The Drug Industry:

Pharmaceuticals and Biopharmaceuticals

Presenter

Prof. Geoffrey Poitras

Simon Fraser University

Vancouver, BC

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Disclosure

SIMON FRASER UNIVERSITY
VANCOUVER, CANADA

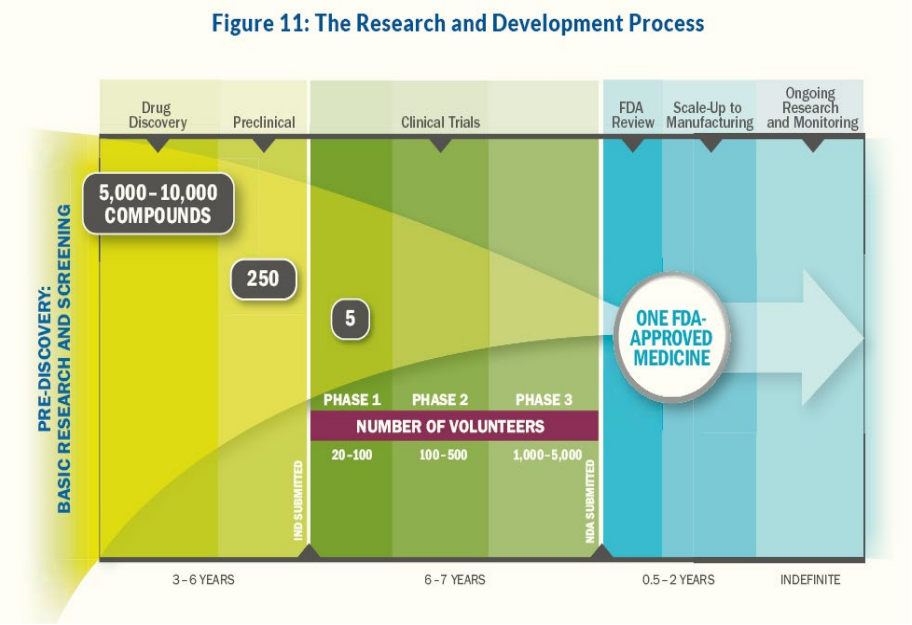
- Geoffrey Poitras is a Professor of Finance at Simon Fraser University in Vancouver, BC, Canada. He currently has a nominal common stock position in Pfizer, Viatris and Novo Nordisk, and in the past has been a shareholder of Amgen.

- Information in this presentation has been prepared from publicly available sources and is provided solely for educational purposes.

Agenda

- Industry Analysis
  - Industry Structure, Market Leaders, M&A, Regulatory Bodies, Current Industry-wide Issues and Future Trends
- Company Developments
  - **Pfizer**
    - Pharma Blockbusters going off patent
    - Vaccine Profitability
  - **Amgen**
    - Large Biotech vs. Traditional Big Cap Pharma
  - **Zogenix, Moderna and Novavax**
    - Stages II, III and EUA/CMA results for Vaccine Startups
  - **Valeant Pharmaceuticals, Purdue Pharma and SPACs**
    - Controlling Bad Actors?

Current Industry Landscape



- 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."

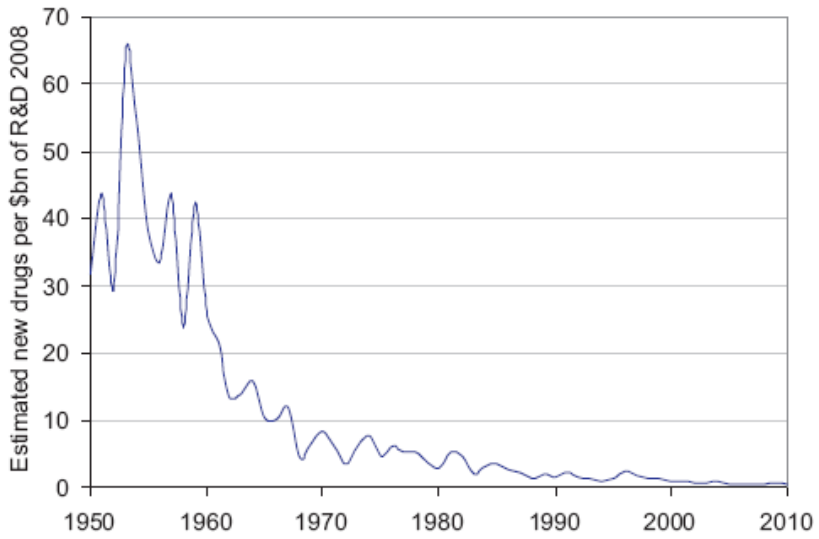
The **2017** *10-K* filing (p.4) for Pfizer changes this observation somewhat because the R&D data has also changed:

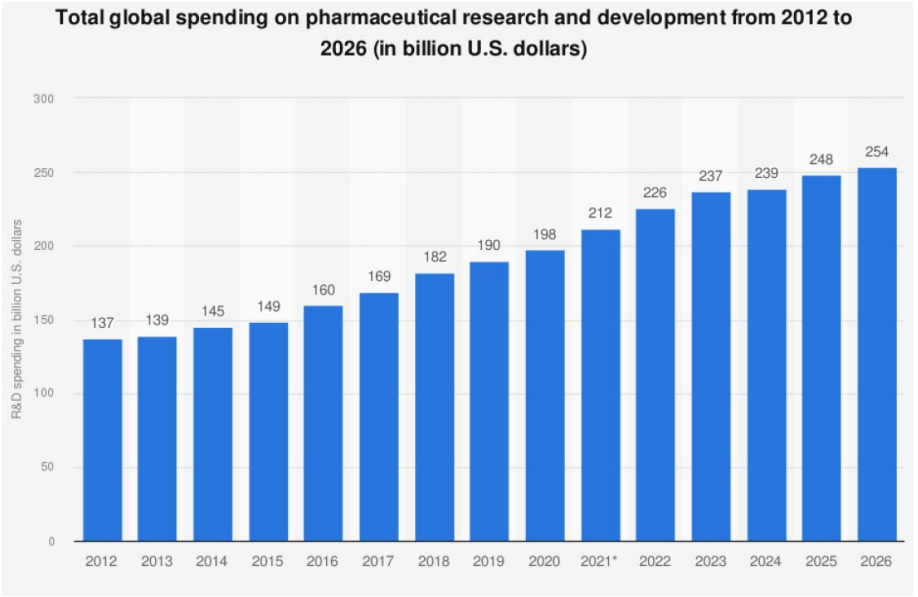
… out of 17 compounds entering preclinical development, on average, only one is approved by a regulatory authority in a major market ... The process from early discovery or design to development to regulatory approval can take more than ten years. Drug candidates can fail at any stage of the process and candidates may not receive regulatory approval even after many years of research and development

Development of a single compound is often pursued as part of multiple programs. While these drug candidates may or may not eventually receive regulatory approval … In addition to discovering and developing new products, our R&D efforts seek to add value to our existing products by improving their effectiveness, enhancing ease of dosing and by discovering potential new indications for them.

Similar statement does not appear in 2020 10-K only: “The discovery and development for drugs and biological products are time-consuming, costly and unpredictable.”

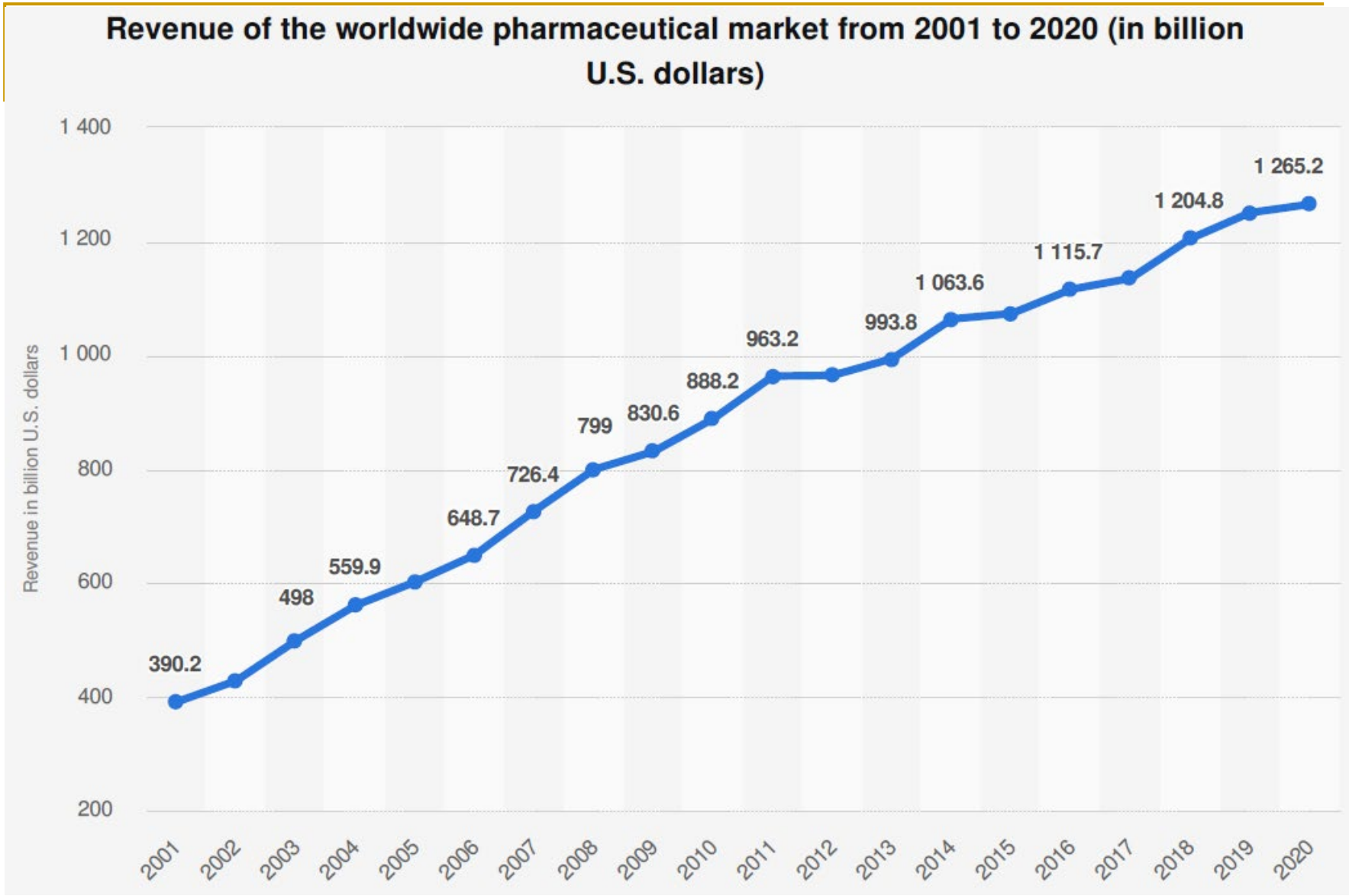
Increasing financial pressures leads to conflict with traditional 'patient centered' medical ethics and objectives





- Serious Decline of R&D productivity
  - Shifting of early-stage research costs to start-ups

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*



Source: Statista

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 are global and in most or all sectors
- Difference between Biotech and Pharma
  - Variation in Definition
    - US Industry Trade Association, the Pharmaceutical Research and Manufacturers of America (PhRMA), combines reference to pharmaceutical and biotechology products as "biopharmaceuticals"
- Different numbers and Types of Firms
  - Increasing prevalence of small firms in initial stage 'research'

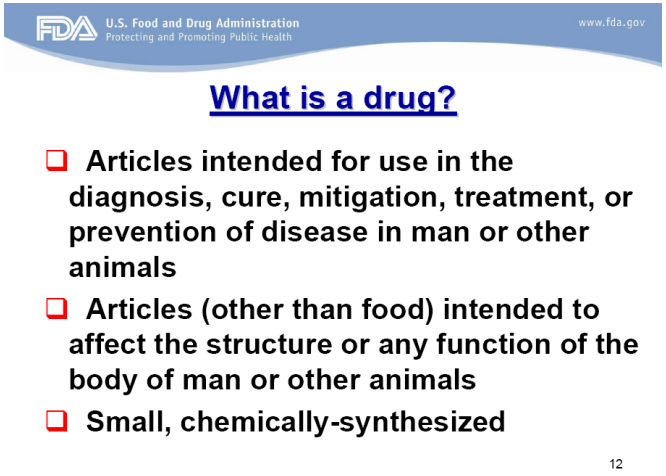
Pharmaceuticals and Biotechnology

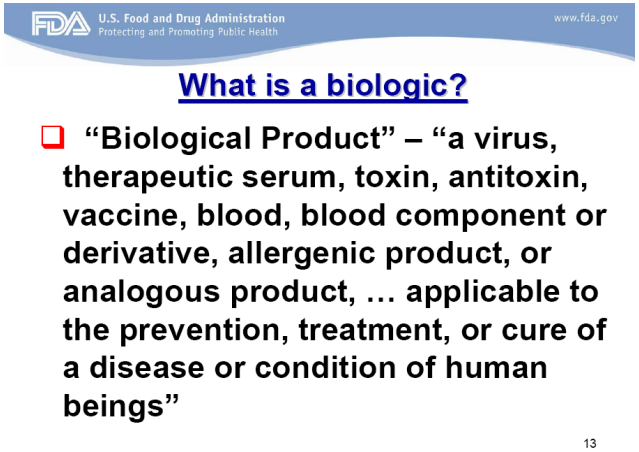
The 'Drug' Industry can be defined with reference to the regulatory framework. While 'drugs' and 'biologics' are distinguished for US regulatory purposes (BLA vs. NDA), there is a blurring line between the commercial activities of biotech and pharmaceutical firms

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 (2015 data)

Traditional 'Big Cap' pharma company Pfizer is increasingly transitioning to biologics

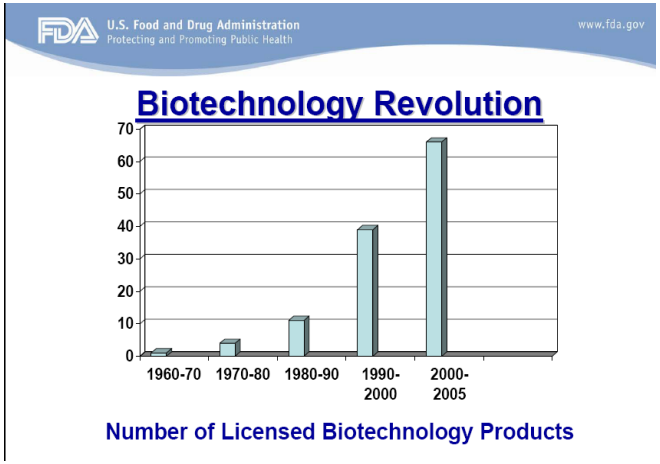
Slides from HMS Webinar, *FDA: Historical Perspective and Overview,* Mar. 13, 2014, B-Elective. Rankings for J&J from company website.

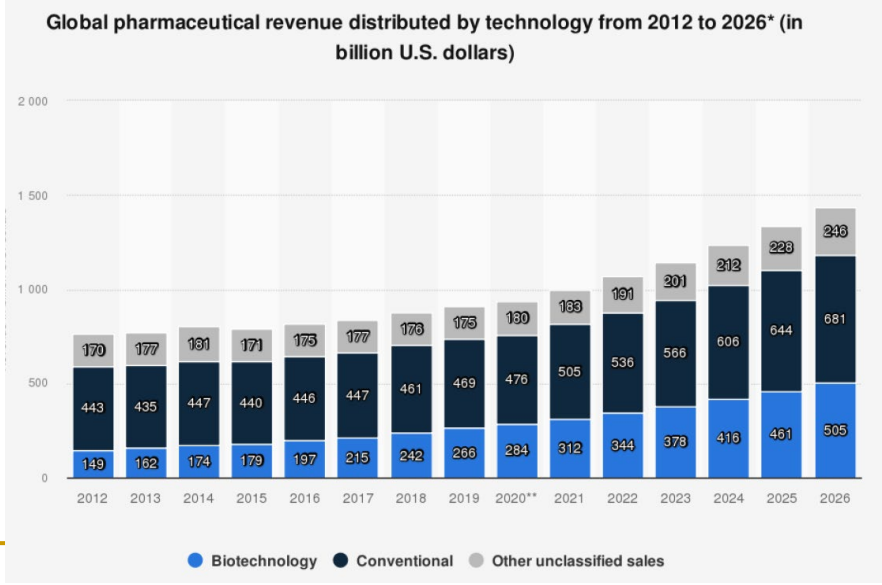




The Biopharmaceutical Industry?

- 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





Traditional 'Pharma' Companies

Equity Market Capitalization 2006 + 2022 (billions US$)

Company (Ticker)	2006	2022 (rank) 01/01/23
Pfizer (PFE-N)	$182.15	$287.6 (3)*
Johnson & Johnson (JNJ-N)	$180.88	$461.8 (1)*
GlaxoSmithKlein (GSK-N)	$141.87	$71.9 (10)*
Roche Holding (RHHBY-O)	$135.28	$267.4 (5)*
Novartis AG (NVS-N)	$128.65	$200.7 (7)*
Sanofi-Aventis (SNY-N)	$122.80	$122.8 (9)*
AstraZeneca (AZN-Q)	$ 75.70	$210.1 (6)*
Merck (MRK-N)	$72.71	$281.3 (4)*
Eli Lilly & Co. (LLY-N)	$64.67	$347.6 (2)*
Wyeth (now PFE)	$62.78*	
Bristol Myers Squib (BMY-N)		$153.0 (8)
Comparables		
Bayer (BAYRY-O)		$50.5
Amgen (AMGN-Q)		$140.1

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;

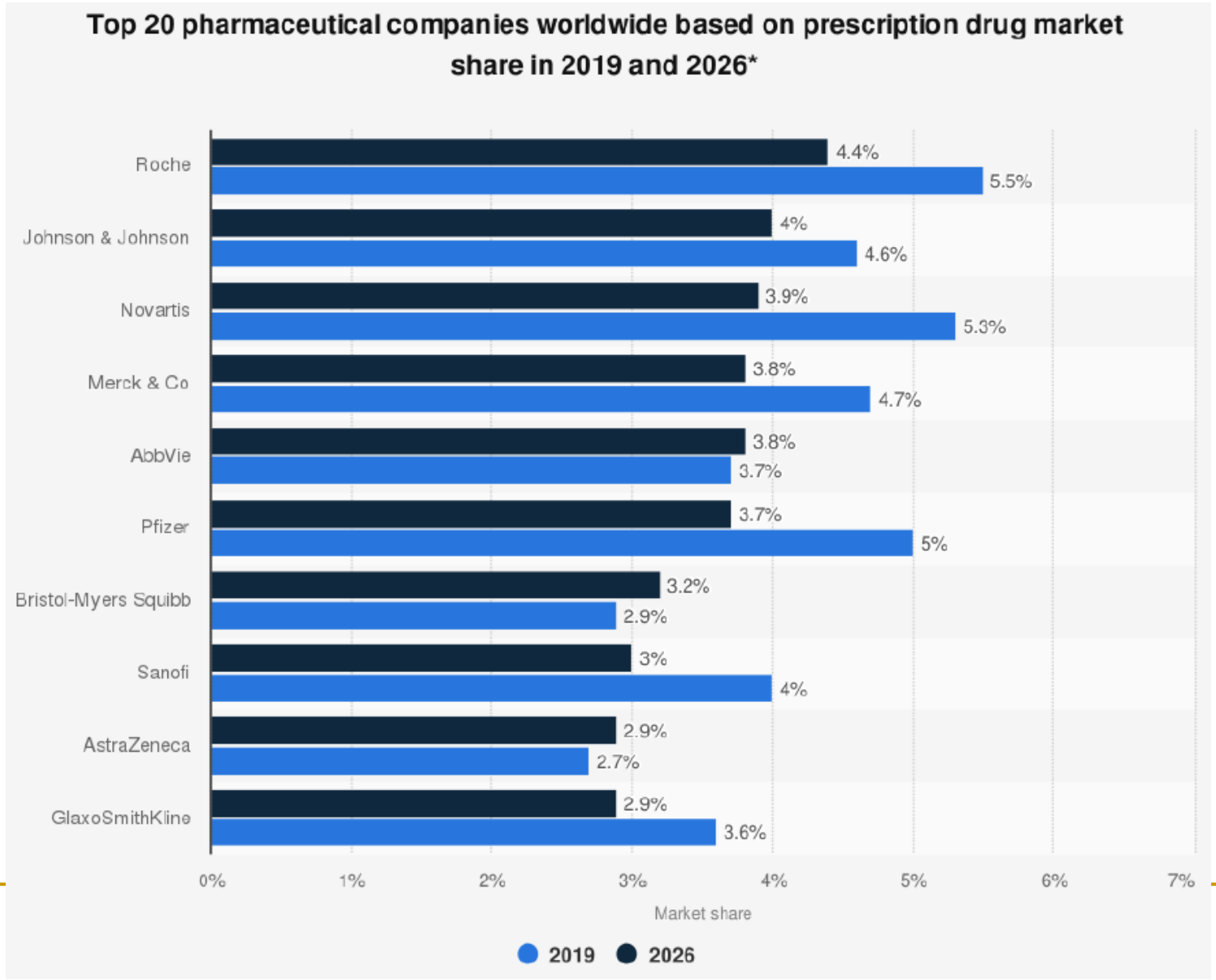
Traditional Biotechnology Companies 2015/2022

Company	Equity Capitalization		Largest Seller(s)
(Ordered by 3/14/14 Cap.)	12/1/15	1/1/23	
Novo Nordisk (NVO-N)	$117.2 B	$306.3B	Diabetes drugs
Gilead Sciences (GILD-Q)	$146.7B	$107.7B	HIV/AIDS/HepC
Amgen (AMGN-Q)	$117.0 B	$140.1B	Enbrel
AbbVie (ABBV-N)	$101.0 B	$285.8B	Humira
Celgene (CELG-Q)	$94.6 B	####	Thalomid/Revlimid
Biogen Idec (BIIB-Q)	$83.0 B	$40.0B	Rituxin
CSL (CSL-AU)	A$41.0 B	A$138.8B	Vaccines/Blood Pr.
Regeneron (REGN-Q)**	$41.3 B	$78.6B	Eylea/Arcalyst

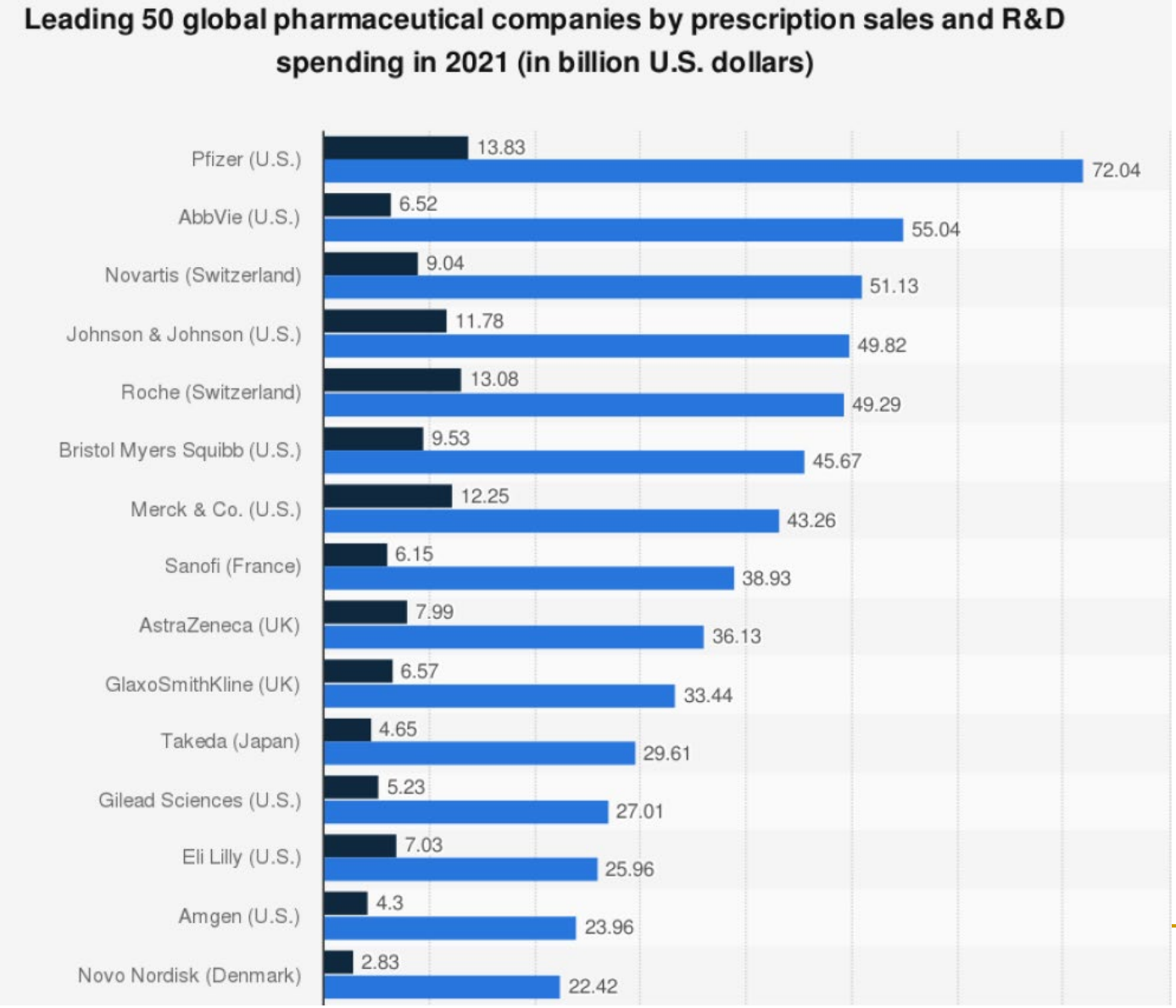
Source: Globe Investor; Financial Times; ** Eylea is joint with Bayer AG. ### Acquired by Bristol-Myers 1/20.

An alternative measure for size: Market Share for 2019

Source: Statista



Significant change in rankings for 2021



Significant Big Cap Biopharma 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)
  - Genezyme was third largest global biotechnology firm

Different Responses to the Landscape (2013)

- 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 3rd 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

Important Events in 2014

- Actavis Plc acquires Allergan, Inc. in Nov. ($66 B)
  - Adds Botox and Restasis (dry eye treatment)
    - Valeant and Bill Ackman (Pershing Square hedge fund) hostile offer outbid
      - Name of the combined company is Allergan (ticker AGN)
- 3-way deal between Novartis, GlaxoSmithKline and Eli Lilly in Apr. ($25 billion total)
  - GlaxoSmithKline (GSK) sells cancer-products business to Novartis ($14.5 billion); Novartis sells animal health division to Eli Lilly ($5.4 billion); GSK purchases some of Novartis vaccine business; GSK and Novartis set up joint venture for OTC drugs
- Failed Tax Inversion Deals
  - Pfizer fails in $100 B. bid for AstraZeneca (Apr.)
  - Shire and Abbvie abandon merger ($54 B.) after US Treasury ruling

Important Events in 2015-16

2015 was a record breaking year for mergers and acquisitions in Healthcare/Pharma with over $680B in deals (Chicago Tribune 28/12/15)

- Jan. 2016 Shire agrees to acquire Baxalta for cash and stock deal for $32B
  - (Deal completed June 3, 2016)

- Feb. 2015 Valeant acquires Salix Pharmaceuticals (gastrointestinal drugs) for $14.5B
- Sept. 2015 the drug re-pricing practices of Valeant Pharmaceuticals attract political attention in US of House Committee on Oversight and Government Reform, Hilary Clinton, and two US Attorney offices.
- Oct 2015 Citron Research precipitates a sharp drop in Valeant stock associated with mis-representation of sales figures through the use of speciality pharma company Philidor

- Nov. 2015, Pfizer and Allergan Plc agree to merger of $160 billion, if completed deal would be the largest pharmaceutical and third largest corporate merger.
  - **April 2016 deal is canceled; Pfizer pays break fee following ruling regarding the tax inversion benefits of the transaction**

And the Large Deals go on! 2016-17

- Sept. 2016, Bayer announces takeover of Monsanto in a $66 billion all-cash deal – completing negotiations that started in May 2016 with a $60 billion offer
  - This is the largest all-cash deal corporate M&A to date exceeding the $60 billion for Anheuser-Busch by InBev in 2008
  - Monsanto is the world's largest supplier of genetically modified seeds and the widely used herbicide Roundup
    - Deal redirects Bayer toward the agricultural sector

- Dec. 2016, J&J announces commencement of negotiations to acquire Swiss biotechnology company Actelion – estimated deal value of $29 billion
  - Actelion is one of Europe's biggest biotechs with a drug portfolio for pulmonary arterial hypertension.

Largest Deals in 2018

- April 2018, Japanese company Takeda Pharmaceuticals reaches agreement to acquire Dublin-based Shire PLC for $62 billion (cash + shares) after a long period of negotiations where previous bids were rejected
  - Brief period where Allergan also expressed interest and possible bidding war
  - Shire is maker of Adderall– amphetamine-related drug used to treat narcolepsy and ADHD
  - Approved by shareholder vote on Dec. 6, 2018 (closed Jan. 2019)
- Other Deals
  - Celgene acquires Impact Biomedicines for $7 billion (myelofibrosis)
  - Celgene acquires Juno Therapeutics for $9 billion (cancer CAR-T)
  - Sanofi acquires Bioverativ for $11.6 billion (hemophilia)

Major Deals in 2019

- Bristol-Myers /Celgene
  - Cash and Stock Deal to acquire Celgene for $74 B announced Jan. 2019, approved by shareholders April. 3 after considerable resistance from large investors.
  - Aims to establish BMY as the leader in oncology drugs
  - July 29, Deal receives EU approval
  - Completed 11/19, largest ever biopharma acquisition transaction
- Abbvie / Allergan
  - June 25 Abbvie announces $63 B acquisition of Allergan
  - Abbvie facing impending expiration of blockbuster Humira
  - Divestures of some drugs in order to receive regulatory approval.
  - Deal completed 5/20

Deals in 2020 and 2021

- Slowdown of megadeals in 2020-1 – ten largest deals in 2020 valued at $91B vs. $207B in 2019
  - Slowdown likely due to a combination of COVID and size of deals done in 2019
- Two largest acquisitions in 2020:
  - AstraZeneca acquires Alexion Pharmaceuticals for $39B
  - Gilead acquires Immunomedics for $21B
- Largest deals in 2021 were mostly smaller despite companies accumulating significant cash stockpiles
  - Merck to acquire Acceleron Pharma. (cardio drugs) for $11.5B
  - Pfizer to acquire Arena Pharma. (oncology drugs) for $6.7B
  - Some large deals in the medical IT and services space, e.g., Thermo Fisher acquires PPD for $17.4B
  - 12/21 CSL acquires Vifor for $11.7B (iron deficiency; renal)

Spinoff + Merger: VIATRIS

- In Nov. 2020 Pfizer previously used spinoff of Upjohn subsidiary (acquired as part of the Pharmacia takeover) that featured key off-patent drugs and a generic business that was merged with Mylan (epipen) to create Viatris
  - Deal valued at $18.5 Billion
  - Mylan + PFE joint owners of epipen
  - PFE also provided branded drugs (Viagra, Zoloft; Lipitor, etc.)
  - Mylan also provided generics and specialty pharms
  - VTRS ownership PFE 57% + Mylan 43%
  - Sold biosimilar business in 2022 for $3B to Biocon Biologics (India)

Largest Deals in 2022

- Biggest Deal of 2022: Amgen acquires Horizon Therapeutics for $26.4B
  - Horizon is a rare disease biotech with two significant drugs: Krystexxa (gout treatment) and Tepezza (thyroid eye treatment)
  - Amgen also acquires ChemoCentryx in Oct. ($3.7B; autoimmune);
- Pfizer acquires Biohaven Pharmaceutical for $11.6B
  - Biohaven has products in the areas of migraine and pain; neurological disorders; and neurodegeneration
  - Deal is unusual: Pfizer will spin-off products – mostly in the development stage – that do not fit with the Pfizer strategic plan
  - Incentive for spinoff is to avert possible anti-trust issues
  - Pfizer also purchased Global Blood Therapeutics, $5.7B
- BMS acquires Turning Point Therapeutics (oncology) $4.1B
- Range of smaller deals (GSK, Abbvie, Halozyne) from $2 to $1B

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 Lily)	$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

Global Prescription Drug Sales, 2014

Sales ($ billions)	Drug Name	Treatment	Company
$12.54	.Humira	arthritis	Abbott Labs
$10.28	Sovaldi	hepatitis c	Gilead
$9.24	Remicade	Crohn's Disease	Johnson & Johnson
$8.68	Rituxan	cancer, leukemia	Genentech
$8.54	Enbrel	arthritis	Wyeth
$7.28	Lantus Solostar	diabetes	Sanofi-Aventis
$6.96	Avastin	cancer	Roche
$6.79	Herceptin	breast cancer	Roche
$6.43	Advair Diskus	asthma	GlaxoSmithKline
$5.87	Crestor	cholesterol	AstraZeneca
$5.86	Neulasta	chemotherapy	Amgen
$5.27	Abilify	schizophrenia	Otsuka Pharma

Source: Genetic Engineering News;qz.com; Vaughan's summaries.

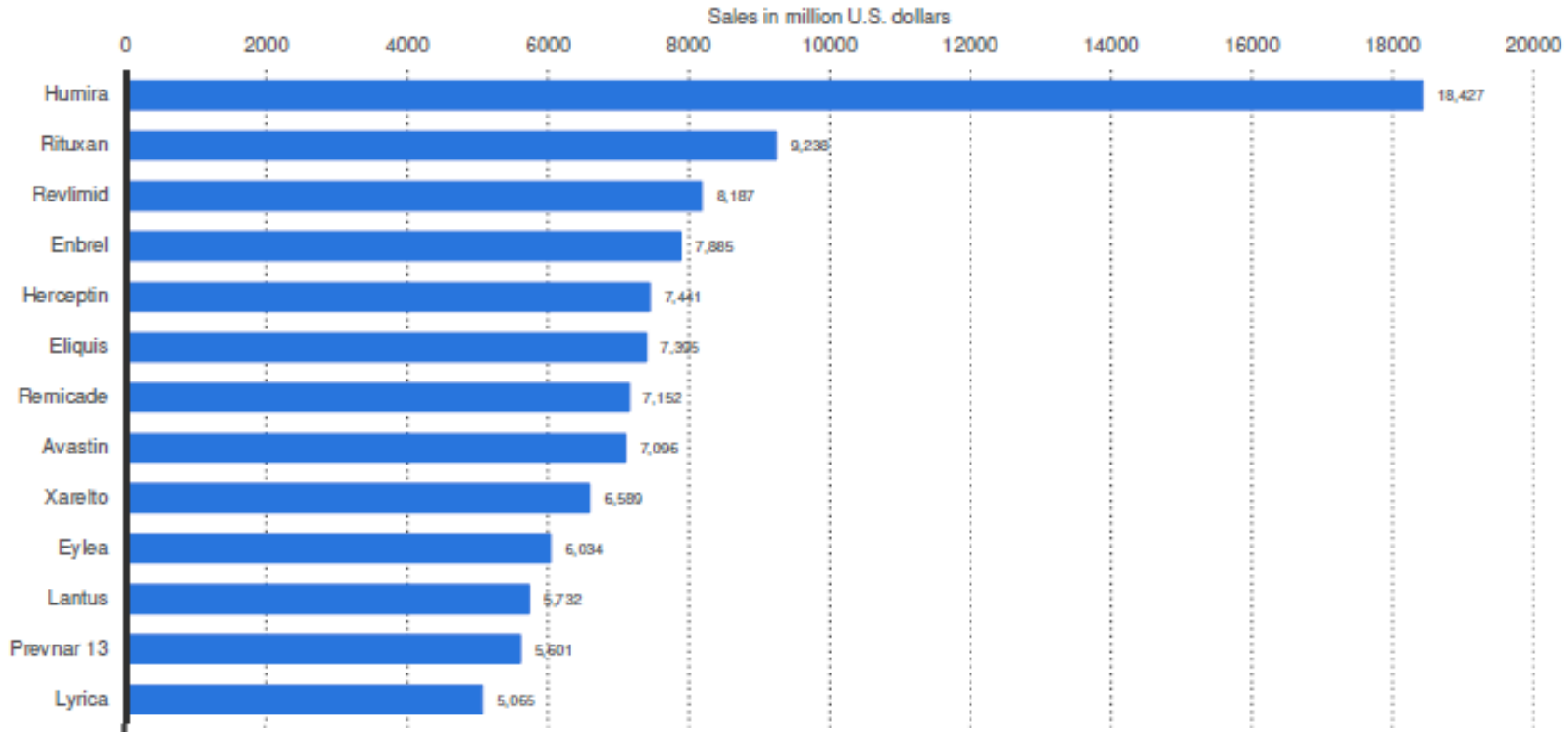
Top-Selling Biopharmaceuticals, 2015 (Global)

Harvoni	$18.4 B	Anti-viral (Hep.C)	Gilead
Humira	$14.95B	Arthritis/Psoriasis	AbbVie
Lantus	$11.46B	Diabetes	Sanofi-Aventis
Enbrel	$9.47B	Arthritis/Psoriasis	Amgen
Crestor	$8.61B	Cholesterol	Aztra-Zeneca
Remicade	$8.2B	Crohn's/Colitis	Janssen
Seretide	$8.0B	Asthma/COPD	Glaxo-S-K
Sovaldi	$6.58	Anti-viral (Hep.C)	Gilead
Mabthera	$6.3B	Lymph Cancer	Roche
Avastin	$6.18B	Cancer/Eye Dis.	Genentech
Lyrica	$6.04B	Pain	Pfizer

Compare list for 2017 (year-end 2016) with 2015 – collapse of Hep-C and rise of Eylea

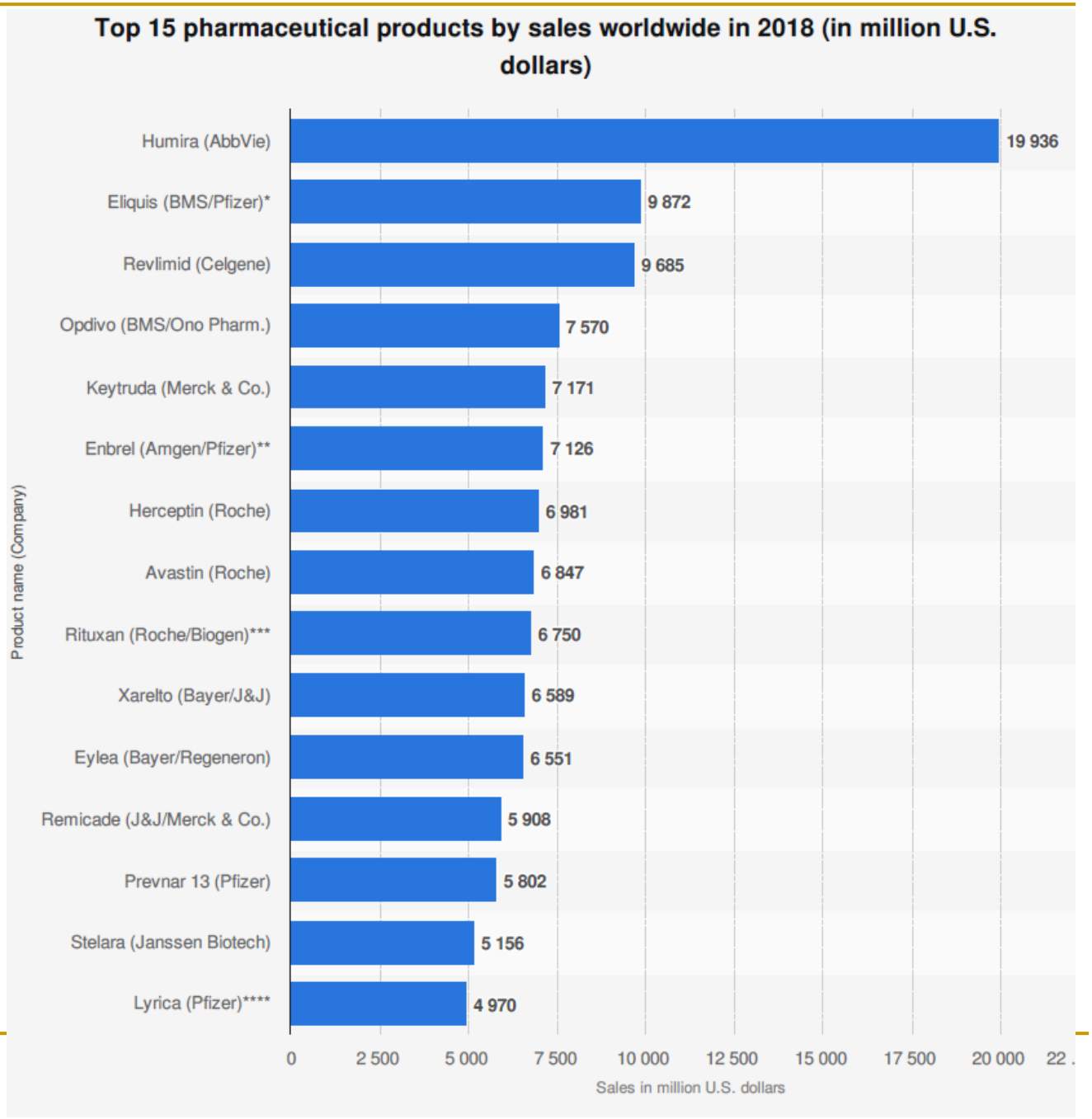
Top pharmaceutical products by sales worldwide 2017

Top 15 pharmaceutical products by sales worldwide in 2017 (in million U.S. dollars)



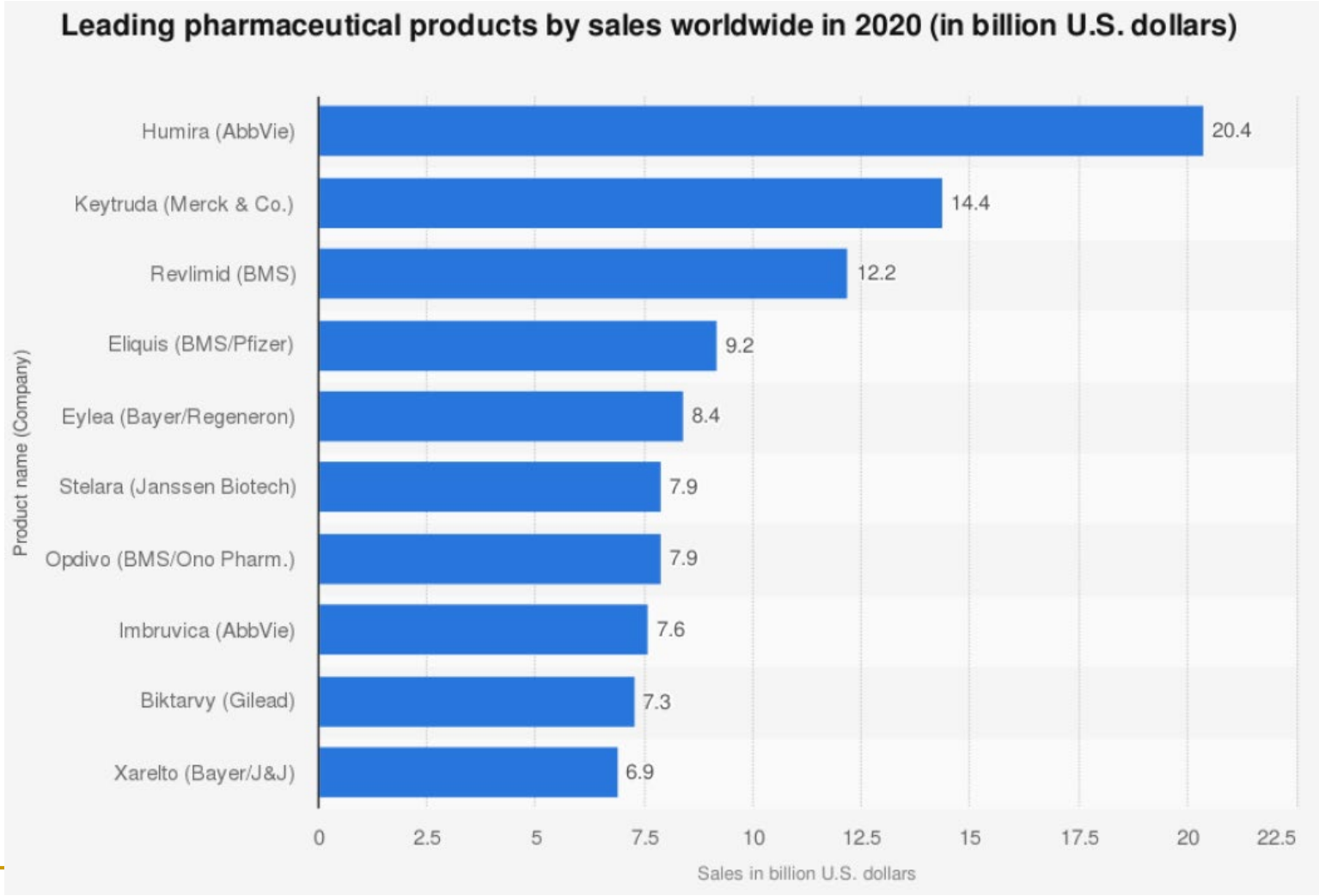
Humira still #1 in 2018

No 'falling angels' (dramatic declines in big blockbusters) in this reporting year

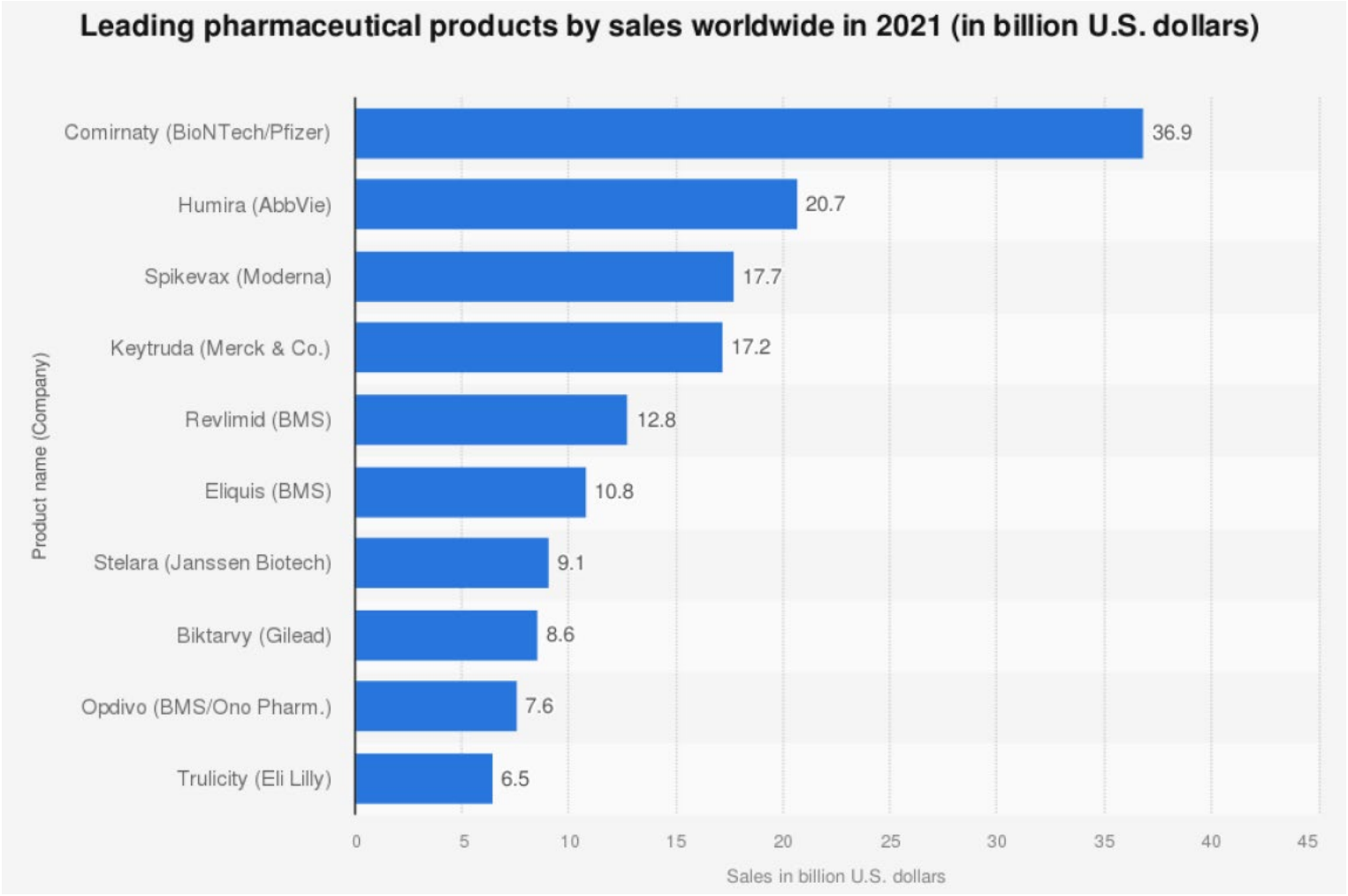


Humira still #1 in 2020

Some falling angels and emergence of new rising stars

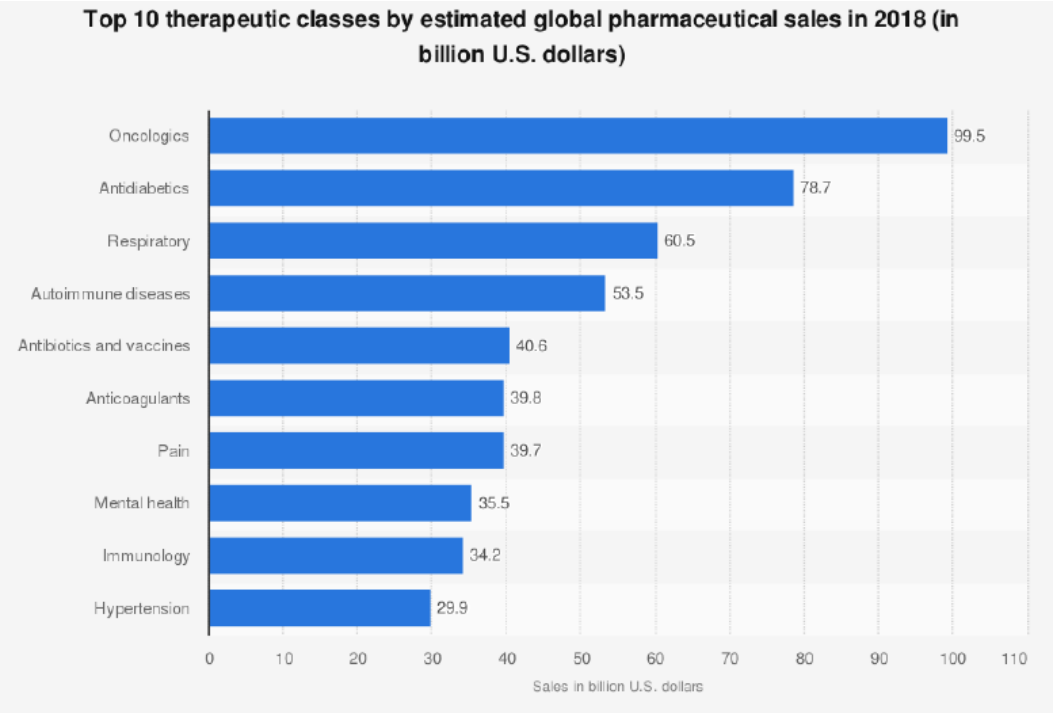


Significant changes in 2021



Therapeutic Class Sales Breakdown (2018 Global Sales)

- Oncologics $99.5B
- Anti-diabetics $78.7B
- Respiratory Agents $60.5 B
- Autoimmune Agents $53.5 B
- Anti-bacterials $40.6 B
- Cardiovascular $39.8 B
- Pain $39.7B
- Mental Health $35.5 B
- Immunology $34.2 B
- Hypertension $29.9 B



Source: Statista

Important Changes: Pain was #2 area in 2017 ($76.1 B) falling to #7 in 2018 ($39.7 B); Respiratory Agents rising from #6 ($38.6 B) to #3 ($60.5 B).

Note: Data on revenues vary across sources; Statista reports Oncologic revenues of $145B in 2019

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

Age group and Multum Lexicon Plus therapeutic class[1] (common indications for use)	Total			Male			Female		
	1988–1994	1999–2002	2007–2010	1988–1994	1999–2002	2007–2010	1988–1994	1999–2002	2007–2010
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)[3]	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)[2]	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)[5]	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”.

Prescription drug use for 55-64 Age Bracket (CDC, *Health 2014*)

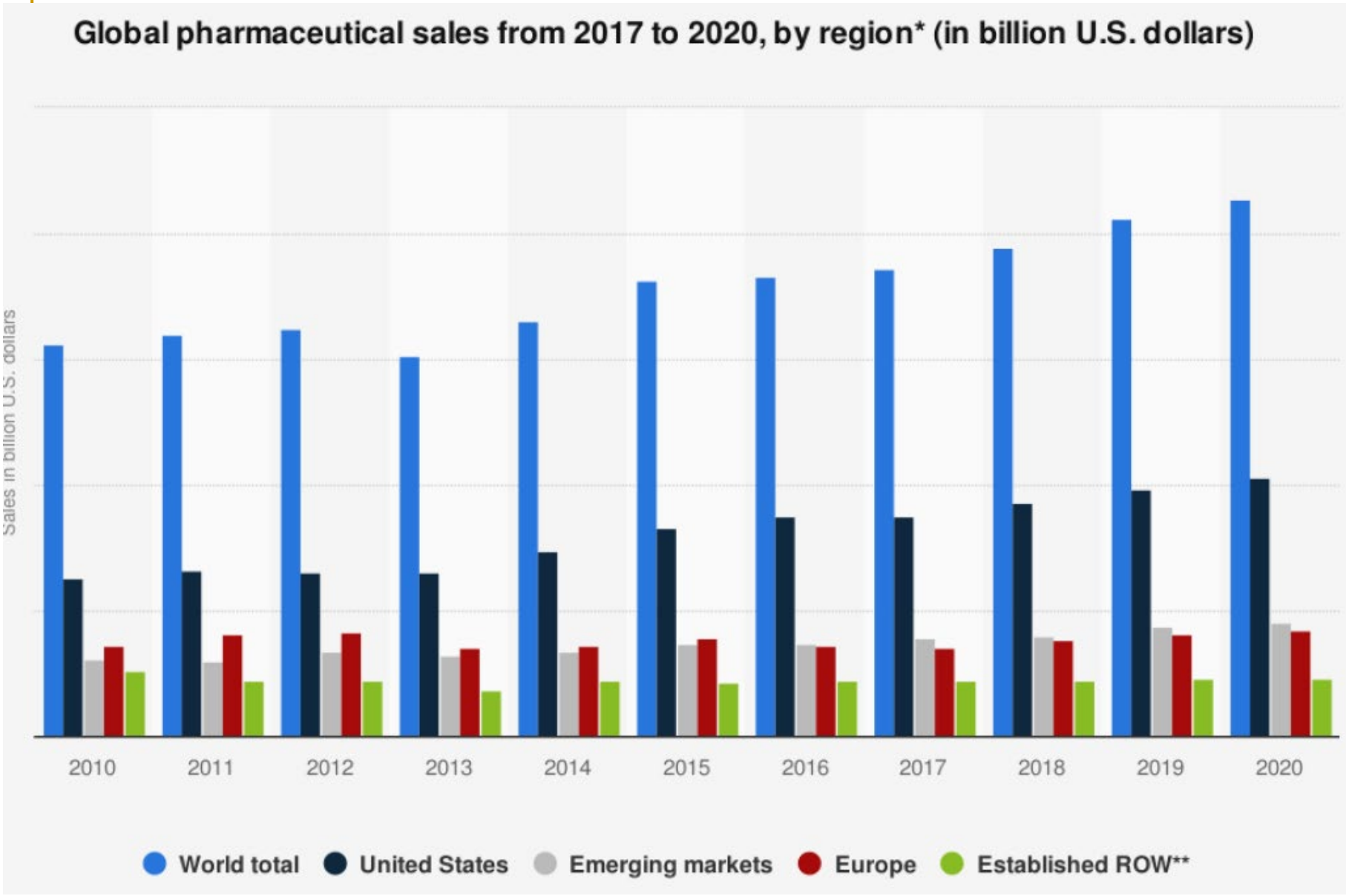
Data table for Figure 28. Prescription drug use in the past 30 days among adults aged 55–64, by number of drugs and selected drug class: United States, 1999–2002 and 2009–2012

Excel and Powerpoint: http://www.cdc.gov/nchs/hus/contents2014.htm#fig28

Characteristic	1999–2002		2009–2012	
	Percent	SE	Percent	SE
Number of prescription drugs in past 30 days[1]				
No prescription drugs	26.9	1.5	24.2	1.4
1–4 prescription drugs	55.4	1.8	55.6	1.4
5 or more prescription drugs	17.7	1.7	20.3	1.3
Prescription drug use in past 30 days, by selected Multum Lexicon Plus therapeutic drug class (common indications for use)[2]				
Cardiovascular (heart, blood pressure, and kidney disease)	41.3	2.0	45.0	2.2
Cholesterol-lowering (high cholesterol)	20.6	1.7	31.8	1.7
Gastric reflux (gastroesophageal reflux disease [GERD], anti-acid reflux, ulcers)	9.0	1.6	16.0	1.2
Analgesic (pain, inflammation, blood clot prevention)	16.8	1.4	15.0	1.7
Antidepressant (depression, anxiety, perimenopausal symptom, pain)	10.3	1.2	14.4	1.2
Antidiabetic (high glucose [blood sugar])	10.0	1.1	12.9	0.9

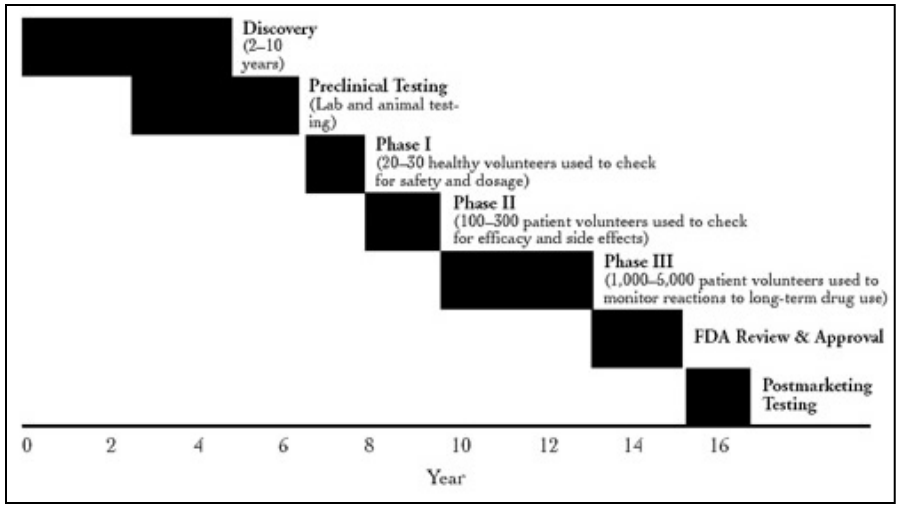
SE is standard error.

[1]Respondents were asked if they had taken a prescription drug in the past 30 days. Those who answered "yes" were asked to show the interviewer the medication containers for all prescriptions. If no container was available, the respondent was asked to verbally report the name of the medication. Each drug's complete name was recorded and classified.



Source: Statista; IMS Health; Astra-Zeneca

New Drug and Biologic Development and Marketing Approval

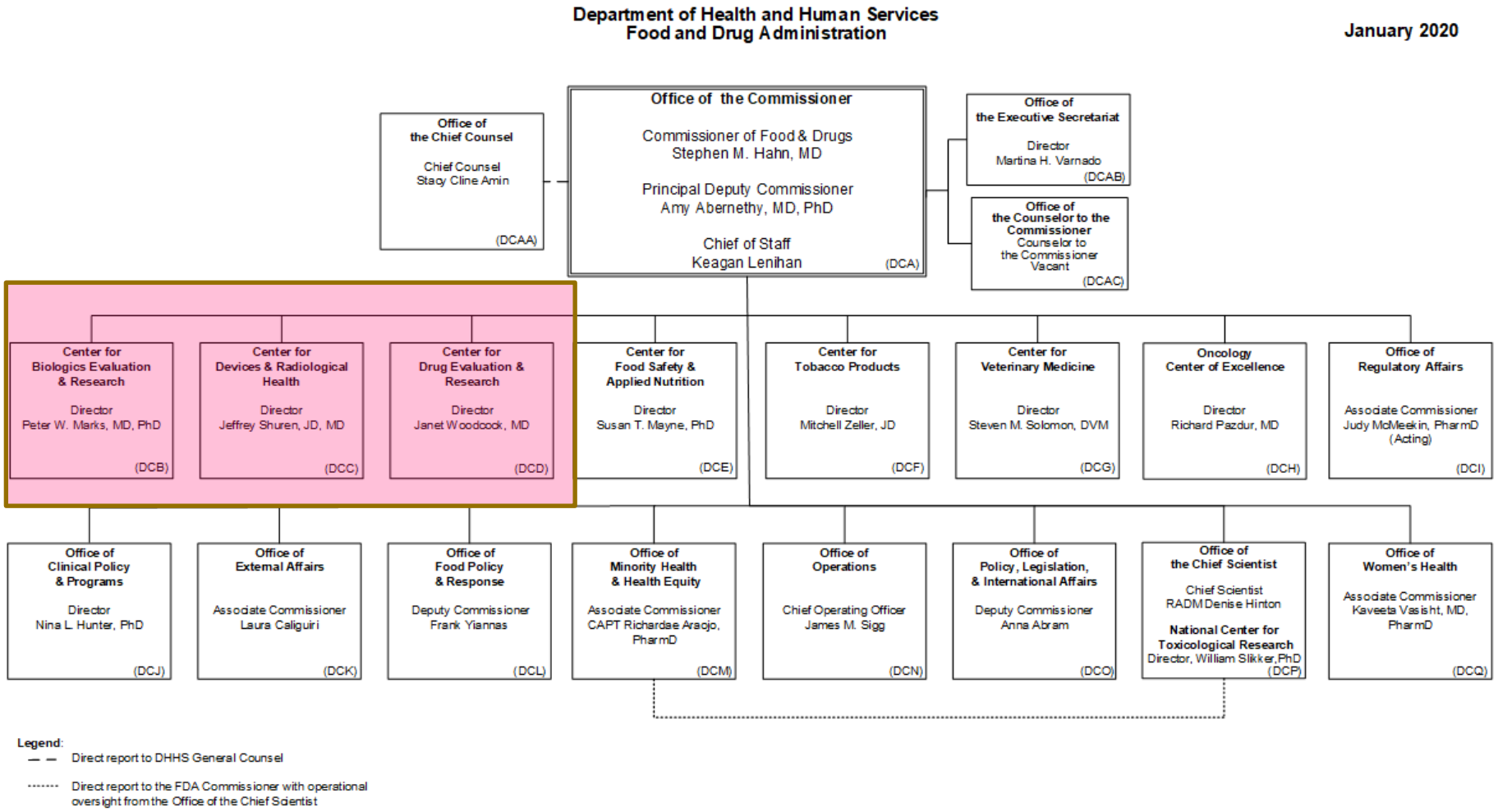


Patent

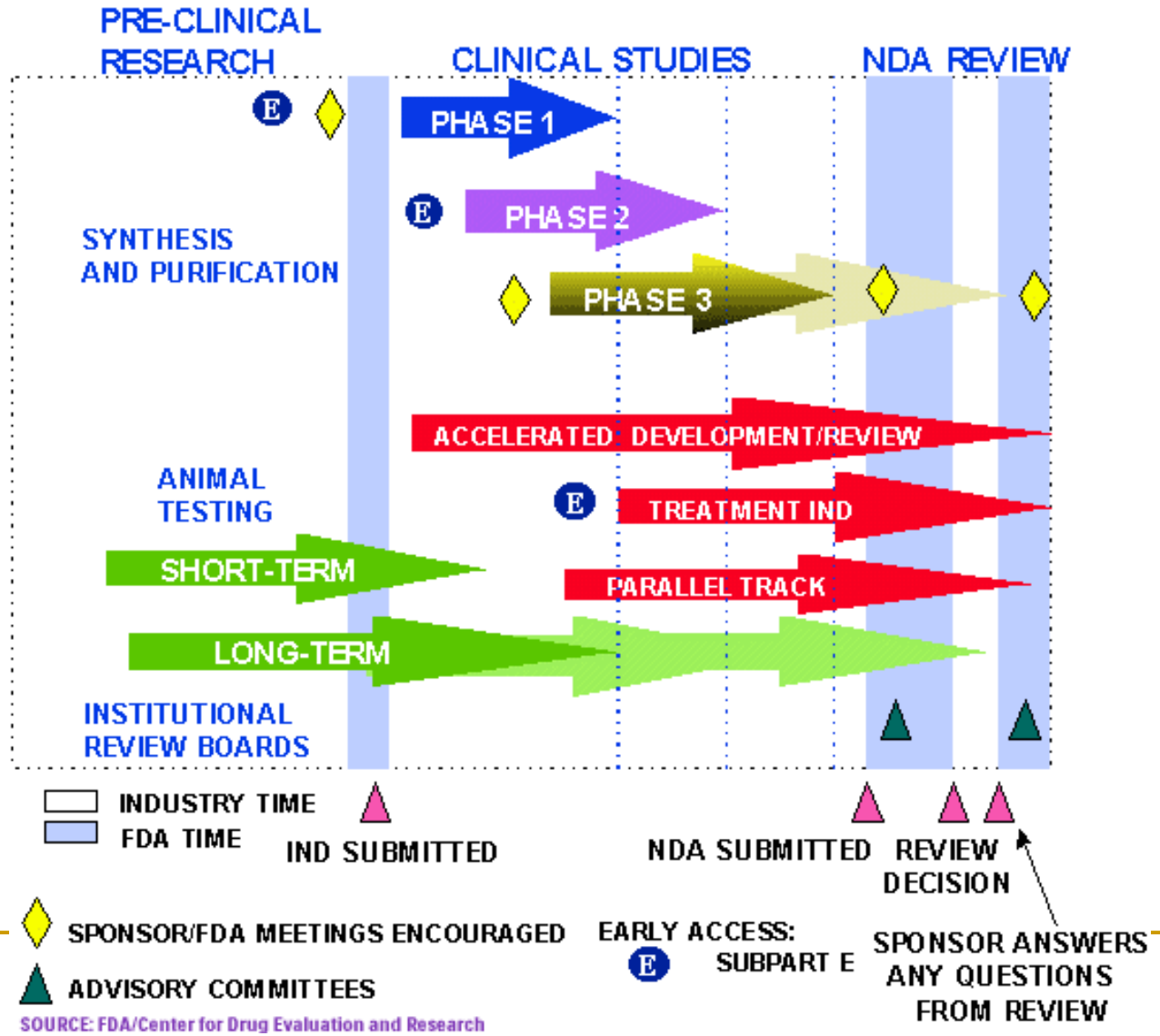
- Generally last 20 years
- Since most companies file for patent during pre-clinical trials, usually the patent is only good for another 10 years or so after it gains FDA approval
- What can be patented
  - Product
  - Method
  - Use
- Examples
  - DNA and RNA sequences
  - Proteins, enzymes, antibiotics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

- For US (FDA) and EU (EMA) Accelerated Clinical Development and Approval Process see:
  https://cddf.org/files/2017/06/0850-Jan-Gross.pdf

Organization Chart for FDA (Approval sections highlighted)



FDA: Center for Drug Evaluation and Research (CDER)



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

- Difficult to determine precisely the number of 'new' drugs and biologics
  - Essential US sources from

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm

  - IND – Investigational New Drug Application (to start human trials)
  - NDA (New Drug Application) and Biologics License Application See Calendar Year Approvals
  - New Molecular Entity (NME) Drug and New Biologic Approvals

Biologic License Application (BLA) Approvals:

BLA NUMBER	PROPRIETARY NAME	PROPER NAME	APPLICANT	REVIEW CLASSIFICATION
BLA 761032/0.0	SILIQ	BRODALUMAB	VALEANT PHARMACEUTICALS LUXEMBOURG S.A.R.L. (VPL)	S
BLA 761049/0.0	BAVENCIO	AVELUMAB	EMD SERONO, INC.	P,O
BLA 761053/0.0	OCREVUS	OCRELIZUMAB	GENENTECH, INC.	P
BLA 761055/0.0	DUPIXENT	DUPILUMAB	REGENERON PHARMACEUTICALS, INC.	P
BLA 761052/0.0	BRINEURA	CERLIPONASE ALFA	BIOMARIN PHARMACEUTICAL INC.	P,O

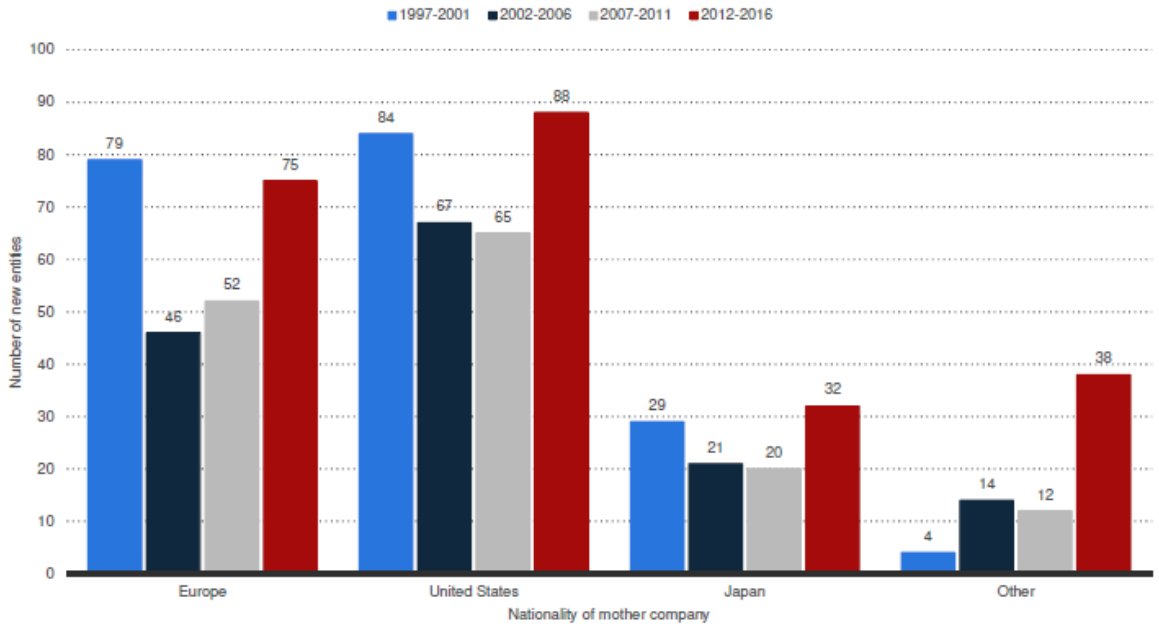
Reporting system recognizes P (Priority, Significant improvement), S (Standard) and O (Orphan) status

In 2012, 2017 and 2020 BLA and NDA approvals were:

(2021) 6P, 3 (P,O), 2S, 4 (S,O) BLA; 20P, 25 (P,O), 57S, 4 (S,O) NDA
(2017) 4P, 5 (P,O), 4S, 3(S,O) BLA; 21P, 17 (P,O), 78S, 13 (S,O) NDA
(2012) 3P, 2 (P,O), 1S, 0 (S,O) BLA; 7P, 4 (P,O), 15S, 6 (S,O) NDA

Pharmaceutical industry - number of new substances 1992-2016

Number of new chemical or biological entities developed between 1992 and 2016, by region of origin



European Medicines Agency (EMA): History and Approvals

- Process of approval and marketing is different in Europe
  - Since 1995, there has been a centralized agency (EMA) aimed at harmonizing the work of the medicine regulatory bodies of the member states (first joint EU legislation in 1965)
    - Prior to 2004, EMA was named the European Agency for the Evaluation of Medicinal Products

- Three pathways for biopharmaceutical approval
  - Centralized procedure where application is made to EMA and marketing approval given for all member states
    - Compulsory for certain medicines and process of choice for most innovative products; majority of medicines do **not** meet criteria for centralized procedure
  - Decentralized procedure
    - Application for simultaneous authorization in more than one EU country (not currently approved in any EU state) and not required to be compulsory
  - Mutual-Recognition Procedure
    - Where a medicine has been approved in one EU state and application is made for recognition by other EU members

- NOTE: Rules and Requirements for approval of biopharmaceuticals are the same regardless of the procedure used for approval

EMA and EU Legislation: Recent Developments

- 2012 -- Pharmacovigilance legislation came into force in the EU.
  - Key changes: establishment of a new Pharmacovigilance Risk Assessment Committee within the EMA, responsibility for reviewing and making recommendations on product safety issues. Introduces possibility for regulators to require pharmaceutical companies to conduct post-authorization efficacy studies at the time of approval, or at any time afterwards in light of scientific developments. There are also additional requirements regarding adverse drug reaction reporting and additional monitoring of products.

- 2014 -- EU has been active recently implementing legislation on clinical trials and post-authorization
  - May 2014 -- EU adopted a new Clinical Trials Regulation in May 2014, came into effect December 2017.
    - Regulation aimed at simplifying and harmonizing governance of clinical trials in the EU and will require increased public posting of clinical trial results.

- 2015 -- January 1 EMA adopted a new policy on Publication of Clinical Data for Medicinal Products for Human Use.
  - Under this policy, the EMA proactively publishes clinical trial data from application dossiers for new marketing authorizations, including data from trials taking place outside the EU, after the EMA decides on marketing authorization.

What happened with Brexit?

- June 2016: UK electorate votes to leave EU
- March 2017, U.K. government notifies the European Council of intention to leave the EU triggering Article 50 of Lisbon Treaty to begin the two-year negotiation process
- November 2017, announcement that EMA will be relocating from London, U.K. to Amsterdam by expected date of Brexit in March 2019
- March 2019, relocation of EMA to Amsterdam
- Currently: The UK Medicines and Healthcare products Regulatory Agency (MHRA) broke away from the EMA in Dec. 2020 in order to accelerate the approval of COVID vaccines; MHRA now operates as a separate regulator.

Useful webpages from the EMA site:

- https://www.ema.europa.eu/en/about-us/united-kingdoms-withdrawal-european-union-brexit
- https://www.ema.europa.eu/en/about-us/uks-withdrawal-eu/relocation-amsterdam

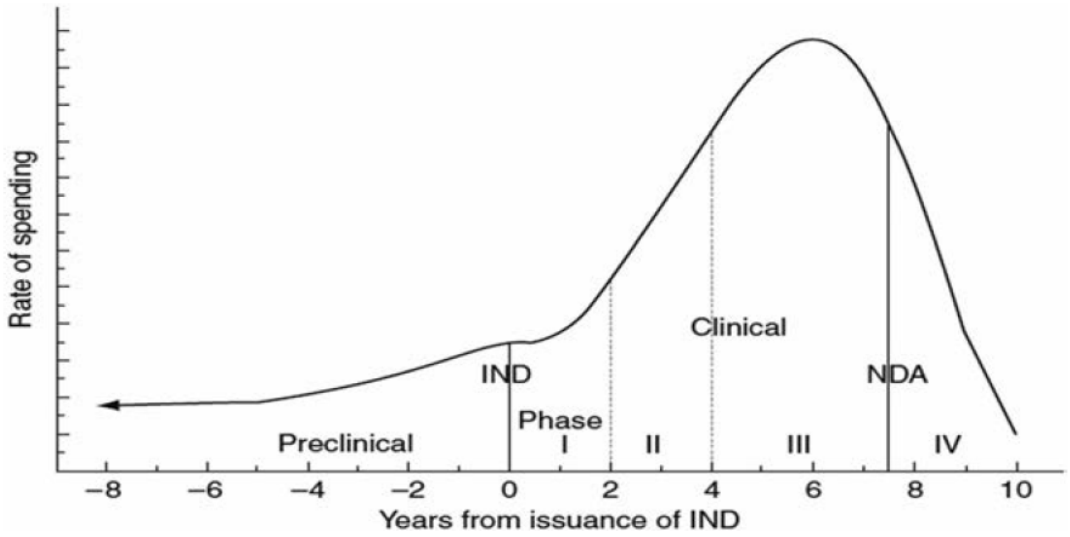
Costing the Clinical Process

- 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.

Costing from IND to Stage 4

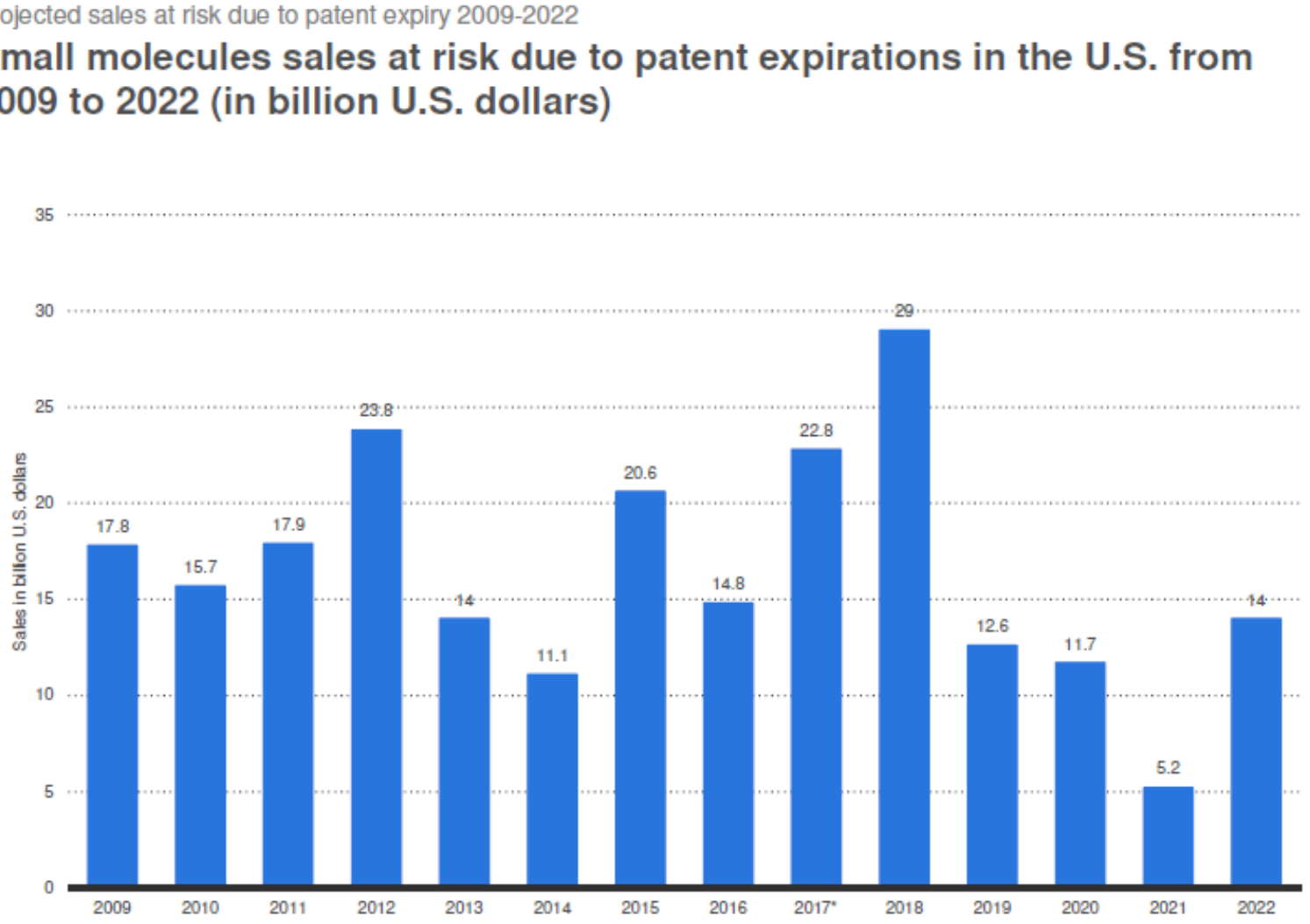
- Preclinical costs can be highly variable – much is sourced to startups that are merged or acquired with large bio-pharma companies at a later stage
- IND (Investigational New Drug) application to FDA for receiving permission to begin human trials
- NDA approval required for drug to move to commercial distribution



- Large biopharma companies increasingly relying on mergers and acquisitions to deal with declining R&D productivity – startups especially prominent in biotech

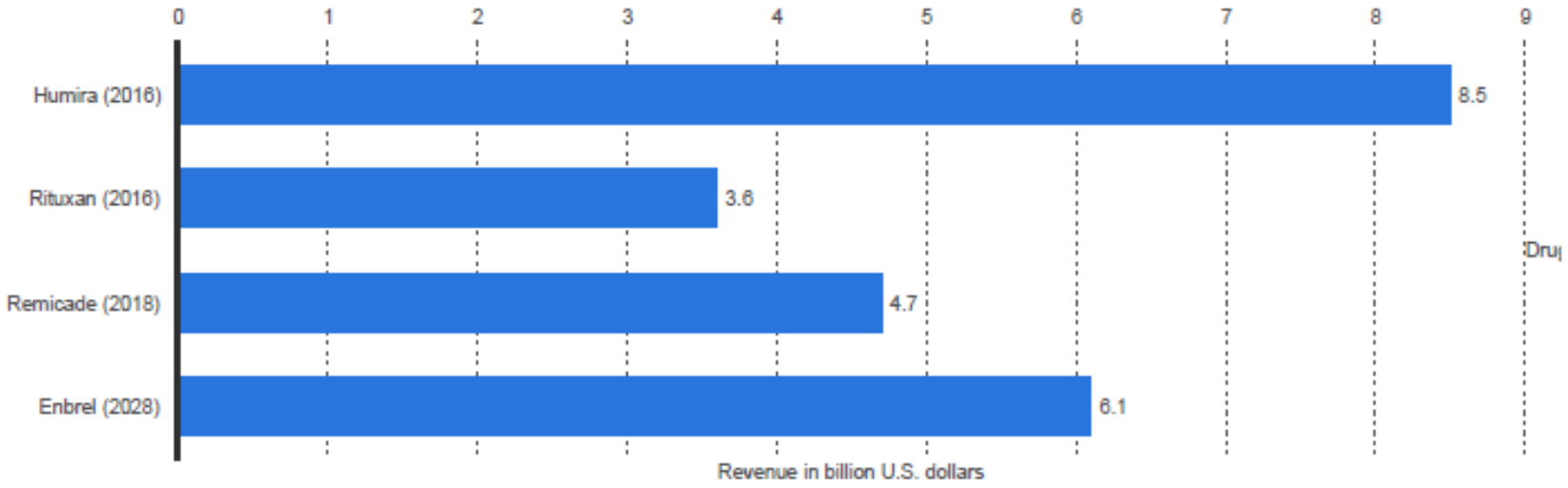
Small molecule patents at risk of expiration in US

Source: Statista

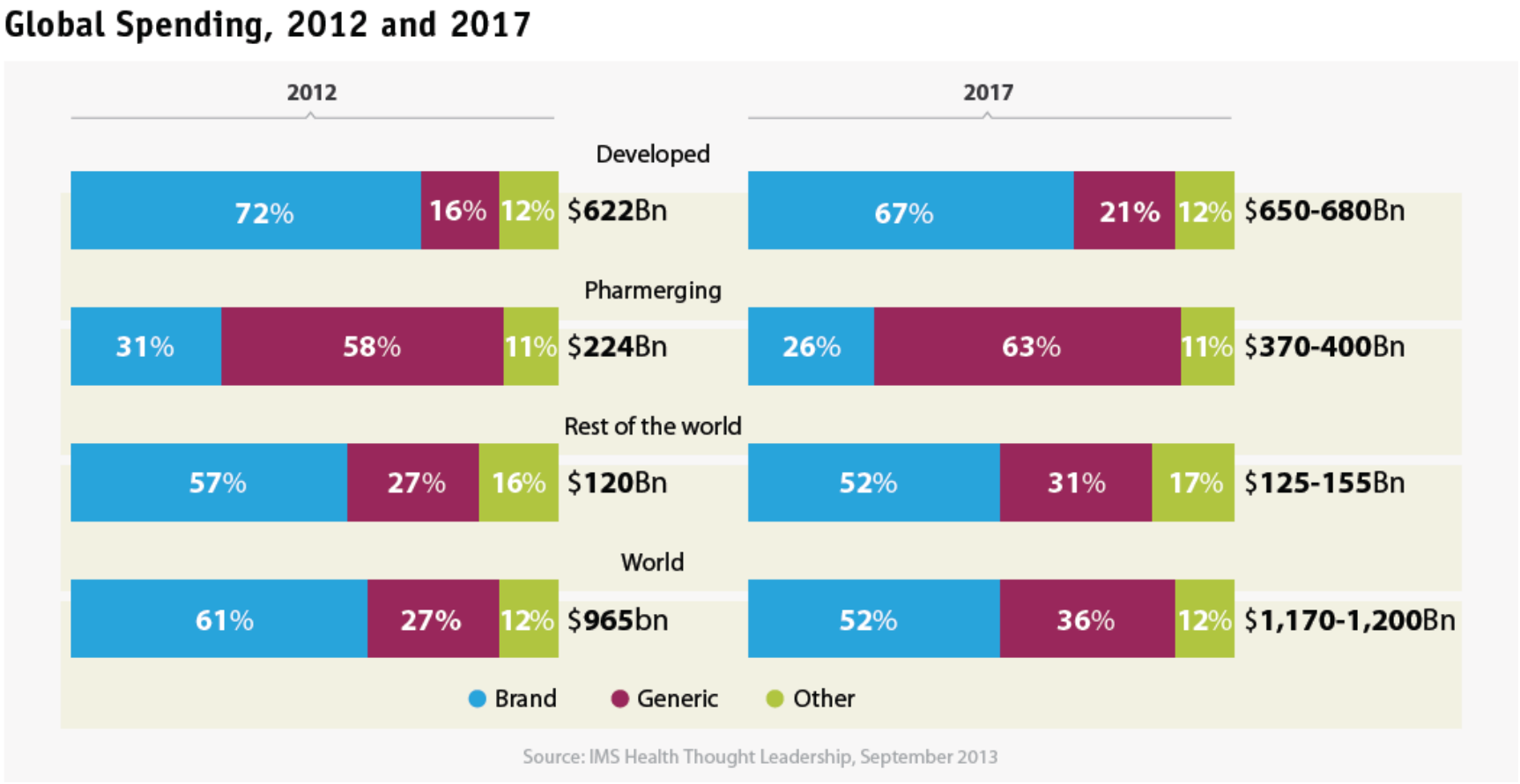


Biologics not as susceptible to switching to biosimilars

Selected top branded biologic drugs in the United States that will go generic between 2016 and 2028, by revenue (in billion U.S. dollars)*

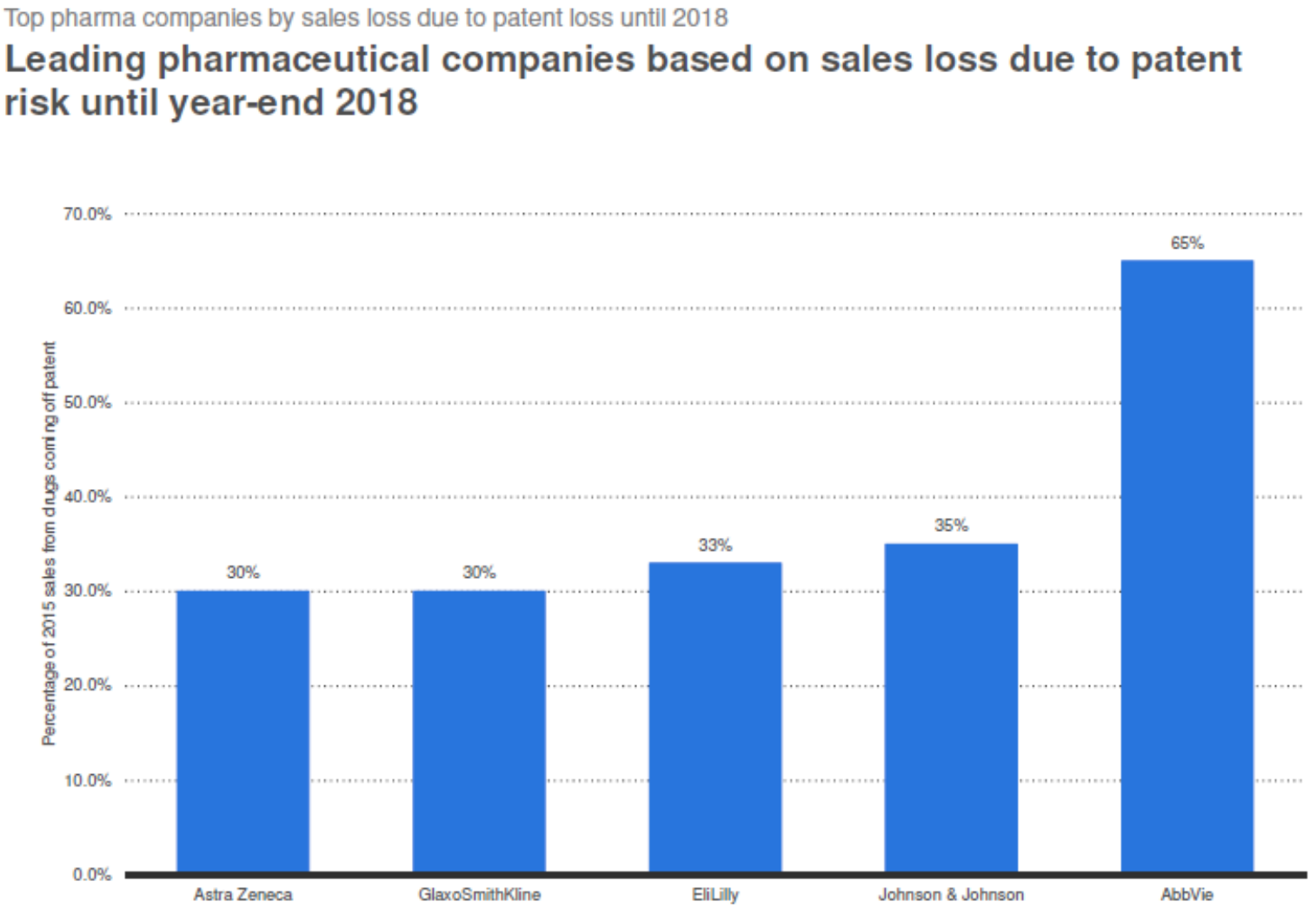


Generic Drug Sales



Risk of patent expiration for selected companies

Source: Statista



Patent Protection

- Drugs and Biologics may have several patents
  - Specific delivery method
    - e.g., in 2021 Mylan FDA got S approval for injectable acetaminophen
  - Specific product/molecule
  - Specific manufacturing process
  - Specific medical indication
    - How molecules react
  - Specific Combination
    - Fixed dose/combination of several molecules; Gilead with Harvoni

Source: www.southcentre.org

Large Capitalization Biopharmaceutical Companies

Pfizer:

- Small Molecule Blockbusters going off-patent
- Seeking Takeovers: Allergan and After
- Transitioning the Biologics

Amgen:

- Large Biotech vs. Large Pharma
- Protection Against Generics

Pfizer: Reacting to Patent Expiration

- 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 – 2018 shares in Eliquis (#2), Embrel (#6) and full share of Prevenar (#13) + Lyrica (#15)
- 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

Major Acquisitions

June 2019 Acquired Array BioPharma for $11.1B (oncology)

Feb. 2015, Acquired Hospira for $17.B (injectable drugs and biosimilars)

Sept. 2016, acquires Medivation for $14.B (oncology)

Product	U.S. Basic Product Patent Expiration Year[1]	Major Europe Basic Product Patent Expiration Year[1]	Japan Basic Product Patent Expiration Year[1]
Chantix/Champix	2020[2]	2021[2]	2022
Sutent	2021[3]	2022[3]	2024
Inlyta	2025	2025	2025
Xeljanz	2025	2028[4]	2025
Prevnar 13/Prevenar 13	2026	[5]	2029
Eliquis[6]	2026	2026	2026
Ibrance	2027	2028	2028
Xtandi[7]	2027	[7]	[7]
Vyndaqel/Vyndamax/Vynmac	2024 (2028 pending PTE)	2026	2026/2029[8]
Xalkori	2029	2027	2028
Besponsa	2030	2028	2028[4]
Braftovi[9]	2031 (2031 pending PTE)	[9]	[9]
Mektovi[9]	2031[10]	[9]	[9]
Bavencio[11]	2033	2032	2033
Lorbrena	2033	2034	2036
Prevnar 20/Apexxnar	2033 (2035 pending PTE)	2033	2033[12]
Cibinqo	2034	2034[13]	2034 (2038 pending PTE)
Comirnaty	[14]	[14], [15]	[14]
Paxlovid	[16]	[16]	[16]

Pfizer products with revenues greater than $2.4B in 2021 -- Nov. 2020 Pfizer creates Viatris spinoff that includes legacy off-patent brands plus Epipen

(MILLIONS)

Product	Global Revenues	Region	Revenue Year Ended Dec. 31, 2021	2020
Comirnaty[a]	$36,781	U.S.	$ 7,809	$ 154
	*	Int'l.	28,972	—
		Worldwide	$ 36,781	$ 154
Eliquis	$5,970	U.S.	$ 3,160	$ 2,688
	Up 19%	Int'l.	2,810	2,260
	(operationally)	Worldwide	$ 5,970	$ 4,949
Ibrance	$5,437	U.S.	$ 3,418	$ 3,634
	Flat	Int'l.	2,019	1,758
	(operationally)	Worldwide	$ 5,437	$ 5,392
Prevnar family	$5,272	U.S.	$ 2,701	$ 2,930
	Down 11%	Int'l.	2,571	2,920
	(operationally)	Worldwide	$ 5,272	$ 5,850
Xeljanz	$2,455	U.S.	$ 1,647	$ 1,706
	Flat	Int'l.	808	731
	(operationally)	Worldwide	$ 2,455	$ 2,437

(MILLIONS OF DOLLARS)

PRODUCT	PRIMARY INDICATION OR CLASS	Year Ended December 31, 2018	2017	2016
TOTAL REVENUES		**$ 53,647**	$ 52,546	$ 52,824
PFIZER INNOVATIVE HEALTH (IH) [a]		**$ 33,426**	$ 31,422	$ 29,197
Internal Medicine		**$ 9,996**	$ 9,684	$ 8,858
Lyrica IH [b]	Epilepsy, post-herpetic neuralgia and diabetic peripheral neuropathy, fibromyalgia, neuropathic pain due to spinal cord injury	**4,622**	4,511	4,165
Eliquis alliance revenues and direct sales	Atrial fibrillation, deep vein thrombosis, pulmonary embolism	**3,434**	2,523	1,713
Chantix/Champix	An aid to smoking cessation treatment in adults 18 years of age or older	**1,085**	997	842
BMP2	Development of bone and cartilage	**279**	261	251
Toviaz	Overactive bladder	**271**	257	258
Viagra IH [c]	Erectile dysfunction	**—**	823	1,181
All other Internal Medicine	Various	**306**	312	447
Vaccines		**$ 6,332**	$ 6,001	$ 6,071
Prevnar 13/Prevenar 13	Vaccines for prevention of pneumococcal disease	**5,802**	5,601	5,718
FSME/IMMUN-TicoVac	Tick-borne encephalitis vaccine	**184**	134	114
Trumenba	Meningococcal Group B vaccine	**116**	88	84
All other Vaccines	Various	**230**	177	155
PFIZER ESSENTIAL HEALTH (EH) [d]		**$ 20,221**	$ 21,124	$ 23,627
Legacy Established Products (LEP) [e]		**$ 10,540**	$ 10,894	$ 11,197
Lipitor	Reduction of LDL cholesterol	**2,062**	1,915	1,758
Norvasc	Hypertension	**1,024**	926	962
Premarin family	Symptoms of menopause	**832**	977	1,017
Xalatan/Xalacom	Glaucoma and ocular hypertension	**318**	335	363
Effexor	Depression and certain anxiety disorders	**311**	297	278
EpiPen	Epinephrine injection used in treatment of life-threatening allergic reactions	**303**	290	386
Zoloft	Depression and certain anxiety disorders	**298**	291	304

Compare 2012-14 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)			Year Ended December 31,		
PRODUCT	PRIMARY INDICATIONS	Business[a]	2014	2013	2012
Lyrica[b]	Epilepsy, post-herpetic neuralgia and diabetic peripheral neuropathy, fibromyalgia, neuropathic pain due to spinal cord injury	GEP/GIP	$ 5,168	$ 4,595	$ 4,158
Prevnar family	Vaccines for prevention of pneumococcal disease	V	4,464	3,974	4,117
Enbrel (Outside the U.S. and Canada)	Rheumatoid, juvenile rheumatoid and psoriatic arthritis, plaque psoriasis and ankylosing spondylitis	GIP	3,850	3,774	3,737
Celebrex	Arthritis pain and inflammation, acute pain	GEP	2,699	2,918	2,719
Lipitor	Reduction of LDL cholesterol	GEP	2,061	2,315	3,948
Viagra[c]	Erectile dysfunction	GEP/GIP	1,685	1,881	2,051
Zyvox	Bacterial infections	GEP	1,352	1,353	1,345
Sutent	Advanced and/or metastatic renal cell carcinoma (mRCC), refractory gastrointestinal stromal tumors (GIST) and advanced pancreatic neuroendocrine tumor	O	1,174	1,204	1,236
Norvasc	Hypertension	GEP	1,112	1,229	1,349
Premarin family	Symptoms of menopause	GEP	1,076	1,092	1,073
BeneFIX	Hemophilia	GIP	856	832	775
Vfend	Fungal infections	GEP	756	775	754
Pristiq	Depression	GEP	737	698	630
Genotropin	Replacement of human growth hormone	GIP	723	772	832
Chantix/Champix	An aid to smoking cessation treatment	GIP	647	648	670
Refacto AF/Xyntha	Hemophilia	GIP	631	602	584

Revenues — Major Human Health Products

(MILLIONS OF DOLLARS) PRODUCT	PRIMARY INDICATIONS	YEAR ENDED DEC. 31, 2005	2004	2003	% CHANGE 05/04	04/03
Cardiovascular and metabolic diseases:						
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	—
Central nervous system disorders:						
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[a]	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
Arthritis and pain:						
Celebrex[b]	Arthritis pain and inflammation, acute pain	1,730	3,302	1,883	(48)	75
Bextra[b]	Arthritis pain and inflammation	(61)	1,286	687	*	87
Infectious and respiratory diseases:						
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
Urology:						
Viagra	Erectile dysfunction	1,645	1,678	1,879	(2)	(11)
Detrol/Detrol LA	Overactive bladder	988	904	544	9	66
Oncology:						
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
Ophthalmology:						
Xalatan/Xalacom	Glaucoma and ocular hypertension	1,372	1,227	668	12	84
Endocrine disorders:						
Genotropin	Replacement of human growth hormone	808	736	481	10	53
All other:						
Zyrtec/Zyrtec-D	Allergies	1,362	1,287	1,338	6	(4)
Alliance revenue[c]	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)

[a] Represents direct sales under license agreement with Eisai Co., Ltd.
[b] Includes direct sales under license agreement with Pharmacia prior to the acquisition.
[c] 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 massive 2021 revenue and earnings increase after revenue in 2019 and 2020 flatlined; R&D to SGA improvement

Consolidated Statements of Income
Pfizer Inc. and Subsidiary Companies

(MILLIONS, EXCEPT PER COMMON SHARE DATA)	Year Ended December 31, 2021	2020	2019
Revenues	$ 81,288	$ 41,651	$ 40,905
Costs and expenses:			
Cost of sales[a]	30,821	8,484	8,054
Selling, informational and administrative expenses[a]	12,703	11,597	12,726
Research and development expenses[a]	13,829	9,393	8,385
Amortization of intangible assets	3,700	3,348	4,429
Restructuring charges and certain acquisition-related costs	802	579	601
(Gain) on completion of Consumer Healthcare JV transaction	—	(6)	(8,107)
Other (income)/deductions—net	(4,878)	1,219	3,497
Income from continuing operations before provision/(benefit) for taxes on income	24,311	7,036	11,321
Provision/(benefit) for taxes on income	1,852	370	583
Income from continuing operations	22,459	6,666	10,738
Discontinued operations—net of tax	(434)	2,529	5,318
Net income before allocation to noncontrolling interests	22,025	9,195	16,056
Less: Net income attributable to noncontrolling interests	45	36	29
Net income attributable to Pfizer Inc. common shareholders	$ 21,979	$ 9,159	$ 16,026
Earnings per common share—basic:			

Rebuilding Pfizer by acquisition

- Aug.1, 2019 **GSK completes transaction with Pfizer to form new world-leading Consumer Healthcare Joint Venture**
- Aug. 2016
  - Pfizer announces purchase of the biotech firm Medivation specializing in oncology for $14B
    - Medivation has one successful late stage prostrate cancer drug (Xtandi) and two promising late stage cancer drugs (breast cancer and lymphoma)
- Sept. 2015
  - Pfizer purchases Hospira for $17B
    - One of largest providers of biosimilars in Europe

Dramatic improvement in Cash from Operations in 2021

Consolidated Statements of Cash Flows
Pfizer Inc. and Subsidiary Companies

(MILLIONS)	Year Ended December 31, 2021	2020	2019
Operating Activities			
Net income before allocation to noncontrolling interests	**$ 22,025**	$ 9,195	$ 16,056
Discontinued operations—net of tax	**(434)**	2,529	5,318
Net income from continuing operations before allocation to noncontrolling interests	**22,459**	6,666	10,738
Adjustments to reconcile net income before allocation to noncontrolling interests to net cash provided by operating activities:			
Depreciation and amortization	**5,191**	4,681	5,755
Asset write-offs and impairments	**276**	2,049	2,889
TCJA impact	**—**	—	(323)
Gain on completion of Consumer Healthcare JV transaction, net of cash conveyed[3]	**—**	(6)	(8,254)
Deferred taxes from continuing operations	**(4,293)**	(1,575)	561
Share-based compensation expense	**1,182**	755	687
Benefit plan contributions in excess of expense/income	**(3,123)**	(1,242)	(55)
Other adjustments, net	**(1,573)**	(479)	(1,080)
Other changes in assets and liabilities, net of acquisitions and divestitures:			
Trade accounts receivable	**(3,811)**	(1,275)	(1,124)
Inventories	**(1,125)**	(778)	(1,071)
Other assets	**(1,057)**	(137)	847
Trade accounts payable	**1,242**	355	(341)
Other liabilities	**18,721**	2,768	861
Other tax accounts, net	**(1,166)**	(1,240)	(3,074)
Net cash provided by operating activities from continuing operations	**32,922**	10,540	7,015
Net cash provided by/(used in) operating activities from discontinued operations	**(343)**	3,863	5,572
Net cash provided by operating activities	**32,580**	14,403	12,588

Pfizer suspends spending on share buybacks while dividend payments were maintained; large short term investment increase in 2021 related to $11.6B acquisition of Biohaven in 2022

	Year Ended December 31,		
	2021	2020	2019
Investing Activities			
Purchases of property, plant and equipment	**(2,711)**	(2,226)	(2,046)
Purchases of short-term investments	**(38,457)**	(13,805)	(6,835)
Proceeds from redemptions/sales of short-term investments	**27,447**	11,087	9,183
Net (purchases of)/proceeds from redemptions/sales of short-term investments with original maturities of three months or less	**(8,088)**	920	6,925
Purchases of long-term investments	**(1,068)**	(597)	(201)
Proceeds from redemptions/sales of long-term investments	**649**	723	232
Acquisitions of businesses, net of cash acquired	**—**	—	(10,861)
Other investing activities, net[a]	**(305)**	(265)	(223)
Net cash provided by/(used in) investing activities from continuing operations	**(22,534)**	(4,162)	(3,825)
Net cash provided by/(used in) investing activities from discontinued operations	**(12)**	(109)	(120)
Net cash provided by/(used in) investing activities	**(22,546)**	(4,271)	(3,945)
Financing Activities			
Proceeds from short-term borrowings	**—**	12,352	16,455
Principal payments on short-term borrowings	**—**	(22,197)	(8,378)
Net (payments on)/proceeds from short-term borrowings with original maturities of three months or less	**(96)**	(4,129)	2,551
Proceeds from issuance of long-term debt	**997**	5,222	4,942
Principal payments on long-term debt	**(2,004)**	(4,003)	(6,806)
Purchases of common stock	**—**	—	(8,865)
Cash dividends paid	**(8,729)**	(8,440)	(8,043)
Other financing activities, net	**16**	(444)	(342)
Net cash provided by/(used in) financing activities from continuing operations	**(9,816)**	(21,640)	(8,485)
Net cash provided by/(used in) financing activities from discontinued operations	**—**	11,991	—
Net cash provided by/(used in) financing activities	**(9,816)**	(9,649)	(8,485)

Pfizer Sizeable Revenue (> $1B) Products (3 year price chart)

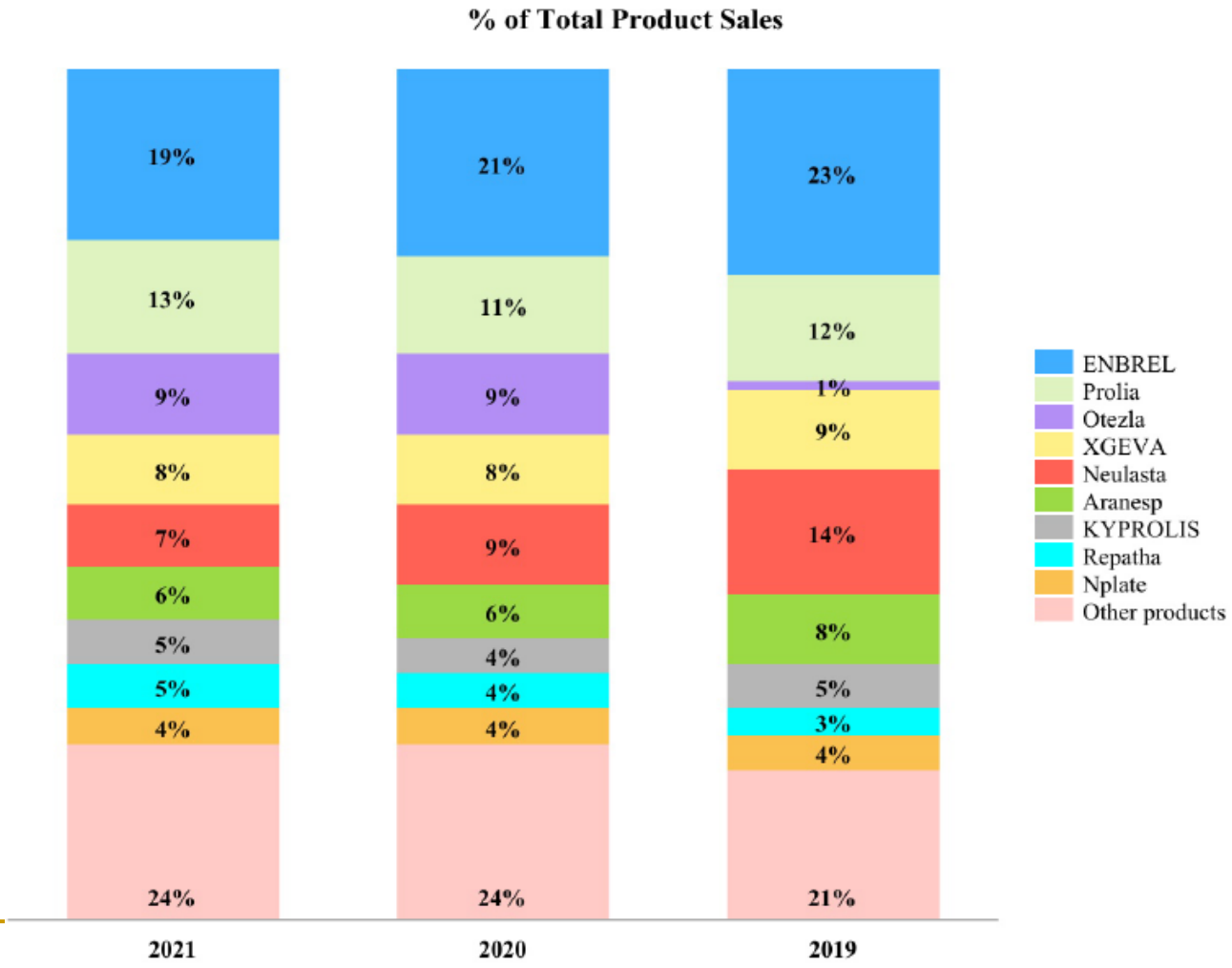
Primary Care	
Comirnaty direct sales and alliance revenues[c]	Active immunization to prevent COVID-19
Paxlovid	COVID-19 infection (high risk population)
Eliquis alliance revenues and direct sales	Nonvalvular atrial fibrillation, deep vein thrombosis, pulmonary embolism
Prevnar family[d]	Pneumococcal disease
Specialty Care	
Vyndaqel/Vyndamax	ATTR-CM and polyneuropathy
Xeljanz	RA, PsA, UC, active polyarticular course juvenile idiopathic arthritis,
Oncology	
Ibrance	HR-positive/HER2-negative metastatic breast cancer

- In the stock market, success in product development revenue generation does not necessarily translate to superior stock price performance

Pfizer, Q3 2022 Revenue Breakdown

(MILLIONS)	Three Months Ended		Nine Months Ended	
PRODUCT	Oct. 2, 2022	Oct. 3, 2021	Oct. 2, 2022	Oct. 3, 2021
TOTAL REVENUES[a]	**$ 22,638**	**$ 24,035**	**$ 76,040**	**$ 57,450**
GLOBAL BIOPHARMACEUTICALS BUSINESS	**$ 22,319**	**$ 23,513**	**$ 75,066**	**$ 56,101**
Primary Care	**$ 15,846**	**$ 16,680**	**$ 55,676**	**$ 35,804**
Comirnaty direct sales and alliance revenues[c]	4,402	12,977	26,477	24,277
Paxlovid	7,514	—	17,099	—
Eliquis alliance revenues and direct sales	1,464	1,346	5,001	4,470
Prevnar family[d]	1,607	1,447	4,601	3,971
Specialty Care	**$ 3,404**	**$ 3,749**	**$ 10,267**	**$ 11,205**
Vyndaqel/Vyndamax	602	501	1,766	1,454
Xeljanz	502	610	1,304	1,734
Oncology	**$ 3,070**	**$ 3,085**	**$ 9,124**	**$ 9,091**
Ibrance	1,283	1,381	3,841	4,039

Amgen: Profile of a Large Cap Biotech



Until 2021 lower ratio of SGA to R&D than PFE; less erosion of revenues from biologics due to appearance of bio-similars

	Year ended December 31, 2021	Change	Year ended December 31, 2020	Change	Year ended December 31, 2019
Cost of sales	$ 6,454	5 %	$ 6,159	41 %	$ 4,356
% of product sales	26.6 %		25.4 %		19.6 %
% of total revenues	24.8 %		24.2 %		18.6 %
Research and development	$ 4,819	15 %	$ 4,207	2 %	$ 4,116
% of product sales	19.8 %		17.4 %		18.5 %
% of total revenues	18.5 %		16.5 %		17.6 %
Acquired in-process research and development	$ 1,505	N/A	$ —	N/A	$ —
% of product sales	6.2 %		— %		— %
% of total revenues	5.8 %		— %		— %
Selling, general and administrative	$ 5,368	(6)%	$ 5,730	11 %	$ 5,150
% of product sales	22.1 %		23.6 %		23.2 %
% of total revenues	20.7 %		22.5 %		22.0 %
Other	$ 194	3 %	$ 189	*	$ 66
Total operating expenses	$ 18,340	13 %	$ 16,285	19 %	$ 13,688

	2021		2020		2019	
Product Sales by Geography:						
U.S.	$ 17,286	71 %	$ 17,985	74 %	$ 16,531	74 %
ROW	7,011	29 %	6,255	26 %	5,673	26 %
Total	$ 24,297	100 %	$ 24,240	100 %	$ 22,204	100 %

Amgen Worldwide Biopharmaceutical Sales

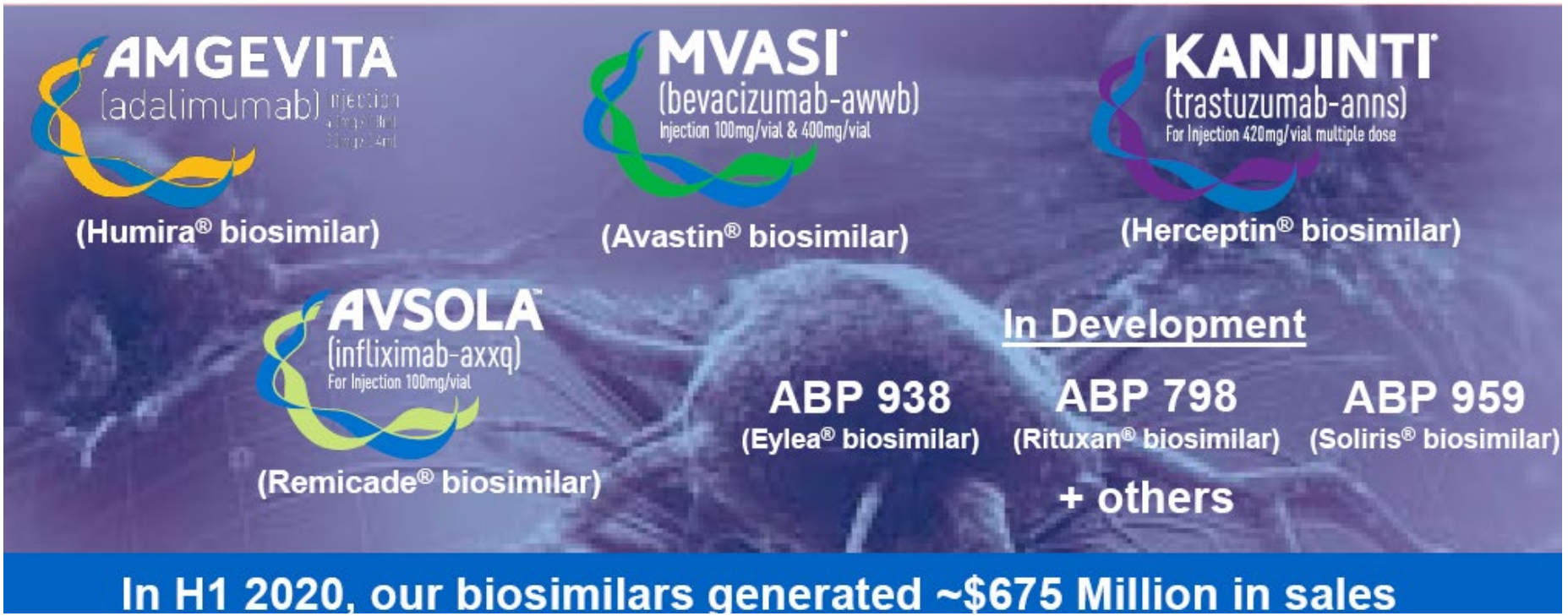
	Year ended December 31, 2021	Change	Year ended December 31, 2020
ENBREL	$ 4,465	(11)%	$ 4,996
Prolia	3,248	18 %	2,763
Otezla	2,249	2 %	2,195
XGEVA	2,018	6 %	1,899
Neulasta	1,734	(24)%	2,293
Aranesp	1,480	(6)%	1,568
Repatha	1,117	26 %	887
KYPROLIS	1,108	4 %	1,065
Nplate	1,027	21 %	850
Other products	5,851	2 %	5,724
Total product sales	$ 24,297	— %	$ 24,240
Total U.S.	$ 17,286	(4)%	$ 17,985
Total ROW	7,011	12 %	6,255
Total product sales	$ 24,297	— %	$ 24,240

Amgen has an impressive pipeline of new biologics

Molecule	
Phase 3 Programs	
Aimovig™	Migraine prevention
Aranesp®	Myelodysplastic syndromes
BLINCYTO®	ALL
ENBREL	Psoriatic arthritis; Rheumatoid arthritis remission
EVENITY™	Postmenopausal osteoporosis; Male osteoporosis
IMLYGIC®	Metastatic melanoma
KYPROLIS®	Multiple myeloma
Omecamtiv mecarbil	Chronic heart failure
Prolia®	Glucocorticoid-induced osteoporosis
Tezepelumab	Asthma
AMG 520 / CNP520	Alzheimer's disease
Phase 2 Programs	
BLINCYTO®	Diffuse Large B-Cell Lymphoma (DLBCL)
Tezepelumab	Atopic dermatitis
AMG 301	Migraine prevention
AMG 557	Primary Sjögren's syndrome
AMG 714	Celiac disease

Amgen is also targeting biosimilars

(Source: Amgen Sept. 2020 Investor Presentation)



Composition of R&D: More D than R

Category	Description
Research and early pipeline	R&D expenses incurred in activities substantially in support of early research through the completion of phase 1 clinical trials, including drug discovery, toxicology, pharmacokinetics and drug metabolism, and process development
Later-stage clinical programs	R&D expenses incurred in or related to phase 2 and phase 3 clinical programs intended to result in registration of a new product or a new indication for an existing product primarily in the United States or the EU
Marketed products	R&D expenses incurred in support of the Company's marketed products that are authorized to be sold primarily in the United States or the EU. Includes clinical trials designed to gather information on product safety (certain of which may be required by regulatory authorities) and their product characteristics after regulatory approval has been obtained, as well as the costs of obtaining regulatory approval of a product in a new market after approval in either the United States or the EU has been obtained

	Years ended December 31,		
	2021	2020	2019
Research and early pipeline	$ 1,670	$ 1,405	$ 1,649
Later-stage clinical programs	1,726	1,365	1,062
Marketed products	1,423	1,437	1,405
Total R&D expense	$ 4,819	$ 4,207	$ 4,116

Revenue generated by the business is growing but profit is stagnant

AMGEN INC.

CONSOLIDATED STATEMENTS OF INCOME

Years ended December 31, 2021, 2020 and 2019

(In millions, except per-share data)

	2021	2020	2019
Revenues:			
Product sales	$ 24,297	$ 24,240	$ 22,204
Other revenues	1,682	1,184	1,158
Total revenues	25,979	25,424	23,362
Operating expenses:			
Cost of sales	6,454	6,159	4,356
Research and development	4,819	4,207	4,116
Acquired in-process research and development	1,505	—	—
Selling, general and administrative	5,368	5,730	5,150
Other	194	189	66
Total operating expenses	18,340	16,285	13,688
Operating income	7,639	9,139	9,674
Other income (expense):			
Interest expense, net	(1,197)	(1,262)	(1,289)
Other income, net	259	256	753
Income before income taxes	6,701	8,133	9,138
Provision for income taxes	808	869	1,296
Net income	$ 5,893	$ 7,264	$ 7,842

In 2021, Amgen increased share buybacks and dividends with little increase in net issue of debt – key item is the purchase in 2019 of Otezla from Celgene for "the only oral, non-biologic treatment for moderate-to-severe plaque psoriasis and psoriatic arthritis" for $13.4B

AMGEN INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

Years ended December 31, 2021, 2020 and 2019

(In millions)

	2021	2020	2019
Cash flows from investing activities:			
Purchases of marketable securities	(8,900)	(8,477)	(9,394)
Proceeds from sales of marketable securities	4,403	2,597	8,842
Proceeds from maturities of marketable securities	8,831	4,381	20,548
Purchases of property, plant and equipment	(880)	(608)	(618)
Cash paid for acquisitions, net of cash acquired	(2,529)	—	(13,617)
Purchases of equity method investments	(157)	(3,219)	(24)
Other	(35)	(75)	(28)
Net cash provided by (used in) investing activities	733	(5,401)	5,709
Cash flows from financing activities:			
Net proceeds from issuance of debt	4,945	8,914	—
Repayment of debt	(4,150)	(6,450)	(4,514)
Repurchases of common stock	(4,975)	(3,486)	(7,702)
Dividends paid	(4,013)	(3,755)	(3,509)
Other	(78)	(90)	(42)
Net cash used in financing activities	(8,271)	(4,867)	(15,767)

Stage II, III and EUA/CMA results for Vaccine Startups and Orphan Drugs

Zogenix

S,O versus P,O Phase III (positive implications)

Moderna: mRNA Technology

Rapid path to Revenue Generation from EUA

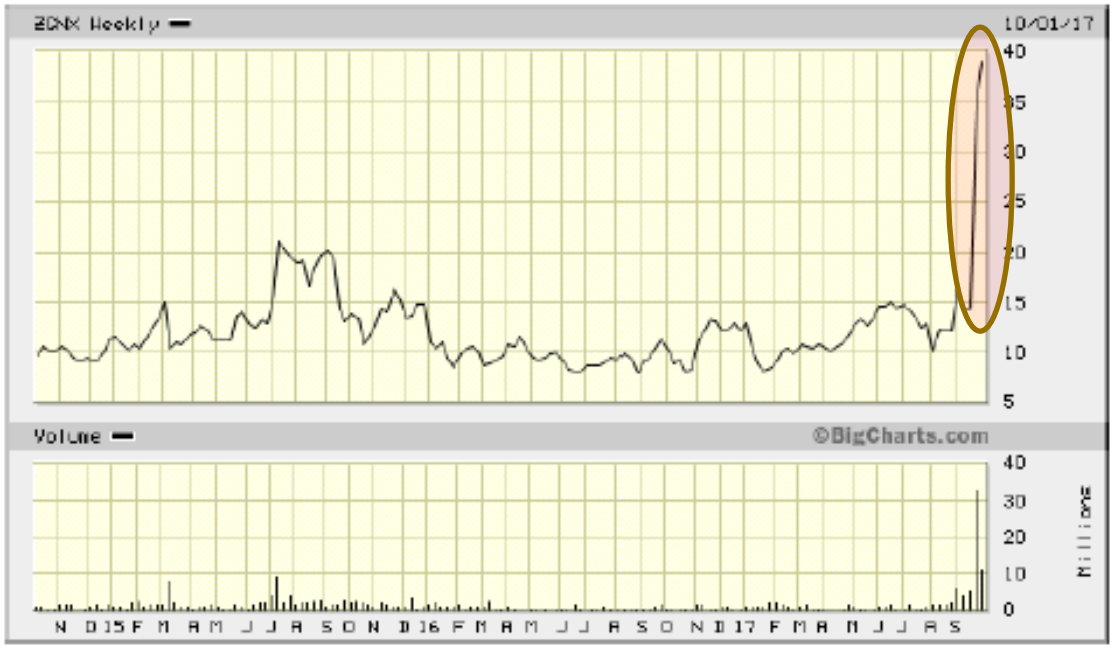
Novavax

Vaccine Awaiting and Acquiring Approval

The Upside of Successful Phase III Orphan Drug – **Zogenix** (ZGNX-Q) – Oct. 3, 2017

ZGNX Zogenix Inc. (NASDAQ) Delayed quote data 10/3/2017 04:00 PM

Last:	Change:	Open:	High:	Low:	Volume:
38.85	-0.05	38.50	40.40	37.80	8,905,075
	Percent Change:	Yield:	P/E Ratio:	52 Week Range:	
	-0.13%	n/a	n/a	7.50 to 41.65	
After Hours Trading 10/3/2017 04:41 PM		Last:	Change:	Volume:	
		39.00	+0.15	32,157	



Company Data

Company Name:	Zogenix Inc.
Dow Jones Industry:	Pharmaceuticals
Exchange:	NASDAQ

Zogenix®

News Release

Zogenix Announces Positive Top-line Results from Pivotal Phase 3 Clinical Trial of ZX008 in Dravet Syndrome

Primary Endpoint Achieved - Statistically Significant Convulsive Seizure Reduction for ZX008 versus Placebo for Adjunctive Treatment of Seizures

ZX008 Also Demonstrated Statistical Significance in All Key Secondary Endpoints

Zogenix to Host Conference Call Today at 8:30 AM Eastern Time/5:30 AM Pacific Time

EMERYVILLE, Calif., Sept. 29, 2017 (GLOBE NEWSWIRE) -- Zogenix, Inc. (NASDAQ:ZGNX), a pharmaceutical company developing therapies for the treatment of rare central nervous system (CNS) disorders, today reported positive top-line results from its first Phase 3 trial (Study 1) for its investigational drug, ZX008 (low-dose fenfluramine hydrochloride), for the treatment of Dravet syndrome. The trial met its primary objective of demonstrating that ZX008, at a dose of 0.8 mg/kg/day, is superior to placebo as adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on change in the frequency of convulsive seizures between the 6-week baseline observation period and the 14-week treatment period ($p<0.001$). ZX008 0.8 mg/kg/day also demonstrated statistically significant improvements versus placebo in all key secondary measures, including the proportion of patients with clinically meaningful reductions in seizure frequency and longest seizure-free interval. The same analyses comparing a 0.2 mg/kg/day ZX008 dose versus placebo also demonstrated statistically significant improvement compared with placebo.

"Dravet syndrome is a rare, but catastrophic form of epilepsy that can be devastating for patients and their families," said Joseph Sullivan M.D., director of the Pediatric Epilepsy Center in UCSF Benioff Children's Hospital San Francisco, and Principal Investigator of Study 1 in the U.S. "These results are truly exciting and demonstrate, in a large multicenter controlled trial, the impressive efficacy of low-dose fenfluramine for patients with Dravet syndrome. If approved, ZX008 could play an important role in treating this devastating condition."

Since the Phase III results: Generating revenues in 21-I but loss per share is double no revenue of 20-1

-- Sizable dilutive equity capital raise in 2020

-- Jan. 2022 Union Chimique Belge (UCB) acquires Zogenix at $26 per share

Moderna and the Rapid EUA timeline

- Company incorporated in 2010, operations commencing in 2011
  - Early financing in 2012 with sizeable Astra-Zeneca investment in 2013 and Merck in 2015
- First in-human dosing of mRNA in 2015 aimed at flu and immuno-oncology
  - First mRNA candidate to enter Phase II in 2018
- MRNA-Q listed on NASDAQ in Dec. 2018 at $23 following an earlier $2.5B capital raise in 2018
- Mar. 2020 MRNA receives Warp-Speed financing
  - mRNA-1273 (COVID vaccine) enters Phase I in July
  - Phase III trials completed in Dec. 2020

MRNA, Current Market Capitalization = $69B

2020 Product Revenues of $275M; Net Income -$747M

Moderna 22-Q3 Revenue Stream and Earnings are from only commercial product: COVID vaccine

MODERNA, INC.
CONDENSED CONSOLIDATED STATEMENTS OF INCOME
(Unaudited, in millions, except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenue:				
Product sales	$ 3,120	$ 4,810	$ 13,576	$ 10,740
Grant revenue	144	140	453	473
Collaboration revenue	100	19	150	47
Total revenue	3,364	4,969	14,179	11,260
Operating expenses:				
Cost of sales	1,100	722	3,498	1,665
Research and development	820	521	2,084	1,343
Selling, general and administrative	278	168	757	366
Total operating expenses	2,198	1,411	6,339	3,374
Income from operations	1,166	3,558	7,840	7,886
Interest income	58	4	113	11
Other expense, net	(7)	(10)	(33)	(22)
Income before income taxes	1,217	3,552	7,920	7,875
Provision for income taxes	174	219	1,023	541
Net income	$ 1,043	$ 3,333	$ 6,897	$ 7,334

The Novavax Saga

- Company formed in 1987 but did not go public (on the AMEX) until 1996
  - Basis of IPO was two products to deliver estrogen (Estrasorb) and testosterone (Androsorb) through the skin
  - Estrasorb reaches Phase III trials in 1999
- 2001 switches listing to NASDAQ in conjunction with plans to market Estrasorb in several countries
- 2002-3 FDA accepts NDA and approves Estrasorb for production and sale
- 2006 transitions to development of influenza vaccine and micellar nanoparticle testosterone medicine (for female hypoactive sex disorder)

The progression to the COVID vaccine

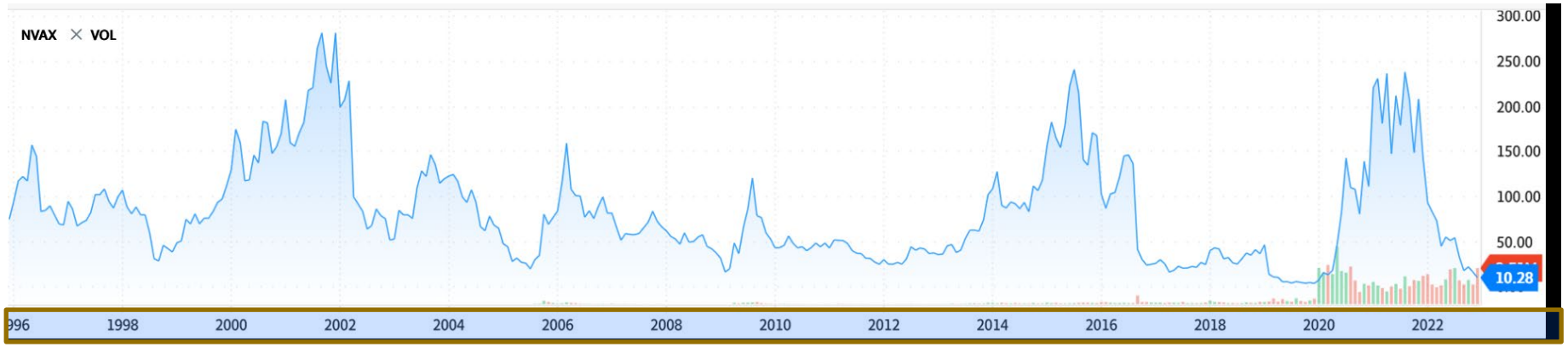
- 2007 Key step taken with acquisition of rights to VLP (virus-like particle) technology
  - 2008 Novavax exits from Estrasorb
- 2008-12 enters agreements with European and Indian companies to develop VLP for influenza
  - Also involved in vaccines for rabies and foot and mouth disease in animals
- 2013 develops vaccine candidate for MERS
- 2016 develops nano-particle vaccine candidate
- Mar. 2020 starts work on COVID vaccine
  - June 2021 Phase III trials in UK and other countries nearing completion with Sept delay in US
  - July 19, 2022 cleared for adult use in US by CDC

NVAX,

Market Capitalization = $4.7B 2020 ($807M 1/1/23)

2020 Product Revenues = $0 Net Income = -$416 M

2020 Grants + Govt. Contracts = $475.6 M



Earnings losses accelerating, Profits coming?

	Year Ended December 31,		
	2021	2020	2019
Revenue:			
Grants	$ 948,709	$ 453,210	$ 15,937
Royalties and other	197,581	22,388	2,725
Total revenue	1,146,290	475,598	18,662
Expenses:			
Research and development	2,534,508	747,027	113,842
Gain on sale of assets	—	—	(9,016)
General and administrative	298,358	145,290	34,417
Total expenses	2,832,866	892,317	139,243
Loss from operations	(1,686,576)	(416,719)	(120,581)
Other income (expense):			
Investment income	1,364	1,014	1,512
Interest expense	(21,127)	(15,145)	(13,612)
Other income (expense)	(8,197)	12,591	(13)
Loss before income tax expense	(1,714,536)	(418,259)	(132,694)
Income tax expense	29,215	—	—
Net loss	$ (1,743,751)	$ (418,259)	$ (132,694)

Novavax Income Statement 22Q3 (10-Q)– finally some non-grant income but still losing money – will the company ever make positive income?

NOVAVAX, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share information)
(unaudited)

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenue:				
Product sales	$ 626,091	$ —	$ 1,267,174	$ —
Grants	106,273	135,007	313,348	854,390
Royalties and other	2,213	43,837	43,951	69,700
Total revenue	734,577	178,844	1,624,473	924,090
Expenses:				
Cost of sales	434,593	—	720,874	—
Research and development	304,297	408,195	977,428	1,571,551
Selling, general, and administrative	122,876	77,793	327,028	214,144
Total expenses	861,766	485,988	2,025,330	1,785,695
Loss from operations	(127,189)	(307,144)	(400,857)	(861,605)
Other expense:				
Interest expense	(4,169)	(5,182)	(15,279)	(15,989)
Other expense	(34,783)	(4,064)	(53,002)	(7,267)
Loss before income tax expense	(166,141)	(316,390)	(469,138)	(884,861)
Income tax expense	2,472	6,041	6,552	12,606
Net loss	$ (168,613)	$ (322,431)	$ (475,690)	$ (897,467)

Valeant Pharmaceuticals, Purdue Pharma and the rise of SPAC's

- Specialty Pharmas and Drug Repricing
  - Hedge Funds and Pharma Takeovers
- Controlling Bad Actors?
  - Legal Implications of the Prescription Opioid Epidemic
  - What are the implications of SPAC funding conduits for early stage bio-tech companies
- SPAC's and Bio-Tech Startup's
  - Another pending Hedge Fund Debacle?

Medical Ethics versus Business Ethics

- Though the present AMA code of ethics and related opinions have evolved considerably from the early beginnings of the Hippocratic Oath and the Percival code (1847), basic principles still remain:
  - physicians should base clinical practice and research on the best science available;
  - individual self-interest is secondary to the well being of the patient;
  - and, medical knowledge is a public trust to be used to the benefit of patients and society.

- The ‘medical profession’ includes not only practicing doctors and associations of doctors but also: the pharmaceutical and medical device industry, providing the drugs and medical technologies that are an essential component of modern medicine
  - Shareholder wealth maximization is the guiding ethical principle for the large corporations that dominate the drugs and devices industry

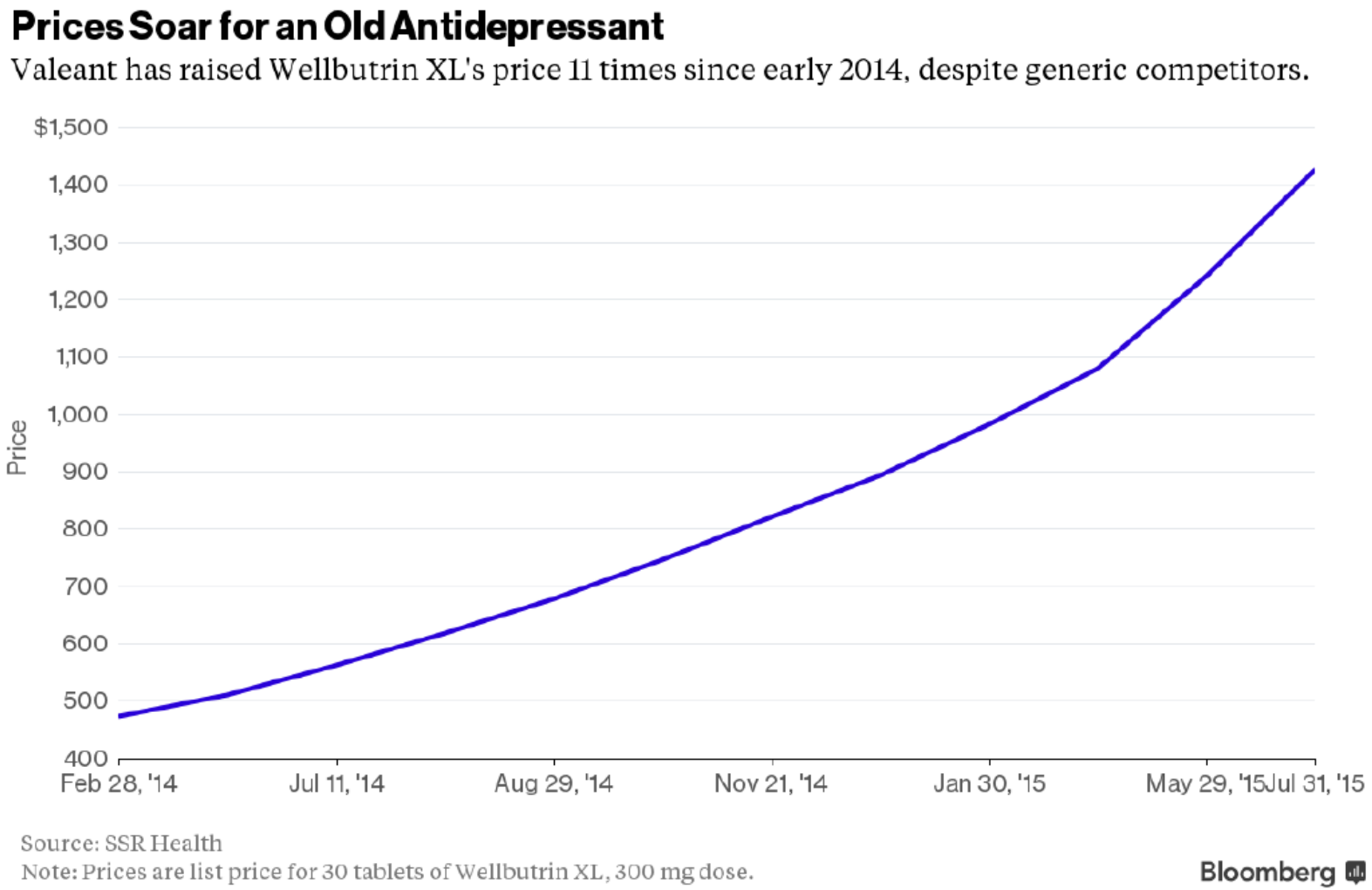
Valeant Pharmaceuticals:

Dramatic Drug Re-pricing Business Strategy

"Valeant is known for buying companies and laying off their employees to achieve savings, while accumulating a debt of about $30 billion. It spends an amount equivalent to only 3 percent of its sales on research and development, which it views as risky and inefficient compared with buying existing drugs. …Valeant also pays extremely low taxes because it is officially based in Canada, although Mr. Pearson operates from New Jersey." *— New York Times 4 October 2015*

Valeant (now Bausch Health) is one of several companies that engaged in purchasing 'unprofitable' older drugs and then dramatically hiking prices – others in 2015 include Turing Pharmaceuticals raising Daraprim (toxoplasmosis) from $13.50 to $750 per pill; Rodelis Therapeutics initially raised Cycloserine (tuberculosis) from $500 for 30 pills to over $10,000 (later rolled back to $1050).

Valeant and the re-pricing of Wellbutrin XL



Valeant Pharmaceuticals:
The Philidor Rx Services LLC Fraud

- An essential feature of the Valeant drug marketing strategy was the wholesale distributor Philidor Rx formed in 2013 with the assistance/subsidization of Valeant
  - See next slide for a diagram of the marketing of US pharmaceuticals
  - The Drug Supply chain in the US is regulated by Title II of the Drug Quality and Security Act a 2013 amendment to the Federal Food, **Drug**, **and** Cosmetic **Act** (https://www.fda.gov/media/93789/download)
- Philidor engaged in various dubious strategies to market Valeant drugs (funneling sales through captive pharmacies, circumventing licensing laws)
- A senior Valeant exec and Philidor CEO sentenced for fraud associated with payment for a Valeant option to buy Philidor
- For results of the federal trial of Tanner (Valeant exec) and Davenport (Philidor CEO) https://www.justice.gov/usao-sdny/pr/former-valeant-executive-and-former-philidor-ceo-sentenced-illegal-kickback-scheme

The U.S. Pharmacy Distribution and Reimbursement System for Patient-Administered, Outpatient Prescription Drugs

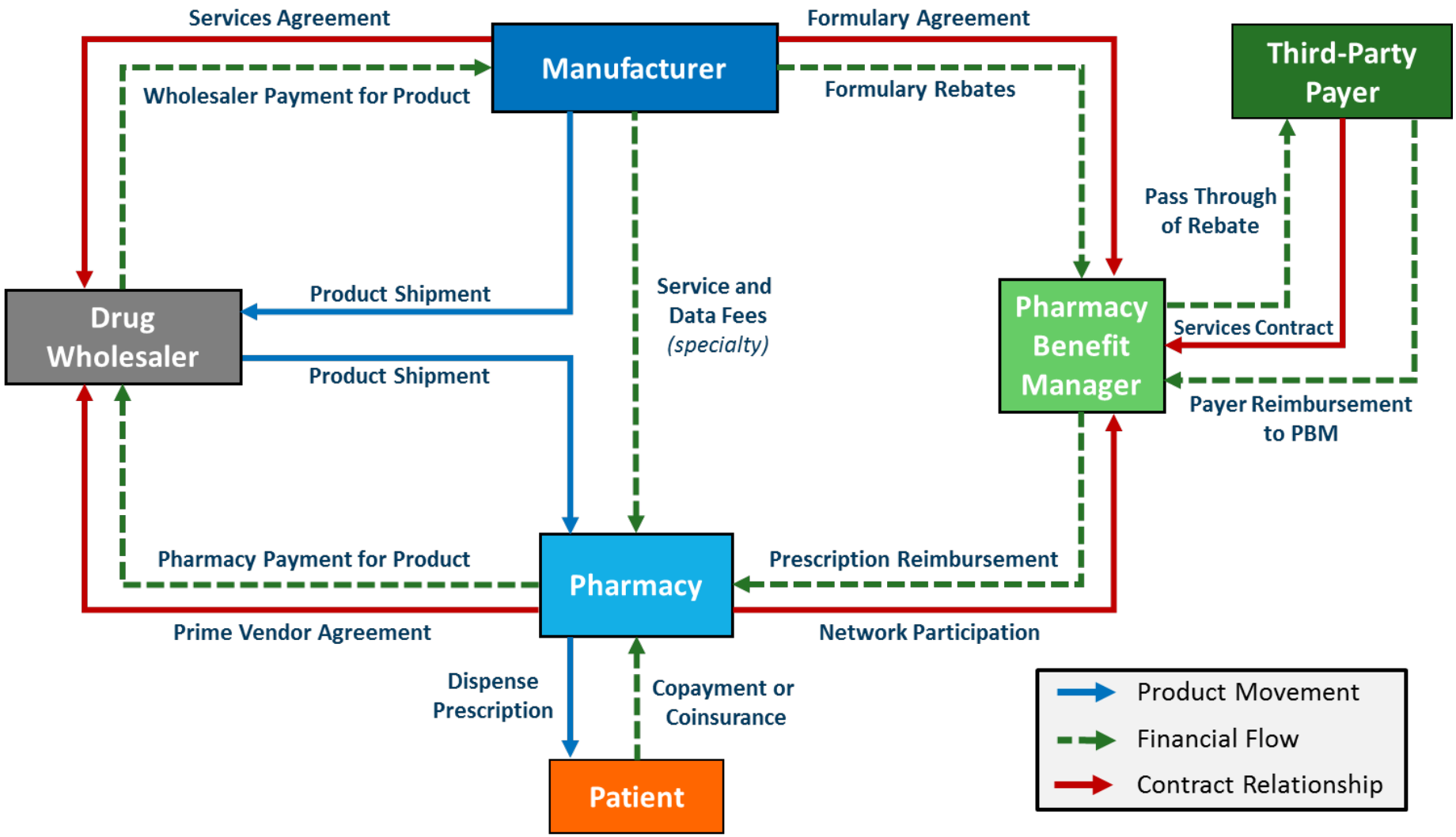


Chart illustrates flows for patient-administered, outpatient drugs. Please note that this chart is illustrative. It is not intended to be a complete representation of every type of financial, product flow, or contractual relationship in the marketplace.

Source: Fein, Adam. J., *The 2016 Economic Report on Retail, Mail and Specialty Pharmacies*, Drug Channels Institute, January 2016. (Available at http://drugchannelsinstitute.com/products/industry_report/pharmacy/)

Valeant Pharma: Assets, Goodwill and Intangibles from an Acquisitions Strategy

VALEANT PHARMACEUTICALS INTERNATIONAL, INC.
CONSOLIDATED BALANCE SHEETS
(All dollar amounts expressed in millions of U.S. dollars)

	As of December 31,	
	2015	2014 (Restated)
Assets		
Current assets:		
Cash and cash equivalents	$ 597.3	$ 322.6
Trade receivables, net	2,686.9	2,075.8
Inventories, net	1,256.6	889.2
Prepaid expenses and other current assets	966.4	650.8
Deferred tax assets, net (Note 3)	—	193.3
Total current assets	5,507.2	4,131.7
Property, plant and equipment, net	1,441.8	1,312.3
Intangible assets, net	23,083.0	11,277.9
Goodwill	18,552.8	9,361.4
Deferred tax assets, net	156.0	54.0
Other long-term assets, net	223.7	167.4
Total assets	$ 48,964.5	$ 26,304.7

Valeant Pharma: Long Term Debt to Equity 5x

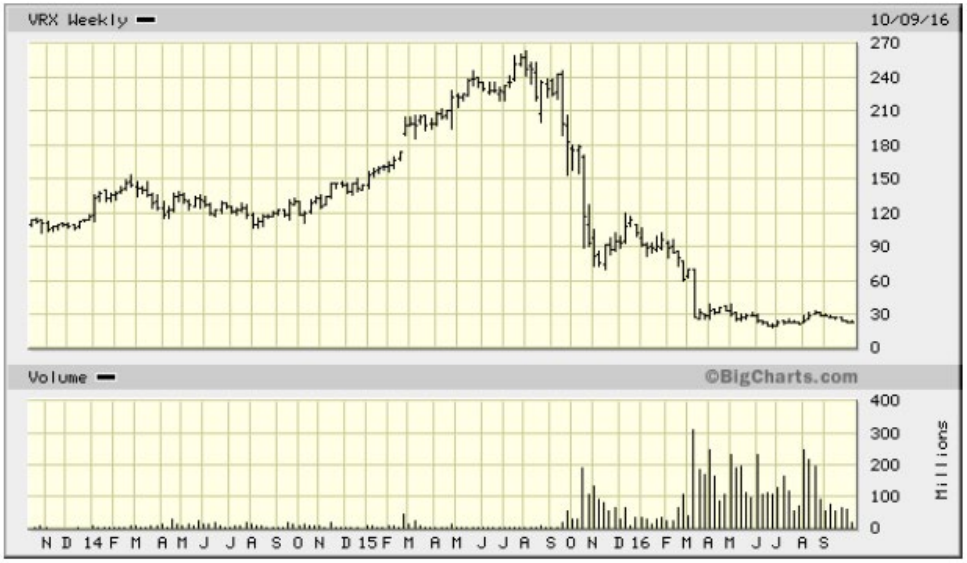
(PFE is about ½ x)

Liabilities		
Current liabilities:		
Accounts payable	$ 433.7	$ 398.0
Accrued and other current liabilities	3,859.1	2,157.0
Acquisition-related contingent consideration	196.8	141.8
Current portion of long-term debt	823.0	0.9
Deferred tax liabilities, net (Note 3)	—	10.7
Total current liabilities	5,312.6	2,708.4
Acquisition-related contingent consideration	959.1	205.8
Long-term debt	30,265.4	15,228.0
Pension and other benefit liabilities	190.4	239.8
Liabilities for uncertain tax positions	120.2	102.6
Deferred tax liabilities, net	5,902.4	2,221.3
Other long-term liabilities	184.6	197.1
Total liabilities	42,934.7	20,903.0
Commitments and contingencies (Notes 21 and 22)		
Equity		
Common shares, no par value, unlimited shares authorized, 342,926,531 and 334,402,964 issued and outstanding at December 31, 2015 and 2014, respectively	9,897.4	8,349.2
Additional paid-in capital	304.9	243.9
Accumulated deficit	(2,749.7)	(2,397.8)
Accumulated other comprehensive loss	(1,541.6)	(915.9)
Total Valeant Pharmaceuticals International, Inc. shareholders' equity	5,911.0	5,279.4
Noncontrolling interest	118.8	122.3
Total equity	6,029.8	5,401.7
Total liabilities and equity	$ 48,964.5	$ 26,304.7

Stock Price Implications of Aggressive Pricing: Valeant, Concordia and Mylan

VRX Valeant Pharmaceuticals International Inc. (NYSE) Delayed quote data 10/12/2016 12:23 PM

Last:	Change:	Open:	High:	Low:	Volume:
22.81	-0.13	22.85	23.36	22.7265	5,652,542
	Percent Change:	Yield:	P/E Ratio:	52 Week Range:	
	-0.57%	n/a	n/a	18.55 to 179.83	

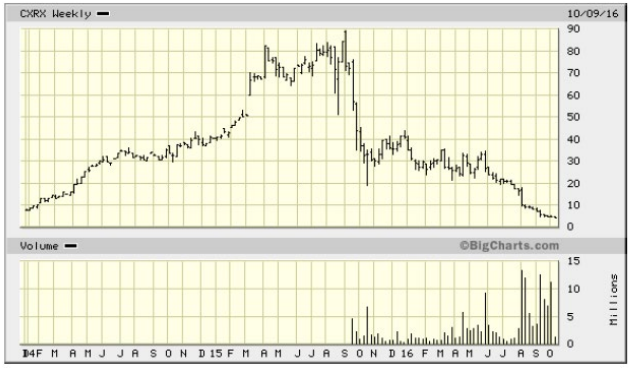


MYL Mylan N.V. (NASDAQ) Delayed quote data 10/12/2016 12:28 PM

Last:	Change:	Open:	High:	Low:	Volume:
37.3011	-1.0089	38.22	38.35	37.08	4,120,008
	Percent Change:	Yield:	P/E Ratio:	52 Week Range:	
	-2.63%	n/a	23.7587	35.58 to 55.505	

CXRX Concordia International Corp. (NASDAQ) Delayed quote data 10/12/2016 12:34 PM

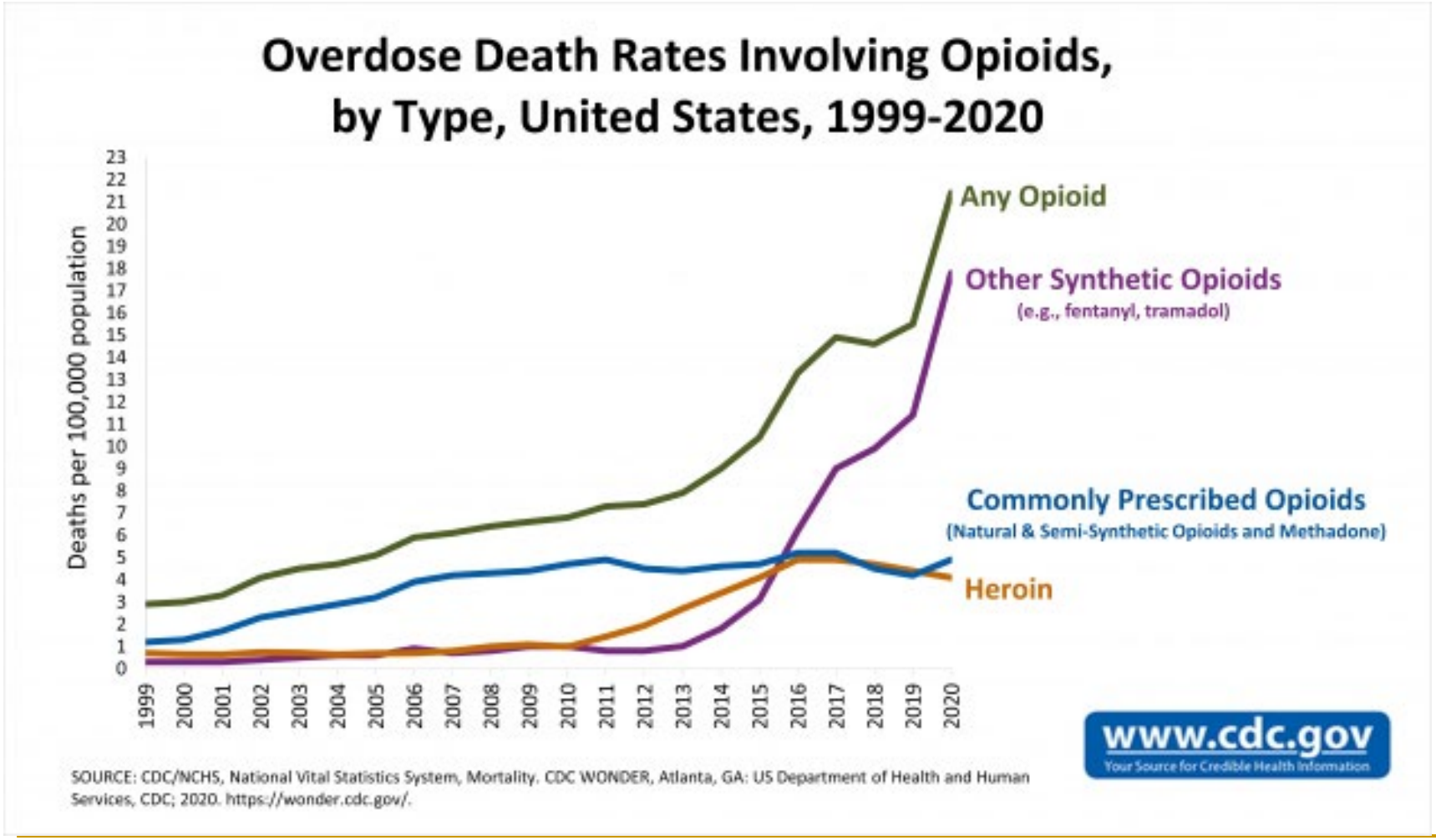
Last:	Change:	Open:	High:	Low:	Volume:
4.34	+0.03	4.27	4.45	4.26	471,840
	Percent Change:	Yield:	P/E Ratio:	52 Week Range:	
	+0.70%	6.91%	n/a	4.26 to 44.00	



The Opioid Epidemic in the US

- From 4/20 to 4/21 more than 100,000 people died in the U.S. from overdoses (75% from opioids), an increase of 28.5% from previous year
- From 1999-2019 nearly 500,000 people in the US died from opioid overdoses (including both licit and illicit sources)
- The CDC reports that 38 Americans die daily from prescription opioid overdoses.
- The epidemic cost the American economy $700 billion in 2018, which was the equivalent of 3.4 percent of gross domestic product that year, according to the Council of Economic Advisers.

Dramatic Changes in the US Opioid Epidemic:
Note: Classification of deaths is problematic, in many deaths multiple drugs are involved, in 2018 8% of drug overdose deaths no specific drug listed on death cert.



Purdue Pharma and the Opioid Epidemic

- Purdue Pharma Is privately held, initially owned by the Sackler family – one of the richest families in America
  - Company is best known for development, promotion and marketing of opioid Oxycontin as 'effective relatively non-addictive form of pain relief' → original formulation of Oxycontin abused by crushing and snorting
  - Launched in 1995, by 2003 Oxycontin sales reached $1.6 billion annually → in 2007 paid $600 million fine (and three executives spend time in jail) for deceptive marketing practices
  - Purdue Pharma subsequently involved in lawsuits by state A-G's and local govt's to recover costs associated with the Opioid Epidemic
  - Sept. 15, 2019 Purdue Pharma files for chapter 11 bankruptcy protection after announcing a tentative deal with about half the states and more than 1,000 local governments.
    - Dec. 16, 2021 federal judge in NY overturns deal that would give legal immunity to Sackler family in exchange for $4.5B payment
  - Mar. 10, 2022 US bankruptcy judge approves $6b settlement with Purdue Pharm and Sackler family

MDL 2804 Developments

- The multitude of civil cases, most of which initiated by government entities, seeking to recover costs of the opioid epidemic resulted in attempt to consolidate most cases into a federal 'National Prescription Opiate' Multidistrict Litigation (MDL) in the Northern Dist. of Ohio, Sept. 29, 2017 https://www.opioidsnegotiationclass.info:
  - 'The largest civil trial in US history' aimed to involve most of the 2500 civil cases → difficult to estimate outcomes as 'bell weather' cases delayed by a COVID continuance – could have a total settlement cost in excess of $250 billion
- Companies involved in legal battles over costs of the epidemic include the drug manufacturers and distribution companies Purdue Pharma (now bankrupt), Endo, Mallinckrodt, Teva , Janssen, Cardinal, McKesson, AmerisourceBergen, CVS and Walgreens
  - Also involves smaller pharmacies and physicians

Recent MDL (2804) developments

In September 2020, the 6th U.S. Circuit Court of Appeals overturned the certification of a so-called "negotiating class" in the vast opioid MDL (MDL 2804). This negotiating class was to be comprised of all the local governments that might receive money in settlements with the opioid defendants.

The National Prescription Opiate Litigation overseen by U.S. District Judge Dan Polster in the Northern District of Ohio proceeds with several bellwether trials, continued due to COVID-19, starting in January through May 2021 in Ohio, West Virginia, and New York.

Ongoing legal wrangling about the key 'public nuisance' theory of the case with some federal and state judges rejecting the theory and maintaining Judge Posner is 'out of step' on this approach

Most recently July 6, 2022 in W. Virginia

MDL and Other Decisions Beginning

- Nov. 23, 2021, federal jury in MDL 2804 finds CVS, Walgreens and Walmart liable for fueling the US opioid crisis (damages to be determined)
  - Likely to influence the thousands of similar cases not incorporated in the MDL that are on-going throughout the US
  - Basis for decision was activities in two counties in Ohio that were the location of large quantities of prescription opioids
  - Speakers for the pharmacy chains claim a ‘flawed verdict’ engineered by judge Polster to favor the plaintiffs
  - Also in Nov., Oklahoma Supreme Court overturned a $400+ million judgment against J&J
    - The basis for the decision was related to the ‘nuisance’ argument that was the basis for the MDL decision
    - State judge in California also declined to hold drug companies liable

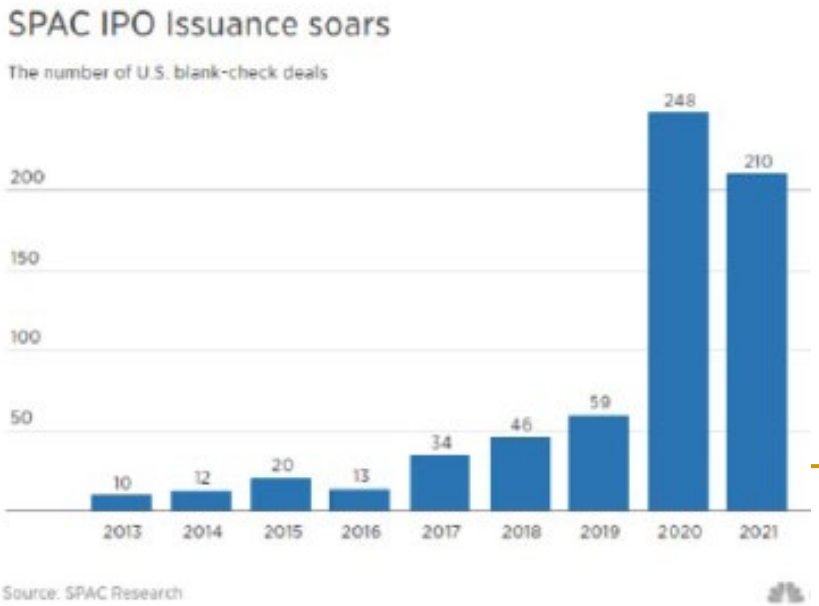
Important Recent Legal Developments

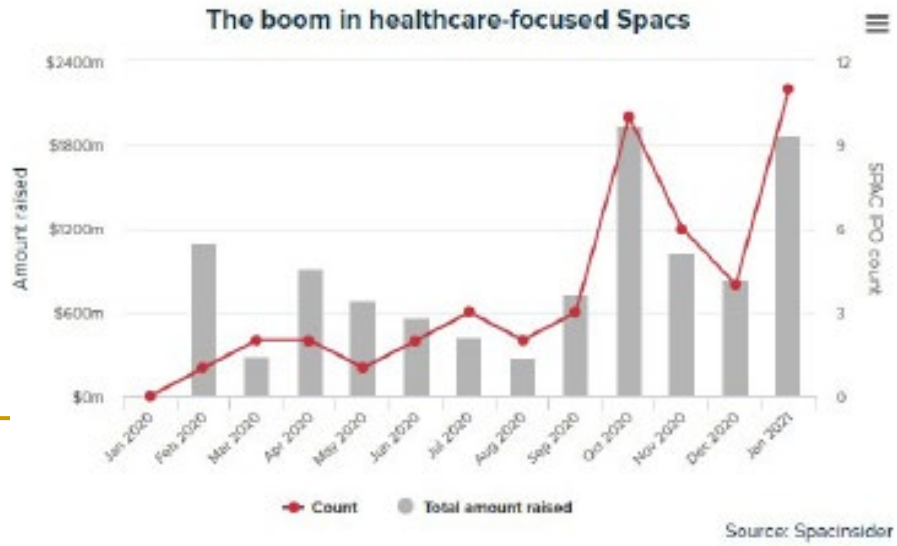
- Opioid litigation cases not yet resolved were in some instances delayed waiting for a SCOTUS decision in Ruan vs. USA (decided June 27, 2022)
  - https://www.supremecourt.gov/opinions/21pdf/20-1410_1an2.pdf
- Ruan is a medical doctor licensed to prescribe controlled substances
  - Ruan tried for violating 21 U. S. C. §841, which makes it a federal crime, 'except as authorized for any person knowingly or intentionally to manufacture, distribute, or dispense a controlled substance.'
  - Prescribing is only legal if "issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his professional practice."
  - Ruan vs. USA introduces a more stringent standard for prosecutors to prove doctors "knowingly" wrote invalid opioid prescriptions
- Walmart and other pharmacies now arguing that Ruan applies to their cases – denying prosecutors the ability to use statistics about number of prescriptions issued.

The 2019 explosion of SPAC's for bio-tech startup funding → Diminishing in 2022

A SPAC is a Special Purpose Acquisition Company – often referred to as a 'blank cheque' company

-- Instead of going the traditional IPO route to raise funds, a SPAC is organized as a publicly traded shell company that aims to acquire a target company (usually privately held)





Questions about the role of SPAC's

- The implications of SPAC's for the financing of start-up bio-tech firms is unclear
  - Why are the 'smart money' players so keen to target this sector?
    - If the motivation is to profit from re-pricing then does this mean that the large cap bio-pharmas will have to pay more? → instead of providing needed capital, the end product may be to discourage development and innovation
- SPAC's are financing vehicles that can avoid the rules and reg's associated traditional IPO's, the use of such corporate shells has a checkered history

Thank you for listening

More info about presenter at
http://www.sfu.ca/~poitras

QUESTIONS (time permitting)?