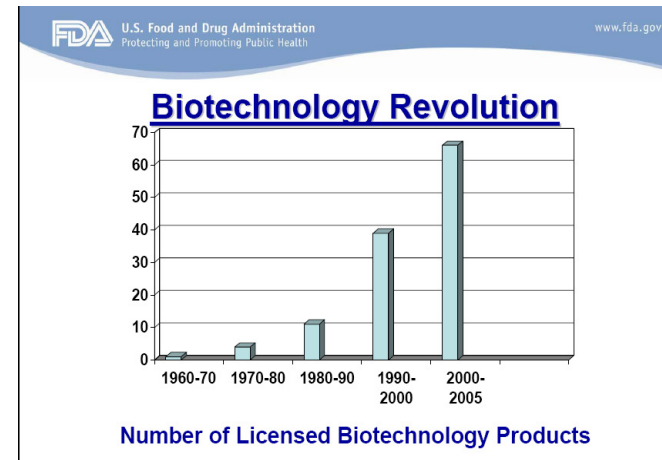
## What is a biologic?

- ❑ "Biological Product" – "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, ... applicable to the prevention, treatment, or cure of a disease or condition of human beings"

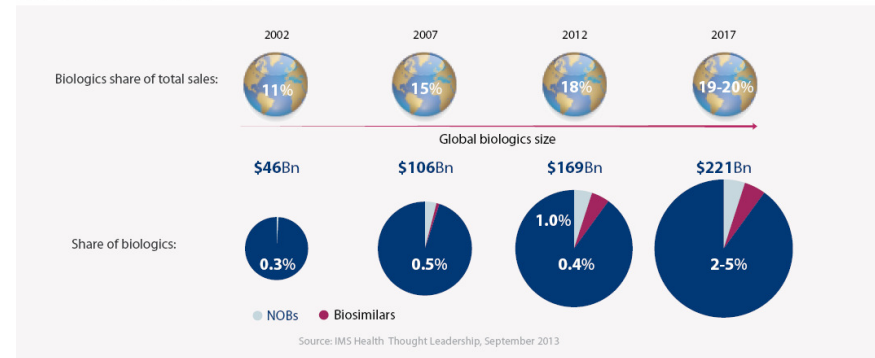
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# The Biopharmaceutical Industry?

- Opportunities in traditional 'small molecule', chemically synthesized pharmaceuticals diminishing relative to potential of 'large molecule' biologics
- Biologics Price Competition and Innovation Act (2010), a legal framework for the approval of 'bio-similars', provides 12 year exclusivity period



## The biologics market





# Top 'Pharma' Companies

Market Capitalization 2006 + 2013 (billions US\$)

Company (Ticker)	2006	2013 (rank)
		18/3/14
■ Pfizer (PFE-N)	\$182.15	\$202.4 (3)*
■ Johnson & Johnson (JNJ-N)	\$180.88	\$261.8 (1)
■ GlaxoSmithKlein (GSK-N)	\$141.87	\$131.8 (7)
■ Roche Holding (RHHBY-O)	\$135.28	\$250.8 (2)*
■ Novartis AG (NVS-N)	\$128.65	\$198.7 (4)*
■ Sanofi-Aventis (SNY-N)	\$122.80	\$132.4 (6)*
■ AstraZeneca (AZN-N)	\$ 75.70	\$ 81.8 (8)
■ Merck (MRK-N)	\$72.71	\$162.8 (5)*
■ Eli Lilly & Co. (LLY-N)	\$64.67	\$ 66.3 (9)
■ Wyeth (now PFE)	\$62.78*	
<i>Comparables</i>		
■ Bayer (BAYRY-O)		\$109.3
■ Amgen (AMGN-Q)		\$92.5

Note: Market Capitalization = (Stock Price) x Shares Outstanding; result varies over time due to changes in: market price, number of shares; and, M&A (\*)

Sources: Bloomberg; Globeinvestor; Yahoo Finance; Genetic Engineering & Biotechnology News

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# Significant Big Cap Pharma Consolidation

- Johnson and Johnson acquires Pfizer Consumer Health Care in 2006 (\$16.6 B)
    - Adds OTC products: Listerine, Benedryl, Bengay
  - AstraZeneca acquires MedImmune in 2007 (\$15.2 B)
    - Adds biologics: flu vaccines and anti-virals for infants
  - Pfizer purchases Wyeth in 2009 (\$68 B)
    - Adds OTC products: Advil and Robitussin
  - Roche Holdings fully acquires Genetech in 2009
    - Roche held a majority stake in Big Cap Biotech since 1990
  - Merck 'acquires' Schering-Plough in Nov. 2009 (\$41.3 B)
    - Adds OTC products: (Claritin, Dr. Scholl's, Coppertone); and, some pharmaceuticals
  - Novartis acquires Alcon in 2010 (\$39.3 B)
    - Adds prescription and OTC eyecare products
  - Sanofi-Aventis acquires Genzyme in 2011 (\$20.1 B)
    - Genzyme was third largest global biotechnology firm
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## Different Responses to the Landscape

- On Jan. 1, 2013 Abbott Labs (\$60 B; ABT-N) completed the 'spin off' of a new research based biopharmaceutical company AbbVie (\$85.1 B; ABBV-N) which has Humira, the 3<sup>rd</sup> highest in 2013 US sales of (bio)pharmaceuticals (\$10.7 B in global sales). Next largest revenue from AndroGel (\$1.03 B)
  - Bayer AG is a combination of Health Care (= Pharmaceuticals + Consumer Health) (€18.9B); Crop Science (€8.8B); and, Material Science (€11.2B). Pharma contains Kogenate and Betaferon with Levitra #12 in revenues. Consumer Health contains Contour, Advantage, Aspirin, Canesten and Aleve
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## Primarily Biotechnology Companies 2013

<b>Company</b>	<b>Market Capitalization</b> <u>3/20/14</u>	<b>Largest Seller(s)</b>
Novo Nordisk (NONOF-O)	\$123.4 B	Diabetes drugs
Gilead Sciences (GILD-Q)	\$116.1 B	HIV/AIDS
Amgen (AMGN-Q)	\$92.5 B	Enbrel
AbbVie (ABBV-N)	\$85.1 B	Humira
Celgene (CELG-Q)	\$60.9 B	Thalomid/Revlimid
Biogen Idec (BIIB-Q)	\$82.0 B	Rituxin
Merck KGaA (MKGAF-O)*	\$36.1 B	Erbix
CSL (CSL-AU)	\$34.4 B	Vaccines/Blood Prod.
Regeneron (REGN-Q)**	\$33.0 B	Eylea/Arcalyst

Source: Bloomberg; (\*) Merck KGaA is a German company, with a historical connection to US company Merck; (\*\*) Eylea is joint with Bayer AG.

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## Top-Selling Biopharmaceuticals, 2004 + 2013 (US Only)

	2004		2013
Lipitor (Pfizer)	\$7.7 B	Abilify (Otsuka Pharma.)	\$6,293 B
Zocor (Merck)	\$4.6 B	Nexium (AstraZeneca)	\$5,974 B
Prevacid (Abbott Labs)	\$3.8 B	Humira (AbbVie)	\$5,428 B
Nexium (AstraZeneca)	\$3.8 B	Crestor (AstraZeneca)	\$5,195 B
Procit (Ortho Biotech)	\$3.2 B	Cymbalta (Eli Lilly)	\$5,083 B
Zoloft (Pfizer)	\$3.1 B	Advair Diskus (GlaxoSK)	\$4,981 B
Epogen (Amgen)	\$3.0 B	Enbrel (Amgen)	\$4,585 B
Plavix (Bristol-Myers Sq.)	\$3.0 B	Remicade (Centocor OB)	\$3,980 B
Advair (GlaxoSmithKlein)	\$2.9 B	Copaxone (Teva Pharma)	\$3,603 B
Zyprexa (Eli-Lilly)	\$2.8 B	Neulasta (Amgen)	\$3,472 B

Source: IMS health and [www.drugs.com/stats/top100/2013/sales](http://www.drugs.com/stats/top100/2013/sales)

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## Therapeutic Class Sales Breakdown (2009 US Sales)

■ Oncologics	\$52.37 B
■ Lipid Regulators	\$35.28 B
■ Respiratory Agents	\$33.59 B
■ Anti-diabetics	\$30.40 B
■ Anti-ulcerants	\$29.61 B
■ Angiotensin II Antagonists	\$25.20 B
■ Anti-psychotics	\$23.24 B
■ Antidepressants	\$19.41 B
■ Autoimmune Agents	\$17.96 B
■ Platelet Aggr. Inhibitors	\$14.60 B
■ HIV Antivirals	\$13.75 B

Source: IMS Health and Fierce Biotech

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# Implications of the Baby Boom for Prescription Drug Demand

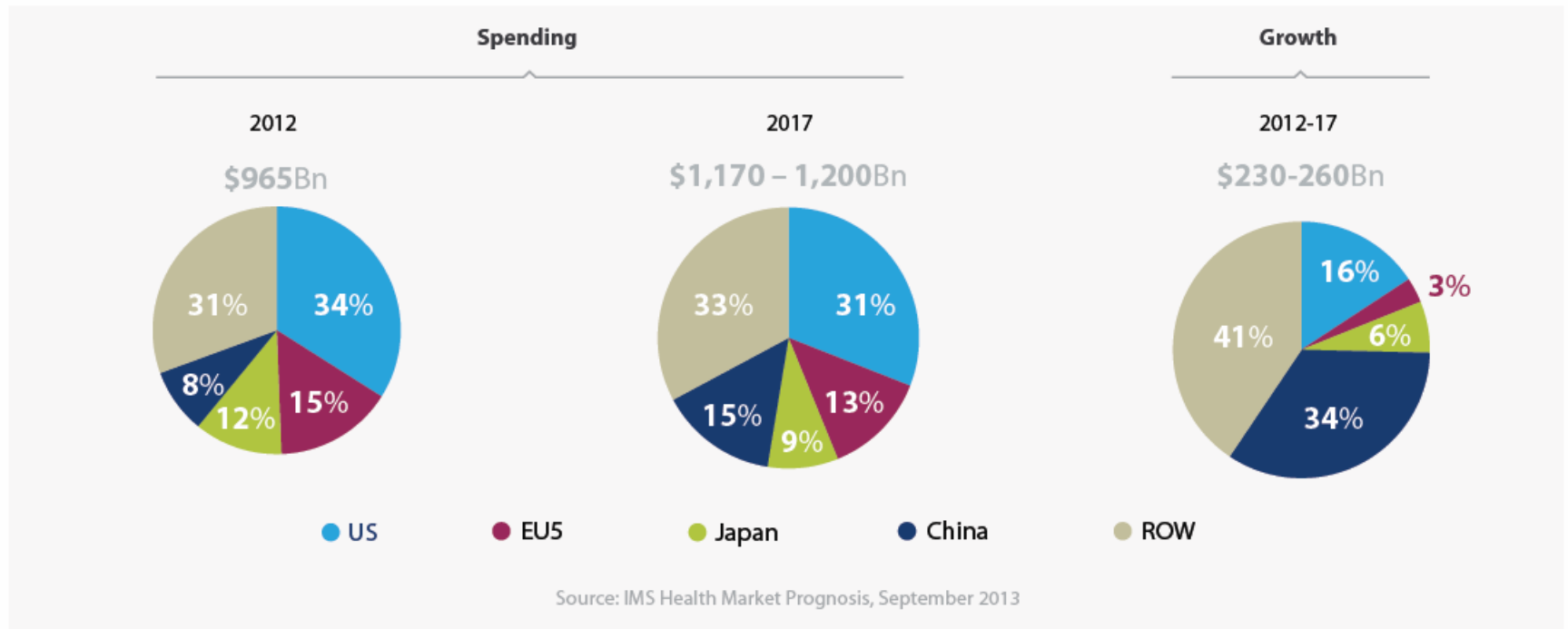
**Table 92 (page 2 of 3). Selected prescription drug classes used in the past 30 days, by sex and age: United States, selected years 1988–1994 through 2007–2010**

<i>Age group and Multum Lexicon Plus therapeutic class<sup>1</sup> (common indications for use)</i>	<i>Total</i>			<i>Male</i>			<i>Female</i>		
	<i>1988– 1994</i>	<i>1999– 2002</i>	<i>2007– 2010</i>	<i>1988– 1994</i>	<i>1999– 2002</i>	<i>2007– 2010</i>	<i>1988– 1994</i>	<i>1999– 2002</i>	<i>2007– 2010</i>
65 years and over									
Antihyperlipidemic agents (high cholesterol) . . . . .	5.9	23.4	46.7	5.3	24.3	53.0	6.4	22.7	41.8
Beta-adrenergic blocking agents (high blood pressure, heart disease) . . . . .	11.8	15.9	32.1	10.4	17.5	35.4	12.8	14.8	29.5
Diuretics (high blood pressure, heart disease, kidney disease) <sup>3</sup> . . . . .	16.2	19.2	22.5	12.2	17.1	22.4	19.1	20.7	22.6
ACE inhibitors (high blood pressure, heart disease) . . . .	9.5	16.9	21.9	9.8	18.0	26.3	9.3	16.1	18.5
Proton pump inhibitors or H2 antagonists (gastric reflux, ulcers) <sup>2</sup> . . . . .	7.5	14.6	21.5	7.2	14.1	20.7	7.7	15.0	22.0
Antidiabetic agents (diabetes) . . . . .	9.0	12.4	18.4	9.0	12.9	20.0	9.0	12.0	17.2
Anticoagulants or antiplatelet agents (blood clot prevention) <sup>5</sup> . . . . .	6.1	9.1	18.1	6.8	11.5	24.0	5.6	7.4	13.5
Analgesics (pain relief) . . . . .	13.8	18.4	17.5	11.4	15.0	17.1	15.6	20.9	17.8
Calcium channel blocking agents (high blood pressure, heart disease) . . . . .	16.1	19.1	17.0	14.5	17.4	16.8	17.3	20.4	17.3
Thyroid hormones (hypothyroidism) . . . . .	7.0	14.3	16.1	3.3	6.7	7.2	9.7	19.8	22.9
Antihypertensive combinations (high blood pressure) . . .	9.6	9.8	15.2	6.0	7.4	11.7	12.2	11.6	18.0
Antidepressants (depression and related disorders) . . . .	3.0	9.3	13.7	*2.3	7.2	9.4	3.5	10.8	17.0
Angiotensin II inhibitors (high blood pressure, heart disease) . . . . .	...	4.8	12.2	...	4.1	11.0	...	5.3	13.1
Antiarrhythmic agents (heart rhythm irregularities) . . . . .	23.1	16.6	11.1	21.6	17.9	12.6	24.3	15.6	9.9

Source: CDC, *Health, United States 2012*, Table 92; numbers in Table represent “percent of population with at least one prescription in the drug class in past 30 days”.

# Global Distribution of Sales

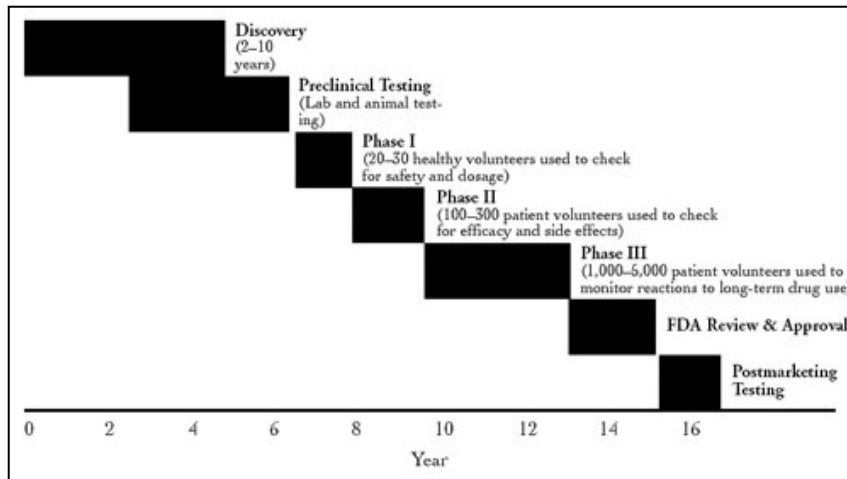
## Geographic distribution of medicine spending



Source: IMS Health



# New Drug Development



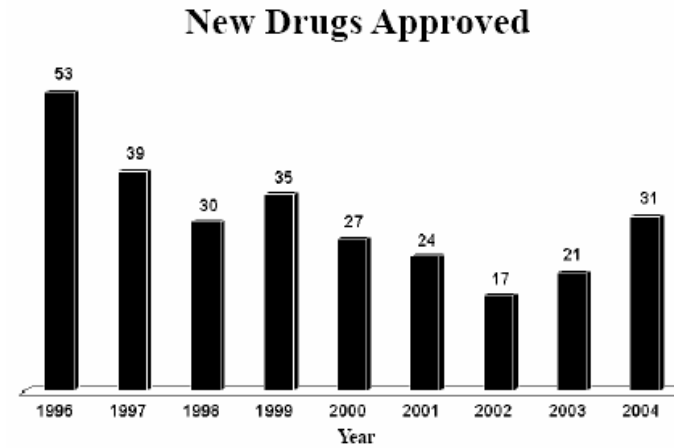
## Patent

- ◆ Generally last 20 years
- ◆ Since most companies file for patent during pre-clinical trials, usually the patent is only good for another 10 years or so after it gains FDA approval
- ◆ What can be patented
  - Product
  - Method
  - Use
- ◆ Examples
  - DNA and RNA sequences
  - Proteins, enzymes, antibiotics
  - Antibodies, antigens
  - Micro-organisms, cell lines, hybrids



- The FDA New Drug Approval Process from Pre-Clinical to Phase 4 discussed in 3-13-14 presentation

# New Drugs and Biologics Approval: New Drug Approvals and Biologics License Approvals



- Difficult to determine precisely the number of ‘new’ drugs and biologics
  - Essential sources from <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm>:
    - NDA and BLA Calendar Year Approvals
    - New Molecular Entity Drug and New Biologic Approvals
- Reporting system recognizes P (Priority, Significant improvement), S (Standard) and O (Orphan) status
  - In 2012, approvals for were:
    - 3P, 2 (P,O) and 1 S for biologics; 7P, 4 (P,O), 15S and 6 (S,O)

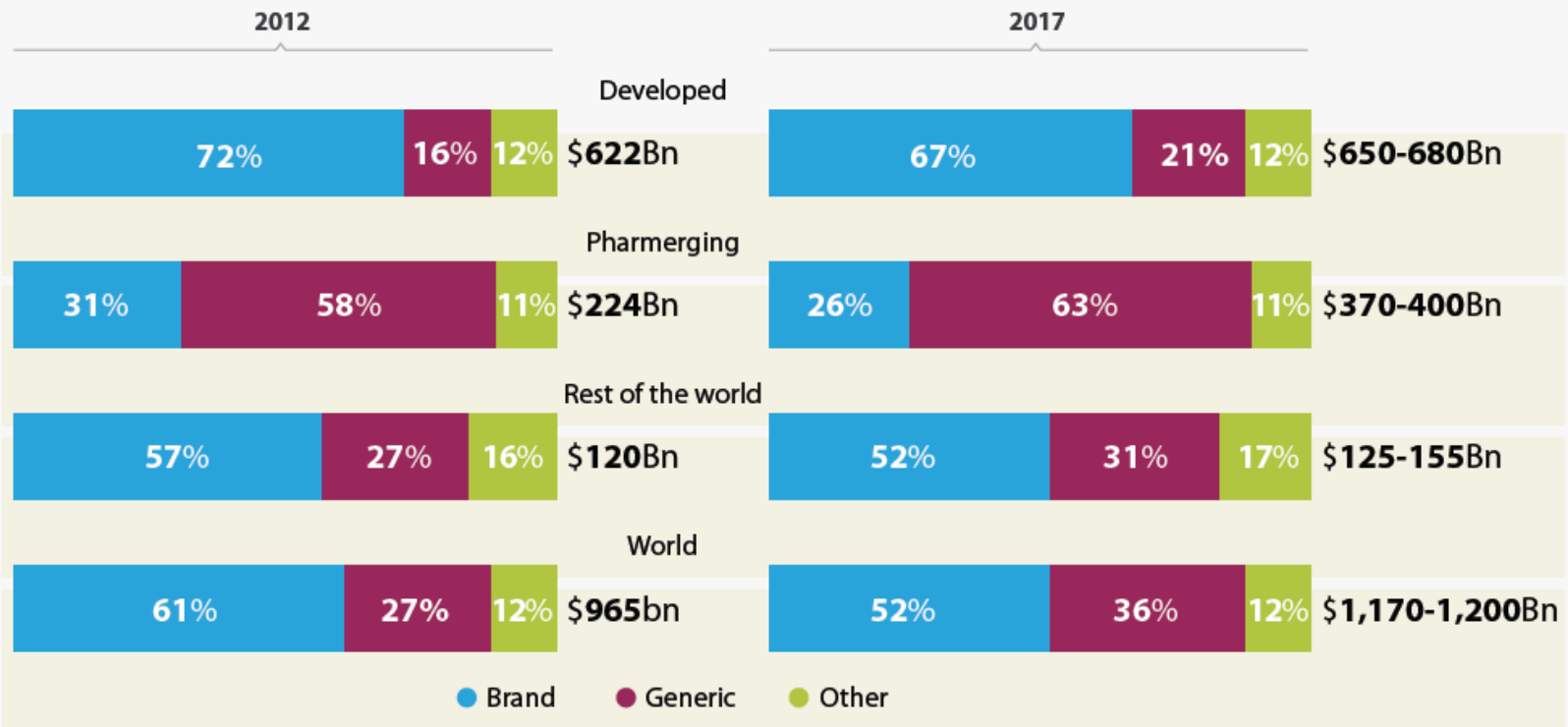
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# Costing the Clinical Process

- Difficult to provide exact estimate of total out-of-pocket expenses for an approved new molecule due to different therapeutic class distributions of biologics and traditional pharmaceuticals
    - Fewer safety issues with biologics due to replacement of substances in the body
  - Di Masi et al. (2003, *J. of Health Economics*) estimate R&D costs for new 'drugs' (including costs of failures and time costs) to \$800 M - \$1 B in 2000 dollars
    - Di Masi and Grabowski (2007) using a relatively small sample for R&D costs of new biologics found "total capitalized cost per approved molecule" to be "nearly the same" for biopharmaceuticals and pharmaceuticals.
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# Generic Drug Sales

## Global Spending, 2012 and 2017



Source: IMS Health Thought Leadership, September 2013

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# Patent Protection

- Drugs and Biologics may have several patents
  - Specific delivery method
  - Specific product/molecule
  - Specific manufacturing process
  - Specific medical indication
    - How molecules react
  - Specific Combination
    - Fixed dose/combination of several molecules

Source: [www.southcentre.org](http://www.southcentre.org)

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## Pfizer: Reacting to Patent Expiration



*We dedicate ourselves to humanity's quest for longer, healthier, happier lives through innovation in pharmaceutical, consumer and animal health products.*

- Circa 2005, Pfizer had the #1, #4 and #10 selling pharmaceuticals, Lipitor (LDL cholesterol control)(\$12+B global); Norvasc (Hypertension) (\$4.9 B global); Zoloft (Depression and anxiety) (\$3.3 B global) -- none in 2013
- How has Pfizer responded to an avalanche of patent expirations?

# Pfizer: Current Patent Expirations

## Major Recent Divestitures

- June 2013, Animal Health business (Zoetis), \$10.3 B gain
- Nov. 2012, sale of Nutrition business to Nestle, \$4.8 B gain

Drug	U.S. Basic Product Patent Expiration Year	Major EU Basic Product Patent Expiration Year	Japan Basic Product Patent Expiration Year
<i>Viagra</i>	2012 <sup>(1)</sup>	2013	2013 <sup>(1)</sup>
<i>Enbrel</i> <sup>(2)</sup>	N/A	2015	2015
<i>Celebrex</i>	2014 <sup>(3)</sup>	2014	2019
<i>Zyvox</i>	2015	2016	2019
<i>Lyrica</i>	2018	2014 <sup>(4)</sup>	2022
<i>Bosulif</i>	2019	2019	N/A <sup>(5)</sup>
<i>Chantix</i>	2020	2021	2022
<i>Inlyta</i>	2020	2020	2025
<i>Xeljanz</i>	2020	N/A <sup>(6)</sup>	2025
<i>Sutent</i>	2021	2021	2024
<i>Eliquis</i> <sup>(7)</sup>	2023	2026	2026
<i>Prevnar 13</i> <sup>(8)</sup>	2026	2026	2026
<i>Xalkori</i>	2029	2025	2028

## Compare 2011-13 Revenues with 2003-5 in the next slide

### Revenues—Major Biopharmaceutical Products

The following table provides revenue information for several of our major biopharmaceutical products:  
(MILLIONS OF DOLLARS)

PRODUCT	PRIMARY INDICATIONS	Year Ended December 31,		
		2013	2012	2011
Lyrica	Epilepsy, post-herpetic neuralgia and diabetic peripheral neuropathy, fibromyalgia and neuropathic pain due to spinal cord injury	\$ 4,595	\$ 4,158	\$ 3,693
Prevnar family	Vaccine for prevention of pneumococcal disease	3,974	4,117	4,145
Enbrel (Outside the U.S. and Canada)	Rheumatoid, juvenile rheumatoid and psoriatic arthritis, plaque psoriasis and ankylosing spondylitis	3,774	3,737	3,666
Celebrex	Arthritis pain and inflammation, acute pain	2,918	2,719	2,523
Lipitor	Reduction of LDL cholesterol	2,315	3,948	9,577
Viagra	Erectile dysfunction	1,881	2,051	1,981
Zyvox	Bacterial infections	1,353	1,345	1,283
Norvasc	Hypertension	1,229	1,349	1,445
Sutent	Advanced and/or metastatic renal cell carcinoma (mRCC), refractory gastrointestinal stromal tumors (GIST) and advanced pancreatic neuroendocrine tumor	1,204	1,236	1,187
Premarin family	Menopause	1,092	1,073	1,013
BeneFIX	Hemophilia	832	775	693
Vfend	Fungal infections	775	754	747
Genotropin	Replacement of human growth hormone	772	832	889
Pristiq	Depression	698	630	577
Chantix/Champix	An aid to smoking cessation treatment	648	670	720
Refacto AF/Xyntha	Hemophilia	602	584	506
Xalatan/Xalacom	Glaucoma and ocular hypertension	589	806	1,250
Detrol/Detrol LA	Overactive bladder	562	761	883
Zoloft	Depression and certain anxiety disorders	469	541	573



## Revenues — Major Human Health Products

(MILLIONS OF DOLLARS)		YEAR ENDED DEC. 31,			% CHANGE	
PRODUCT	PRIMARY INDICATIONS	2005	2004	2003	05/04	04/03
<b>Cardiovascular and metabolic diseases:</b>						
Lipitor	Reduction of LDL cholesterol	\$12,187	\$10,862	\$9,231	12	18
Norvasc	Hypertension	4,706	4,463	4,336	5	3
Cardura	Hypertension/Benign prostatic hyperplasia	586	628	594	(7)	6
Accupril/Accuretic	Hypertension/Congestive heart failure	294	665	706	(56)	(6)
Caduet	Reduction of LDL cholesterol and hypertension	185	50	—	272	—
<b>Central nervous system disorders:</b>						
Zoloft	Depression and certain anxiety disorders	3,256	3,361	3,118	(3)	8
Neurontin	Epilepsy and post-herpetic neuralgia	639	2,723	2,702	(77)	1
Geodon/Zeldox	Schizophrenia and acute manic or mixed episodes associated with bipolar disorder	589	467	353	26	32
Xanax/Xanax XR	Anxiety/Panic disorders	409	378	238	8	59
Aricept <sup>(a)</sup>	Alzheimer's disease	346	308	254	12	22
Lyrica	Epilepsy, post-herpetic neuralgia and diabetic peripheral neuropathy	291	13	—	M+	*
Relpax	Migraine headaches	233	169	85	38	99
<b>Arthritis and pain:</b>						
Celebrex <sup>(b)</sup>	Arthritis pain and inflammation, acute pain	1,730	3,302	1,883	(48)	75
Bextra <sup>(b)</sup>	Arthritis pain and inflammation	(61)	1,286	687	*	87
<b>Infectious and respiratory diseases:</b>						
Zithromax/Zmax	Bacterial infections	2,025	1,851	2,010	9	(8)
Zyvox	Bacterial infections	618	463	181	33	156
Diflucan	Fungal infections	498	945	1,176	(47)	(20)
Vfend	Fungal infections	397	287	200	38	44
<b>Urology:</b>						
Viagra	Erectile dysfunction	1,645	1,678	1,879	(2)	(11)
Detrol/Detrol LA	Overactive bladder	988	904	544	9	66
<b>Oncology:</b>						
Camptosar	Metastatic colorectal cancer	910	554	299	64	86
Ellence	Breast cancer	367	344	216	7	59
Aromasin	Breast cancer	247	143	58	73	145
<b>Ophthalmology:</b>						
Xalatan/Xalacom	Glaucoma and ocular hypertension	1,372	1,227	668	12	84
<b>Endocrine disorders:</b>						
Genotropin	Replacement of human growth hormone	808	736	481	10	53
<b>All other:</b>						
Zyrtec/Zyrtec-D	Allergies	1,362	1,287	1,338	6	(4)
<b>Alliance revenue<sup>(c)</sup></b>						
	Alzheimer's disease (Aricept), neovascular (wet) age-related macular degeneration (Macugen), Parkinson's disease (Mirapex), hypertension (Olmetec), multiple sclerosis (Rebif) and chronic obstructive pulmonary disease (Spiriva)	1,065	721	759	48	(5)

<sup>(a)</sup> Represents direct sales under license agreement with Eisai Co., Ltd.

<sup>(b)</sup> Includes direct sales under license agreement with Pharmacia prior to the acquisition.

<sup>(c)</sup> Includes alliance revenue for Celebrex and Bextra under co-promotion agreements with Pharmacia prior to the acquisition.

M+ Change greater than one-thousand percent.

\* Calculation not meaningful.

# Pfizer is reporting significant improvement in earnings

## Consolidated Statements of Income

Pfizer Inc. and Subsidiary Companies

(MILLIONS, EXCEPT PER COMMON SHARE DATA)	Year Ended December 31,		
	2013	2012	2011
Revenues	\$ 51,584	\$ 54,657	\$ 61,035
Costs and expenses:			
Cost of sales <sup>(a)</sup>	9,586	9,821	12,500
Selling, informational and administrative expenses <sup>(a)</sup>	14,355	15,171	17,581
Research and development expenses <sup>(a)</sup>	6,678	7,482	8,681
Amortization of intangible assets	4,599	5,109	5,465
Restructuring charges and certain acquisition-related costs	1,182	1,810	2,841
Other (income)/deductions—net	(532)	4,022	2,486
Income from continuing operations before provision for taxes on income	15,716	11,242	11,481
Provision for taxes on income	4,306	2,221	3,621
Income from continuing operations	11,410	9,021	7,860
Discontinued operations:			
Income from discontinued operations—net of tax	308	794	885
Gain on disposal of discontinued operations—net of tax	10,354	4,783	1,304
Discontinued operations—net of tax	10,662	5,577	2,189
Net income before allocation to noncontrolling interests	22,072	14,598	10,049
Less: Net income attributable to noncontrolling interests	69	28	40
Net income attributable to Pfizer Inc.	\$ 22,003	\$ 14,570	\$ 10,009
Earnings per common share—basic:			
Income from continuing operations attributable to Pfizer Inc. common shareholders	\$ 1.67	\$ 1.21	\$ 1.00
Discontinued operations—net of tax	1.56	0.75	0.28
Net income attributable to Pfizer Inc. common shareholders	\$ 3.23	\$ 1.96	\$ 1.28

## As Pfizer shrinks, funds expended on R&D also are falling

### Selling, Informational and Administrative (SI&A) Expenses

(MILLIONS OF DOLLARS)	Year Ended December 31,		
	2013	2012	2011
<i>Selling, informational and administrative expenses</i>	\$ 14,355	\$ 15,171	\$ 17,581
<i>As a percentage of Revenues</i>	27.8%	27.8%	28.8%

### Research and Development (R&D) Expenses

(MILLIONS OF DOLLARS)	Year Ended December 31,		
	2013	2012	2011
<i>Research and development expenses</i>	\$ 6,678	\$ 7,482	\$ 8,681
<i>As a percentage of Revenues</i>	12.9%	13.7%	14.2%

(MILLIONS OF DOLLARS)	R&D Expenses		
	Year Ended December 31,		
	2013	2012	2011
Primary Care <sup>(a)</sup>	\$ 969	\$ 1,009	\$ 1,307
Specialty Care and Oncology <sup>(a)</sup>	1,403	1,401	1,561
Established Products and Emerging Markets <sup>(a)</sup>	408	401	441
Consumer Healthcare <sup>(a), (b)</sup>	113	358	88
Worldwide Research and Development/Pfizer Medical <sup>(c)</sup>	2,821	2,839	3,337
Corporate and Other <sup>(d)</sup>	964	1,474	1,947
<i>Total Research and Development Expenses</i>	<i>\$ 6,678</i>	<i>\$ 7,482</i>	<i>\$ 8,681</i>

# Though earnings have increased, cash generated is flat to down

## Consolidated Statements of Cash Flows

Pfizer Inc. and Subsidiary Companies

(MILLIONS)	Year Ended December 31,		
	2013	2012	2011
<b>Operating Activities</b>			
Net income before allocation to noncontrolling interests	\$ 22,072	\$ 14,598	\$ 10,049
Adjustments to reconcile net income before allocation to noncontrolling interests to net cash provided by operating activities:			
Depreciation and amortization	6,410	7,655	9,026
Asset write-offs, impairments and related charges	1,368	1,299	1,198
Gain on disposal of discontinued operations	(10,446)	(7,123)	(1,688)
Gain associated with the transfer of certain product rights to an equity-method investment	(459)	—	—
Deferred taxes from continuing operations	1,726	786	236
Deferred taxes from discontinued operations	(23)	1,412	218
Share-based compensation expense	523	481	419
Benefit plan contributions (in excess of)/less than expense	310	135	(1,769)
Other non-cash adjustments, net	(324)	(130)	18
Other changes in assets and liabilities, net of acquisitions and divestitures:			
Accounts receivable	940	367	140
Inventories	(538)	(631)	1,084
Other assets	(822)	(434)	186
Accounts payable	382	579	(367)
Other liabilities	(3,184)	(2,738)	1,508
Other tax accounts, net	(170)	490	(18)
Net cash provided by operating activities	17,765	16,746	20,240

## Pfizer is spending on share buybacks facilitating option exercise

<u>Investing Activities</u>			
Purchases of property, plant and equipment	(1,206)	(1,327)	(1,660)
Purchases of short-term investments	(42,761)	(24,018)	(18,447)
Proceeds from redemptions and sales of short-term investments	41,127	25,302	14,176
Net (purchases of)/proceeds from redemptions and sales of short-term investments with original maturities of 90 days or less	(4,277)	1,459	10,874
Purchases of long-term investments	(11,020)	(11,145)	(4,620)
Proceeds from redemptions and sales of long-term investments	7,555	4,990	2,147
Acquisitions of businesses, net of cash acquired	(15)	(1,050)	(3,282)
Acquisitions of intangible assets	(259)	(92)	(222)
Proceeds from sale of businesses	—	11,850	2,376
Other investing activities	231	185	501
Net cash provided by/(used in) investing activities	(10,625)	6,154	1,843
<u>Financing Activities</u>			
Proceeds from short-term borrowings	4,323	7,995	12,810
Principal payments on short-term borrowings	(4,234)	(8,177)	(13,276)
Net proceeds from/(payments on) short-term borrowings with original maturities of 90 days or less	3,475	(30)	1,910
Proceeds from issuance of long-term debt <sup>(a)</sup>	6,618	—	—
Principal payments on long-term debt	(4,146)	(1,513)	(6,986)
Purchases of common stock	(16,290)	(8,228)	(9,000)
Cash dividends paid	(6,580)	(6,534)	(6,234)
Proceeds from exercise of stock options	1,750	568	153
Other financing activities	109	(80)	16
Net cash used in financing activities	(14,975)	(15,999)	(20,607)
Effect of exchange-rate changes on cash and cash equivalents	(63)	(2)	(29)
Net increase/(decrease) in cash and cash equivalents	(7,898)	6,899	1,447
Cash and cash equivalents, beginning	10,081	3,182	1,735
Cash and cash equivalents, end	\$ 2,183	\$ 10,081	\$ 3,182

# Amgen: Profile of a Large Cap Biotech



	2013	Change	2012	Change	2011
Neulasta®/NEUPOGEN®	\$ 5,790	8 %	\$ 5,352	3 %	\$ 5,212
ENBREL	4,551	7 %	4,236	14 %	3,701
Aranesp®	1,911	(6)%	2,040	(11)%	2,303
EPOGEN®	1,953	1 %	1,941	(5)%	2,040
XGEVA®	1,019	36 %	748	*	351
Prolia®	744	58 %	472	*	203
Sensipar®/Mimpara®	1,089	15 %	950	18 %	808
Other products	1,135	26 %	900	33 %	677
<b>Total product sales</b>	<b>\$ 18,192</b>	<b>9 %</b>	<b>\$ 16,639</b>	<b>9 %</b>	<b>\$ 15,295</b>
Total U.S.	\$ 14,045	10 %	\$ 12,815	9 %	\$ 11,725
Total ROW	4,147	8 %	3,824	7 %	3,570
<b>Total product sales</b>	<b>\$ 18,192</b>	<b>9 %</b>	<b>\$ 16,639</b>	<b>9 %</b>	<b>\$ 15,295</b>

Much lower ratio of SGA to R&D than PFE; less erosion of revenues from biologics due to appearance of bio-similars

<u>Consolidated Statement of Income Data:</u>	Years ended December 31,				
	2013	2012 <sup>(1)</sup>	2011 <sup>(1)</sup>	2010 <sup>(1)</sup>	2009 <sup>(1)</sup>
	(In millions, except per share data)				
<b>Revenues:</b>					
Product sales	\$ 18,192	\$ 16,639	\$ 15,295	\$ 14,660	\$ 14,351
Other revenues	484	626	287	393	291
Total revenues	18,676	17,265	15,582	15,053	14,642
<b>Operating expenses:</b>					
Cost of sales	3,346	3,199	2,708	2,501	2,372
Research and development	4,083	3,380	3,167	2,894	2,864
Selling, general and administrative	5,184	4,814	4,499	3,996	3,833
Other <sup>(2)</sup>	196	295	896	117	67
Net income	5,081	4,345	3,683	4,627	4,605
Diluted earnings per share	6.64	5.52	4.04	4.79	4.51
Dividends paid per share	1.88	1.44	0.56	—	—

	2013	Change	2012
<b>Product sales:</b>			
U.S.	\$ 14,045	10 %	\$ 12,815
ROW	4,147	8 %	3,824
Total product sales	18,192	9 %	16,639

# Cash generated by the business is growing

**AMGEN INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
**Years ended December 31, 2013, 2012 and 2011**  
**(In millions)**

	2013	2012	2011
<b>Cash flows from operating activities:</b>			
Net income	\$ 5,081	\$ 4,345	\$ 3,683
Depreciation and amortization	1,286	1,088	1,060
Stock-based compensation expense	403	362	341
Deferred income taxes	(189)	28	(328)
Property, plant and equipment impairments	19	178	6
Other items, net	84	(74)	63
<b>Changes in operating assets and liabilities, net of acquisitions:</b>			
Trade receivables, net	(38)	348	(557)
Inventories	(7)	(150)	(383)
Other assets	(59)	124	(204)
Accounts payable	(184)	161	(95)
Accrued income taxes	(326)	87	(20)
Legal reserve	—	(780)	780
Other liabilities	221	165	773
Net cash provided by operating activities	6,291	5,882	5,119



Unlike PFE, Amgen is issuing debt and paying more than cash from operations in acquiring new products

Cash flows from investing activities:			
Purchases of property, plant and equipment	(693)	(689)	(567)
Cash paid for acquisitions, net of cash acquired	(9,434)	(2,390)	(701)
Purchases of marketable securities	(21,965)	(26,241)	(21,183)
Proceeds from sales of marketable securities	19,123	17,372	20,871
Proceeds from maturities of marketable securities	5,090	1,994	749
Change in restricted investments, net	(520)	—	—
Other	(70)	(36)	45
Net cash used in investing activities	(8,469)	(9,990)	(786)
Cash flows from financing activities:			
Net proceeds from issuance of debt	8,054	4,933	10,387
Repayment of debt	(3,371)	(123)	(2,500)
Net proceeds from issuance of commercial paper	—	—	762
Repayments of commercial paper	—	—	(762)
Repurchases of common stock	(832)	(4,607)	(8,315)
Dividends paid	(1,415)	(1,118)	(500)
Net proceeds from issuance of common stock in connection with the Company's equity award programs	296	1,288	242
Other	(6)	46	12
Net cash provided by (used in) financing activities	2,726	419	(674)
Increase (decrease) in cash and cash equivalents	548	(3,689)	3,659
Cash and cash equivalents at beginning of period	3,257	6,946	3,287
Cash and cash equivalents at end of period	\$ 3,805	\$ 3,257	\$ 6,946

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Many of the 2900+ compounds and molecules currently under study are being examined by startups with no product revenues – ‘cash burn’ operations



- Onconova Therapeutics 10-K describes the situation:
    - ***We have incurred significant losses since our inception and anticipate that we will continue to incur losses in the future***
    - ***We currently have no source of product revenue and may never become profitable.***
    - ***We are likely to require additional capital to fund our operations and if we fail to obtain necessary financing, we may be unable to complete the development and potential commercialization of our product candidates.***
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# Onconova Therapeutics (ONTX-Q): The Hazards of Initial Public Offering for Late Stage 'Cash Burn' Biotechnology

ONTX		Onconova Therapeutics Inc. (NASDAQ)		Delayed quote data		3/21/2014 04:00 PM	
Last:	Change:	Open:	High:	Low:	Volume:		
<b>7.12</b>	<span style="color: red;">▼</span> -0.26	7.45	7.45	7.10	260,791		
	Percent Change:	Yield:	P/E Ratio:	52 Week Range:			
	-3.52%	n/a	n/a	7.02 to 31.13			
After Hours Trading		Last:	Change:	Volume:			
3/21/2014 04:53 PM		7.12	<span style="color: blue;">■</span> n/a	5,731			



The company has only one product at an advanced clinical stage *Rigosertib*, being tested for myelodysplastic syndromes, or MDS, and head and neck cancers. ONTX is testing both intravenous and oral formulations of rigosertib, referred to as rigosertib IV (at Phase III) and rigosertib Oral, at Stage II.



## Some Startup IPO Accounting, the Revenue in 2012 and 2013 is from a commercialization agreement with Baxter

### Consolidated Statements of Operations

	Years ended December 31,		
	2013	2012	2011
Revenue	\$ 4,753,000	\$ 46,190,000	\$ 1,487,000
Operating expenses:			
General and administrative	16,793,000	15,707,000	6,436,000
Research and development	50,182,000	52,762,000	22,624,000
Total operating expenses	66,975,000	68,469,000	29,060,000
Loss from operations	(62,222,000)	(22,279,000)	(27,573,000)
Change in fair value of warrant liability	42,000	367,000	1,287,000
Interest expense	(4,000)	(8,608,000)	(19,000)
Other income, net	63,000	608,000	11,000
Net loss before income taxes	(62,121,000)	(29,912,000)	(26,294,000)
Income taxes	435,000	—	—
Net loss	(62,556,000)	(29,912,000)	(26,294,000)
Net loss attributable to non-controlling interest	13,000	—	—
Net loss attributable to Onconova Therapeutics, Inc	(62,543,000)	(29,912,000)	(26,294,000)
Accretion of redeemable convertible preferred stock	(2,320,000)	(3,953,000)	(4,020,000)
Net loss applicable to common stockholders	\$ (64,863,000)	\$ (33,865,000)	\$ (30,314,000)
Net loss per share of common stock, basic and diluted	\$ (6.12)	\$ (15.35)	\$ (14.18)
Basic and diluted weighted average shares outstanding	10,594,227	2,206,888	2,137,403

Onconova common stock began trade on NASDAQ July 25, 2013 under the symbol "ONTX." Prior to that time, the company was privately held. The IPO priced at \$15.00 per share.

### Consolidated Statements of Cash Flows

	Year Ended December 31,		
	2013	2012	2011
<b>Operating activities:</b>			
Net loss	\$(62,556,000)	\$(29,912,000)	\$(26,294,000)
Adjustment to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation and amortization	446,000	319,000	316,000
Loss on asset disposal	—	3,000	—
Amortization of deferred financing fees	—	15,000	21,000
Amortization of debt discount	—	8,176,000	—
Change in fair value of warrant liabilities	(42,000)	(367,000)	(1,287,000)
Treasury note discount amortization	(4,000)	—	—
Stock compensation expense	8,015,000	13,844,000	6,000
Changes in assets and liabilities:			
Grants receivable	—	78,000	1,730,000
Prepaid expenses and other current assets	(2,662,000)	(1,098,000)	253,000
Other assets	—	(15,000)	—
Accounts payable	(1,807,000)	(97,000)	2,230,000
Accrued expenses	1,894,000	2,573,000	1,123,000
Other liabilities	(37,000)	(41,000)	58,000
Deferred revenue	(4,631,000)	8,155,000	7,673,000
<b>Net cash (used in) provided by operating activities</b>	<b>\$(61,384,000)</b>	<b>1,633,000</b>	<b>(14,171,000)</b>

The initial public offering of 5,941,667 shares of the Company's common stock, at \$15.00 per share resulted in net proceeds of \$79,811,000. The balance sheet reveals about \$100 million in liquid assets.

Investing activities:			
Payments for purchase of property and equipment	(609,000)	(279,000)	(256,000)
Security deposits	—	—	15,000
Purchases of marketable securities	(39,990,000)	—	—
Net cash used in investing activities	(40,599,000)	(279,000)	(241,000)
Financing activities:			
Proceeds from initial public offering of common stock, net of issuance costs	79,811,000	—	—
Proceeds from the exercise of stock options	157,000	165,000	154,000
Contribution from non-controlling interest	500,000	—	—
Reverse stock split cash paid in lieu of fractional shares	(4,000)	—	—
Proceeds from stockholder in connection with settlement of stock option exercises	—	3,943,000	—
Settlement of stock options	—	(2,835,000)	—
Proceeds from the exercise of warrants	—	2,167,000	1,918,000
Proceeds from the sale of Series H preferred stock	—	400,000	7,218,000
Proceeds from the sale of Series J preferred stock	—	47,796,000	—
Repayments of long-term debt	—	—	(917,000)
Release of cash restricted for debt repayment	—	—	792,000
Proceeds from stockholder loan and convertible debt	—	25,824,000	620,000
Net cash provided by financing activities	80,464,000	77,460,000	9,785,000
Effect of foreign currency translation on cash	1,000	—	—
Net (decrease) increase in cash and cash equivalents	(21,518,000)	78,814,000	(4,627,000)
Cash and cash equivalents at beginning of period	81,527,000	2,713,000	7,340,000
Cash and cash equivalents at end of period	<u>\$ 60,009,000</u>	<u>\$ 81,527,000</u>	<u>\$ 2,713,000</u>

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# Thank you for listening

More info about presenter at

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## QUESTIONS?