Rising Cost of Pharmacy

Presented by

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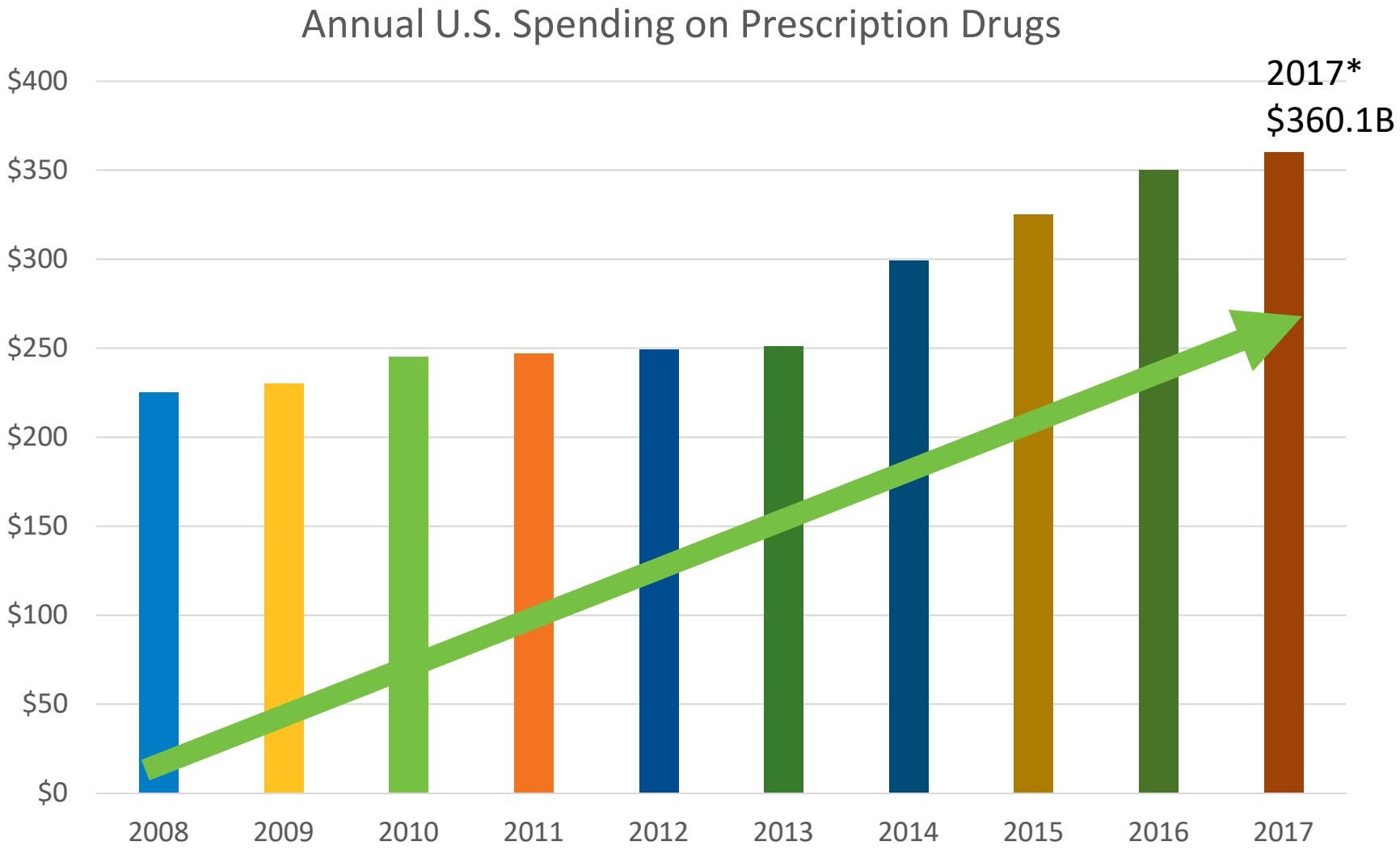
Why Do Drugs Cost So Much?

AGENDA

- Spending in US vs Other Countries
- Lobbying
- Research & Development of Complex Molecules
- Rare Diseases & Technology (Gene Therapy)
- Specialty Medications /Orphan Drug Act
- Formulary & Rebates
- Fewer generic manufacturers
- Predatory Business Practices

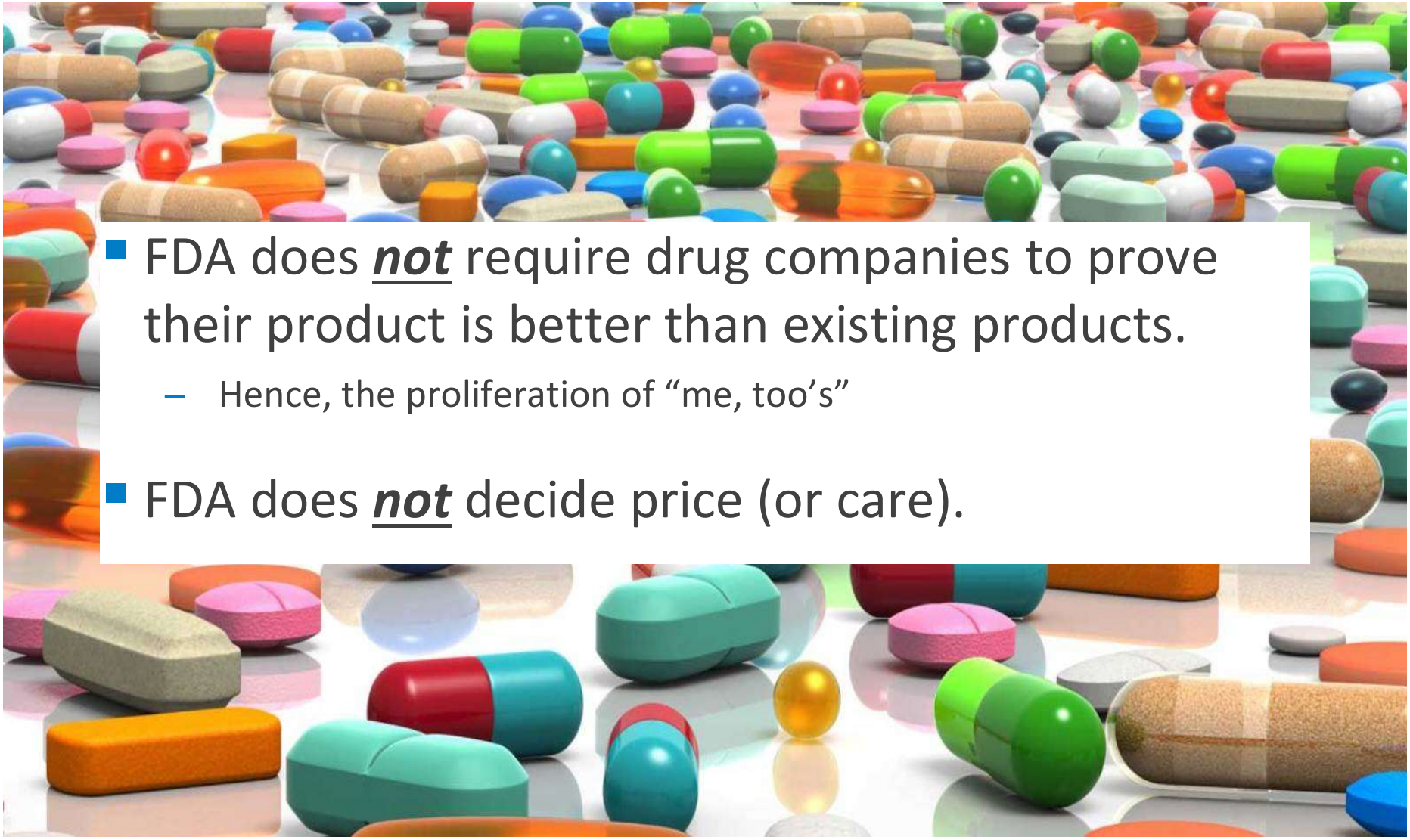
PHARMACEUTICAL COSTS IN THE U.S.

$360B U.S. Drug Spend



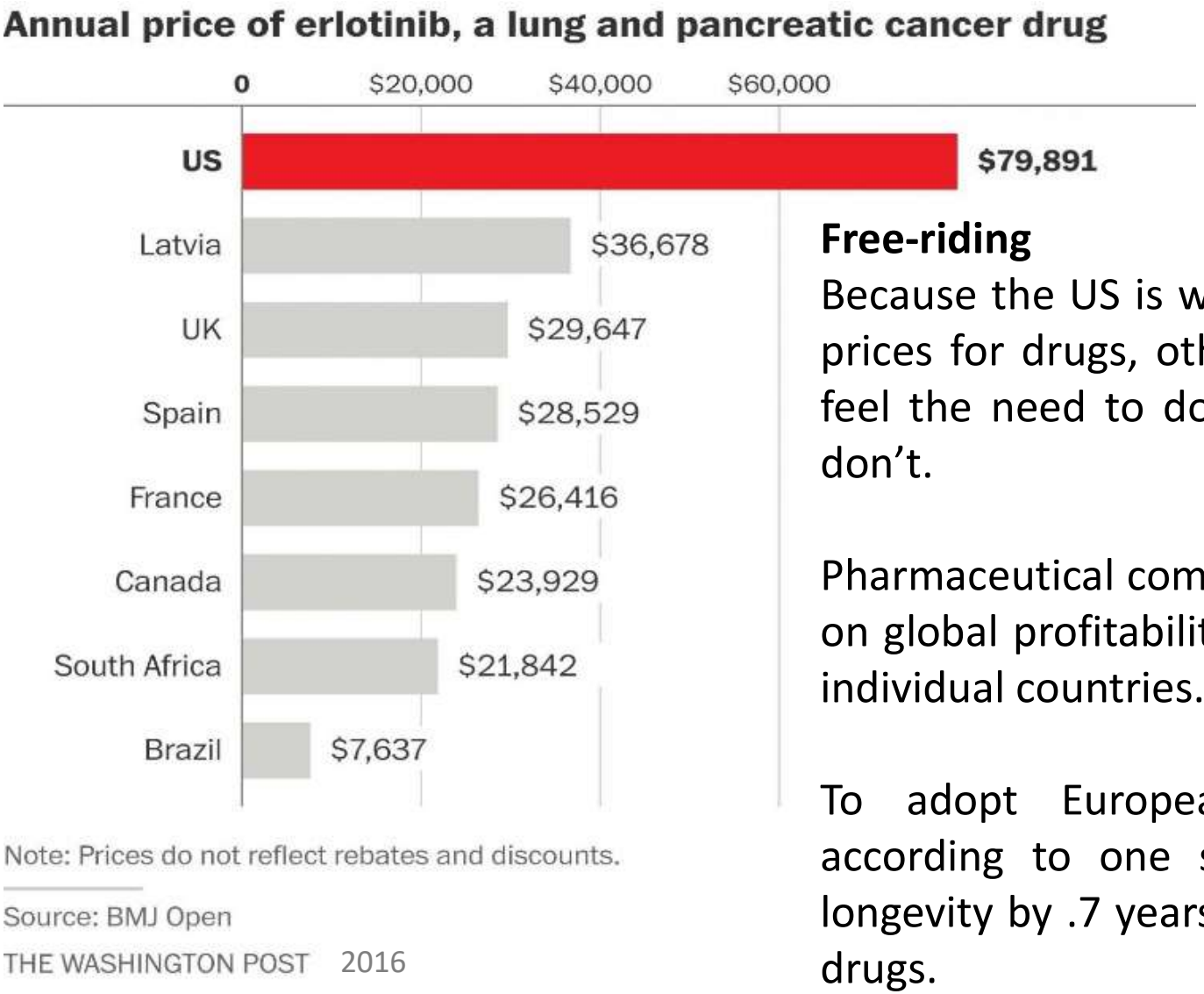
*Estimate; Source: U.S. Centers for Medicare and Medicaid Services U.S. Drug Spending Climbs, Peter Loftus, The Wall Street Journal

What the FDA Does Not Do



- FDA does ***not*** require drug companies to prove their product is better than existing products.
  - Hence, the proliferation of “me, too’s”
- FDA does ***not*** decide price (or care).

Why Does the U.S. Pay More for Drugs?



Free-riding

Because the US is willing to pay higher prices for drugs, other countries don't feel the need to do so and therefore, don't.

Pharmaceutical companies concentrate on global profitability- not profits from individual countries.

To adopt European cost controls, according to one study, would drop longevity by .7 years due to fewer new drugs.

U.S. comprises 42% of global pharmaceutical revenues

Other countries do not face this trade off

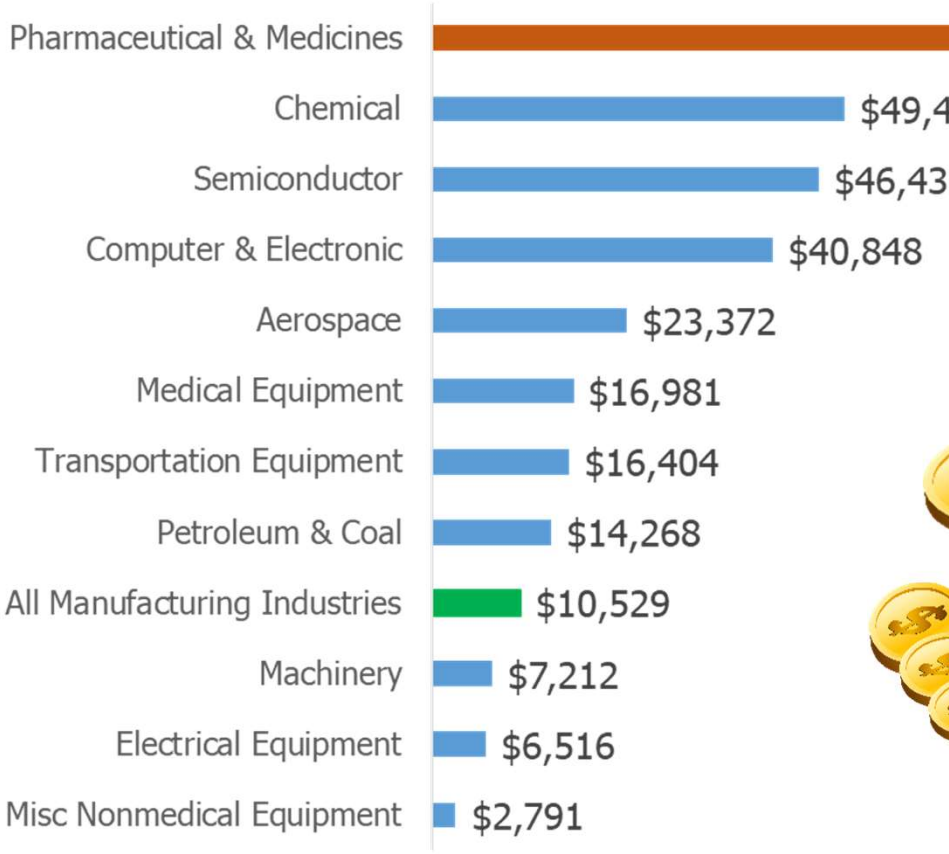
Reducing pharma profits and lowering drug prices….Does this create an innovation- access trade off

- **Only 1 out of 12.5 potential drugs ever reach potential patients**
- **The average drug takes 11-14 years to develop**
- **And, the cost to bring a drug to market is $1 to $2.6 Billion**
- **Individual countries behave - individually**

Source: Anupam Jena, Professor Harvard Medical School, internist Massachusetts General Hospital, faculty research fellow at National Bureau of Economic Research

The Biopharmaceutical Sector is the *Most R&D Intensive* in the U.S.

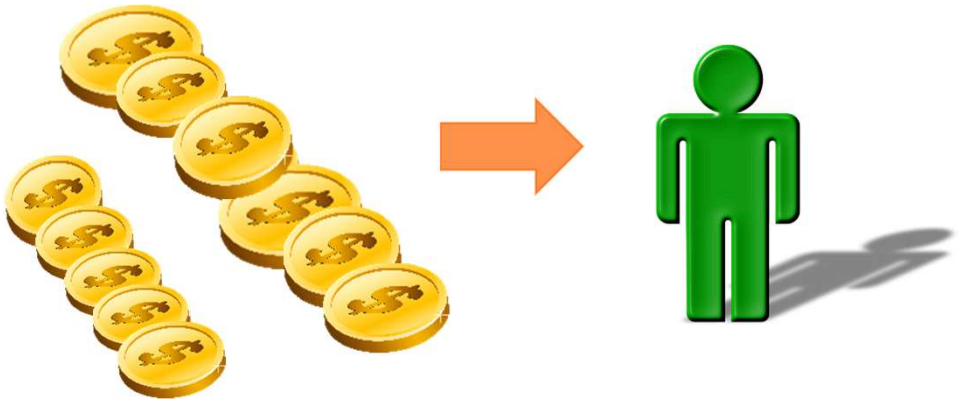
R&D Expenditures per Employee by Manufacturing Sector and Industry 2000-2010



Biopharmaceutical companies invested more than

12 TIMES THE AMOUNT OF R & D PER EMPLOYEE

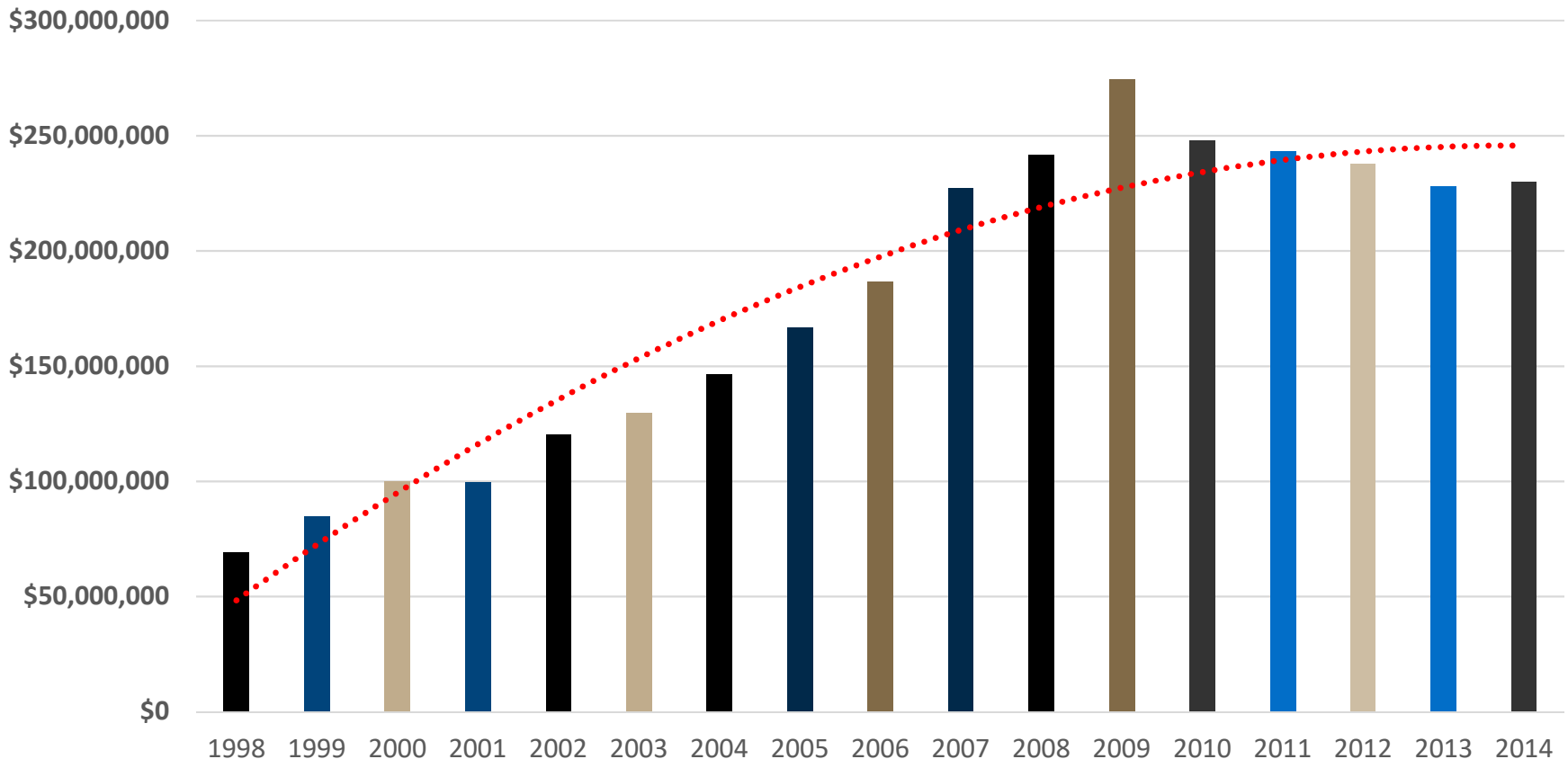
than manufacturing industries overall



Source: IP-intensive manufacturing industries: driving US economic growth. Washington, DC: NDP Analytics; 2015.

Lobbying in the U.S.

Annual Lobbying on Pharm/Health Products



Total for Pharmaceutical/Health Products in 2014: $230,071,063
Total Number of Clients Reported: 350
Total Number of Lobbyists Reported: 1,412
Total Number of Revolvers: 834 (59.1% of Lobbyists)

RARE DISEASES

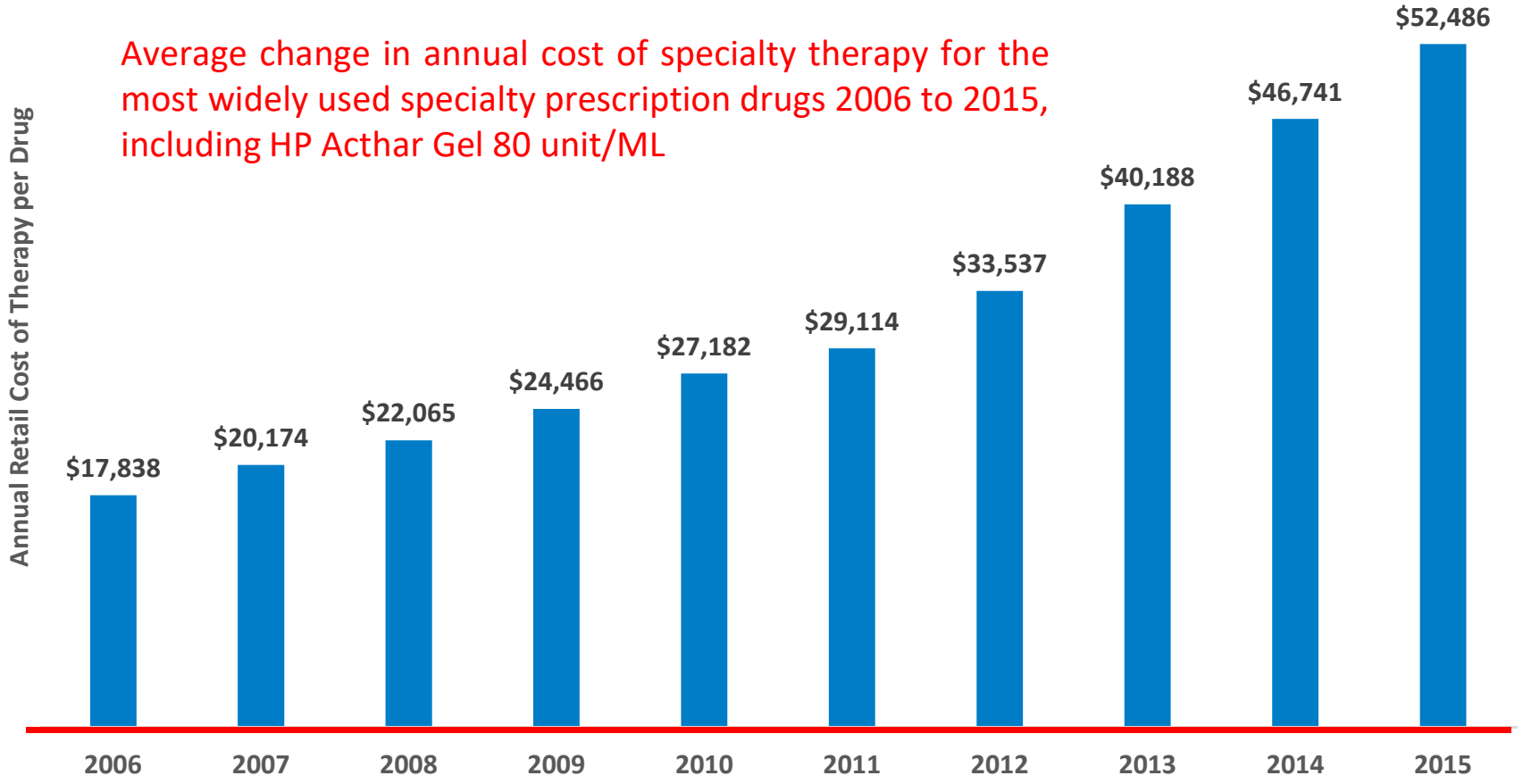
R&D Movement to Rare Diseases

Manufacturer's Focus Shifts to Billion $$ Drugs

- Focus on mass-marketing, i.e. drugs for cholesterol, heart, and diabetes
- Cheap generics eroded billions $$ in annual revenue
- Investors punishing Pharma stock price for relying on one drug and not having a robust pipeline

- Specialty meds and rare disease drugs- cost less to develop & face less competition
- Taking old drugs and remarketing them at egregious prices
- Mergers & acquisitions Bristol-Myers Squibb agreed to pay $74 B in cash and stock for Celegene

Change in Cost of Specialty Therapy



Source: Prepared by the AARP Public Policy Institute and the PRIME *Institute, University of Minnesota, based on data from Truven Health MarketScan® Research Databases.*

Specialty Drug Inflation

Specialty drug prices increased more than 80X faster than general inflation in 2015

Source: AARP's Public Policy Institute, "Trends in Retail Specialty Meds"

Patient Assistance

"Providing help to patients by paying co-pays, helping overcome insurance barriers and even giving it away free helps individual patients, but also insulates the drug company from criticism of its price."

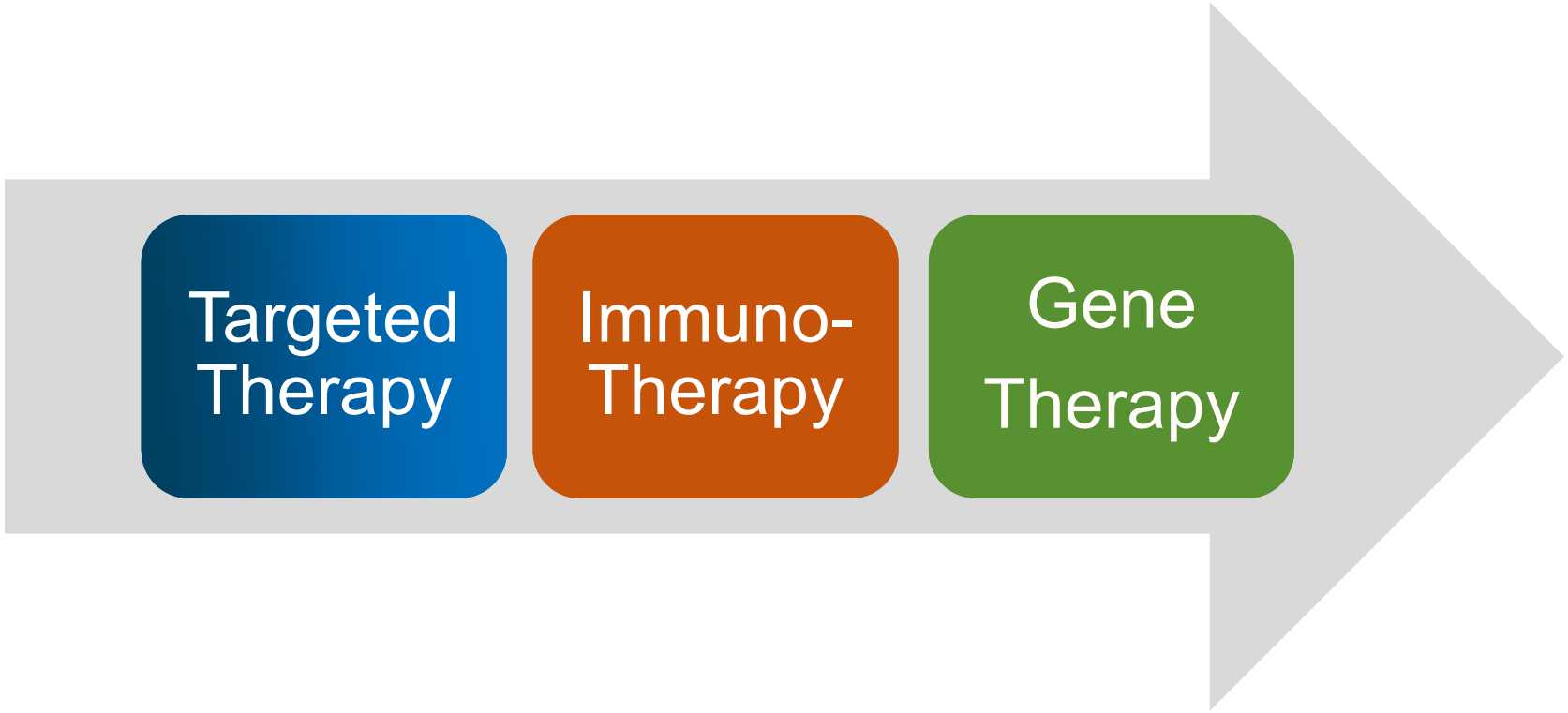
Pharma Invests in Rare Diseases

- Definition of rare disease: affect < 200,000 people in U.S.
  - 7,000 known rare diseases (1 in 10 Americans have a rare disease) = 30M people
- Most rare diseases are caused by a single gene mutation.
- Mapping of the human genome, sophisticated and affordable genetic tests and laboratory robots screening thousands of compounds an hour.
- For most rare diseases, there is no treatment let alone a cure.
- 30% of children die before age 5.

Source: https://rarediseases.info.nih.gov/diseases; FDA.gov

Cancer Therapy is Changing

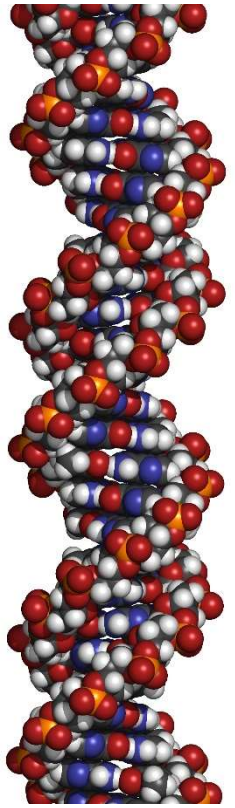
Traditonal Chemotherapy is fading in lieu of the following



What is Gene Therapy?

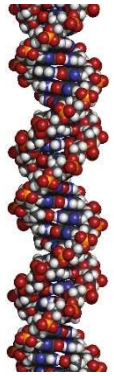
CRISPR Gene Editing- Luxturna cost $850,000

- Gene Therapy delivers a healthy gene to cells that are diseased because they lack that functioning gene.
- The gene carrier is typically an inactive virus. Virus then drops the healthy gene into the diseased cell.
- While the concept is simple, how do you deliver that genetic material (DNA or RNA) to the appropriate cell w/n the affected organ.



CRISPR-Cas9 Therapy

Clustered Regularly Interspaced Short Palindromic Repeats



- Genome editing or the ability to change an organism's DNA
  - Allow genetic material to be added, removed or altered
  - Faster, cheaper and more accurate then other genome editing methods
- Was first adapted using bacteria
- Scientists are still working to determine whether this approach is safe and effective for use in people. It is being explored in research on a wide variety of diseases:
  - Single-gene disorders such as cystic fibrosis, hemophilia, and sickle cell disease
  - Treatment and prevention of more complex diseases, such as cancer, heart disease, mental illness, and human immunodeficiency virus (HIV) infection.

Source: NIH.gov

Car-T Cell Therapy

Successfully used in blood cancers

- Immune system fails to see cancer cells as a threat.
- The healthy T-cells are altered (reprogrammed) and are infused into the patient. The cells include a new gene (CAR receptor), directing T-cells to target and kill leukemia cells.
- Therapy is $450,000 +
- Therapy is a one-time event. Works or doesn't.
- Philadelphia Children's Hospital trials involve juvenile (ALL) acute lymphoblastic leukemias.

Source: "Children's Doctor," Feb 20, 2018

Immunotherapy

Cost $1.7 million

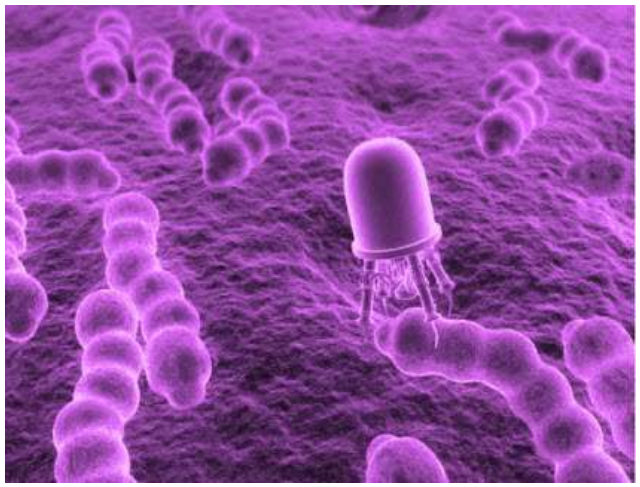
- Yervoy was the first FDA approved immune checkpoint inhibitor for treatment of fully-resected melanoma from BMS. Opdivo and Keytruda are new entrants.
- It works by blocking certain proteins that keep the immune system in check and can keep the body's T cells from killing cancer cells.
- When these proteins are blocked, the "brakes" on the immune system are released and T-cells are able to kill cancer cells better.

Source: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/immune-checkpoint-inhibitor

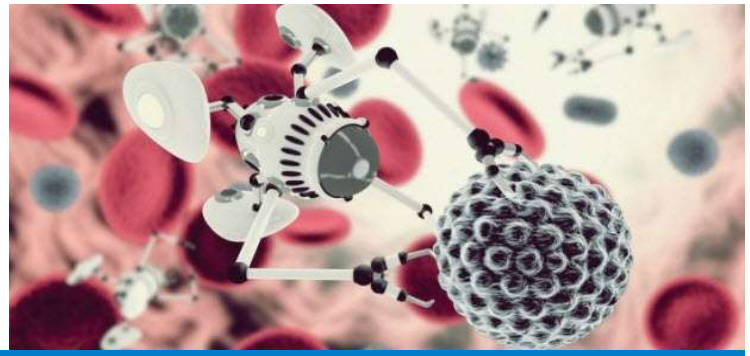
Nanobots

Obstacles for approval are immune responses or blood clots

- They are so tiny that a single drop of water can hold billions of bots. Easily injected into the human bloodstream without damaging any tissue.



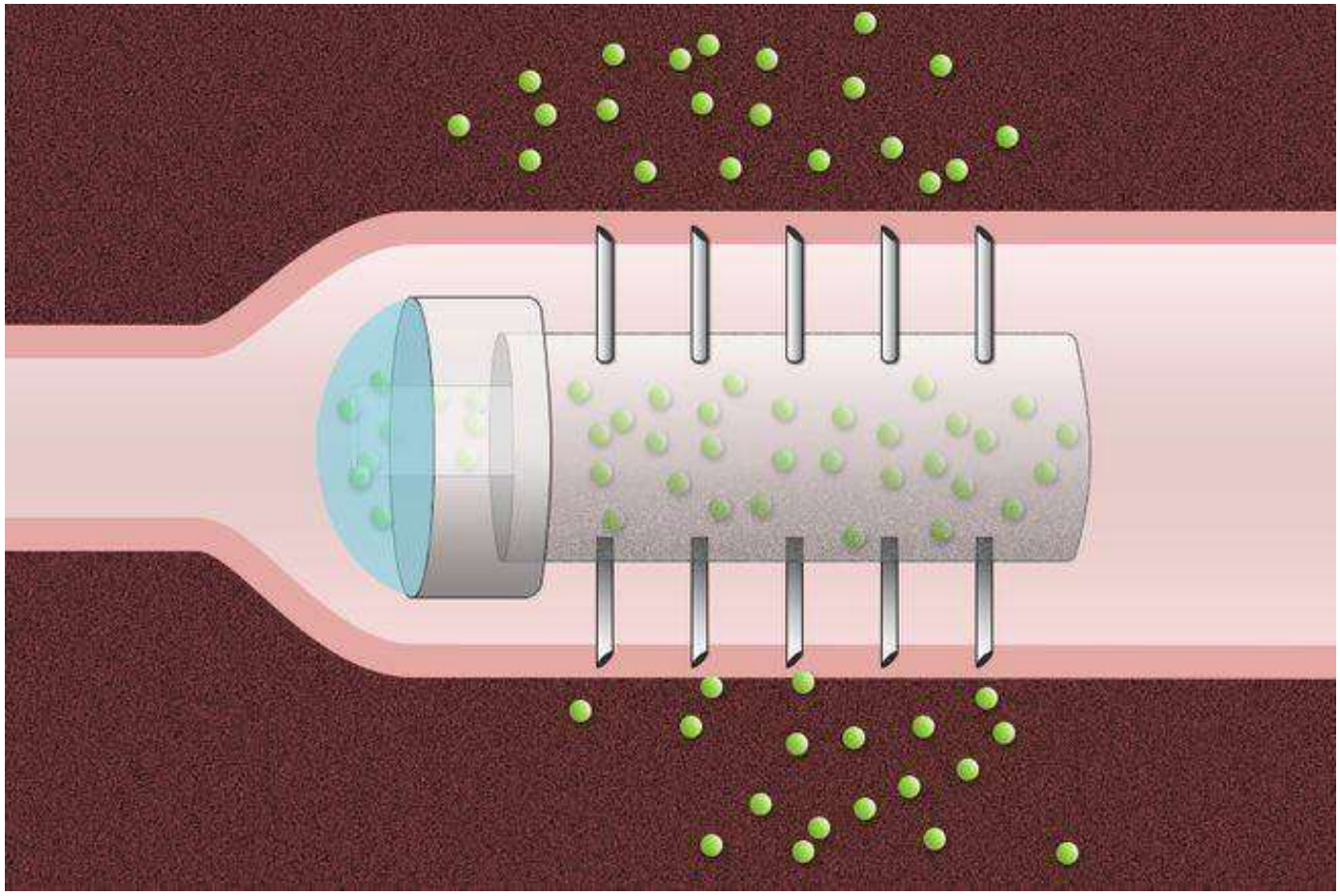
- Effective drug delivery to decrease the side effects of chemo.
- Nanorobots with embedded chemical biosensors are used for detecting the tumor cells in early stages of cancer development inside a patient's body.



Source:https://www.sciencenewsforstudents.org/article/robots-may-soon-actively-crawl-through-your-gut

Gut Jabber

Developed by Researchers at MIT



ABUSE OF ORPHAN DRUG ACT

Perks drive revenue

Orphan Drug Status is Profitable

Why is it Important to Drug-makers to Obtain Orphan Status

- The FDA is more flexible in evaluating drugs for rare diseases - about half of them get through with just one pivotal clinical trial.
  - Clinical trials are smaller and the approval is a different scientific and regulatory experience.
- Each approval gives 7 years of market exclusivity.
  - The FDA cannot approve any new or abbreviated application for the same drug for the same indication during the period of exclusivity and the manufacturer is able to price the drug at what the market can bear.
- Waiver of FDA application fees that can be up to $2m.
- A 50% tax credit for R&D and access to federal grants.
- Public traded company shares soar 30% or more on the news of an approval.

Gralise: Case Study for Orphan Act Abuse

- In 2012, Depomed, Inc. filed suit against the FDA for refusing to give Gralise orphan drug status as a treatment for shingles.
  - Agency wanted proof that the drug was clinically superior to other generic drugs.
- Gralise's active ingredient is gabapentin—

- FDA approved, but denied 7 years of exclusivity.
- Depomed sued and won their case.
- Reason, according to the law, they didn't have to prove their drug was clinically superior to gain the monopoly.
- Sales were $88M in 2016; decreased to $77M in 2017.

Source: Health, Inc. January 2017

The Orphanage is Crowded: Case Study

Mass marketed AbbVie's Humira

- Humira's revenue reached $7.6B in the U.S; $11.8B world wide in 2016.
- Approved by the FDA in 2002 to treat millions with rheumatoid arthritis.
- 3 years later, AbbVie asked for orphan drug status to treat juvenile rheumatoid arthritis affecting 30,000 to 50,000 individuals. Pediatric use was approved in 2008.
- Subsequently, Humira was approved for 4 more rare diseases
  - Crohn's, chronic plaque psoriasis
  - Uveitis, the ophthalmic approval would extend the market exclusivity to 2023.
- This drug counts for 63% of AbbVie's revenue.

Source: Health, Inc.; January 2017

Bio-Similar for Humira

Boehringer won bio-similar challenge in 2017

- AbbVie sued alleging infringement on dozens of Humira patents.
  - Boehringer filed a defense of "unclean hands," arguing that AbbVie unfairly pursued overlapping and non-inventive patents, and used the patent litigation system itself to delay competition. The company says AbbVie's entire infringement lawsuit should be struck aside because of those abuses.
- AbbVie chose to fight the "unclean hands" countersuit.
  - Judge Lloret ordered AbbVie to produce the documents.
  - Boehringer is trying to avoid the fate of eight other bio-similar manufacturers who have to wait to launch through out 2023.

Source: FiercePharma Feb 11, 2019

PROFITABILITY OF PBMS AND BRAND DRUG-MAKERS

Channel Members to Rebates

A Formulary Generates Revenue for PBMs and Drives Up the Cost of Drugs

Let's assume an UNREALISTIC rebate of 50%

(though no one really knows what "it" is)

Amounts based on an actual claim file and a 30-day supply

Formulary Drives Cost

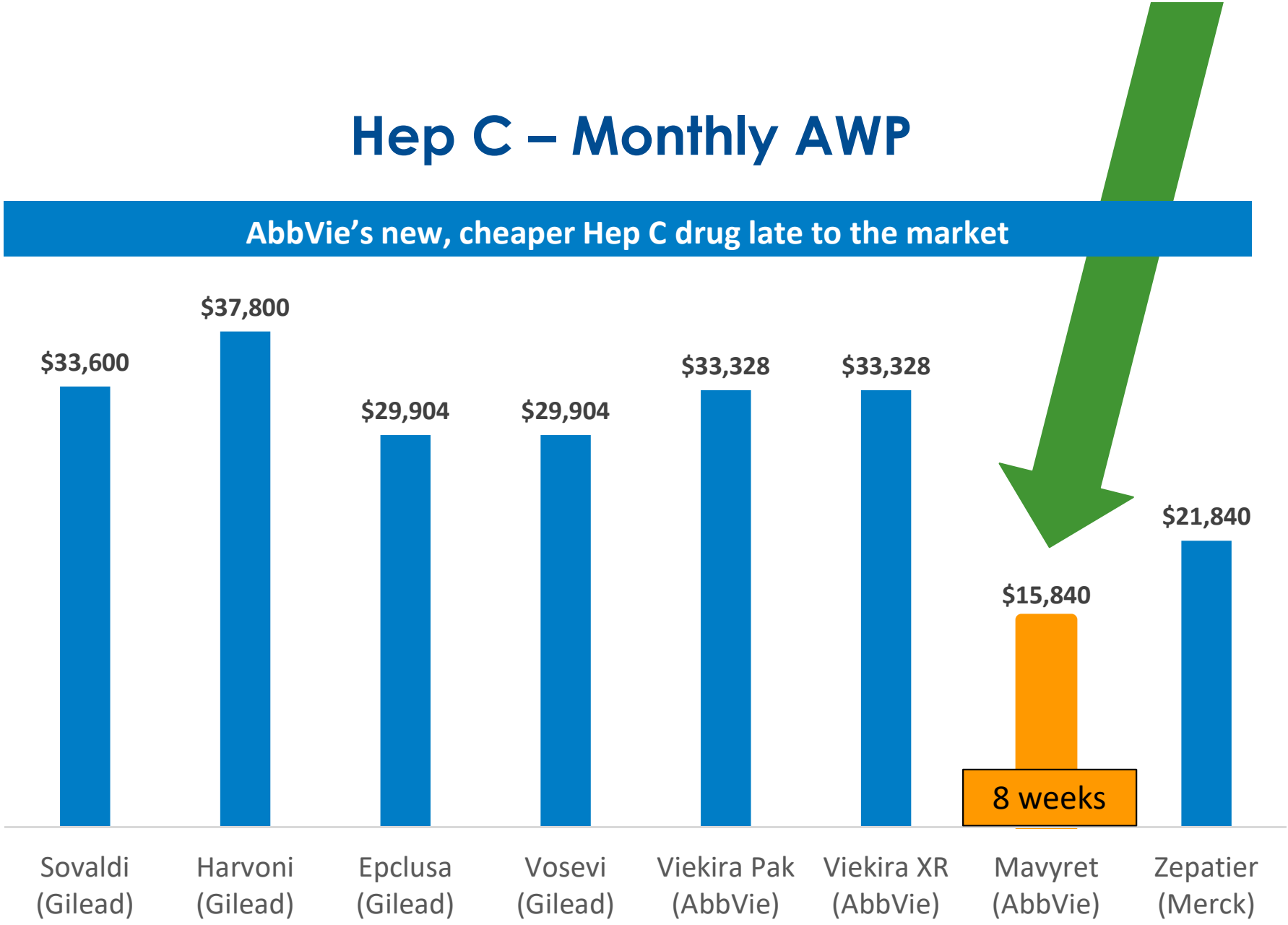
How is this evidence based medicine?

- Example: Jublia
  - Highly advertised by Mario
  - Cost is $8,000 annually
  - Maintenance for 48 weeks
- Ciclopirox is a generic
  - Does the same thing
  - Cost $720 annually

Would you cover this?

Hep C – Monthly AWP

AbbVie's new, cheaper Hep C drug late to the market



Source: Market Watch & Medi-Span

PREDATORY BUSINESS PRACTICES

Manufacturers that don't manufacturer

Martin: Meet the Face of Pharma

Face of Greed & Predatory Practices

Turing, Mylan, Marathon and Horizon

Valeant Pharmaceuticals

Two Top Executives Arrested; Stock Plummeted 90%

OLDER DRUGS RE-INTRODUCED

Periodic Paralysis

Drug Daranide now known as Keveyis

- Daranide was originally approved in 1958 for glaucoma.
- In early 2000, cost was $50 for a bottle of 100; but Merck discontinued making it. Taro, generic manufacturer began producing it.
- In 2015, Sun Pharmaceutical acquired Taro. The cost skyrocketed to $13,650 when it was approved under Orphan Drug Act and received 7 years of exclusivity to treat Periodic Paralysis.
- Then, it was free before skyrocketing again to $15,000 when Stonebridge Biopharma acquired the drug for $8.5M and re-launched it.
- Stonebridge offers free genetic testing.

Source: Carolyn Johnson; This Old Drug was Free, Now it Cost $109,500 a Year; (Washington Post, July 8, 2016)

Generic Price Increases

Predatory or economic

- **Nostrum Pharmaceutical,** more than quadrupled the price of a bottle of *nitrofurantoin* from $474.75 to $2,392 or 400%.
  - The drug was first introduced in 1953 to treat bladder infections.
  - Casper Pharmaceutical had increased their price to $2,800 (182%) in 2015.
- **Emcure's subsidiary, Heritage Pharmaceuticals**, Two former executives pleaded guilty in January to federal charges of conspiring to fix prices and divide up the market for *doxycycline* and the diabetes drug *glyburide*.
- The surge in Mergers and Acquisitions in the last few years has negatively impacted competition and created shortages and price increases.

Source: CNBC: Meg Tirrell; "Beleaguered Price-Hiking Drug CEO Says He Wasn't Defending Shkreli, He was Condemning FDA;" Published 6:10 PM ET Wed, 12 Sept 2018

Egregious Pricing in Diabetes

Valeant Pharmaceutical

Product Name	Drug Type	Ingredient Cost (30 pills)
Glumetza Oral Tablet Extended Release 24 Hour 1000 MG	Brand	$3,407
Metformin HCl ER (MOD) Oral Tablet Extended Release 24 Hour 1000 MG	Generic	$3,066
Fortamet Oral Tablet Extended Release 24 Hour 1000 MG	Brand	$1,075
Metformin HCl ER (OSM) Oral Tablet Extended Release 24 Hour 1000 MG	Generic	$801
Glucophage XR Oral Tablet Extended Release 24 Hour 500 MG	Brand	$34
Metformin HCl ER Oral Tablet Extended Release 24 Hour 500 MG	Generic	$30

Metformin is the generic name of the prescription medications Glucophage, Glumetza, and Fortamet, used to control blood sugar in people with type 2 diabetes.

Hedge Fund Investors Buying Marketing Rights to Older Drugs

Drug Name	Brand/ Generic	Ingred Cost (30 pills)	Manufacturer
Klofensaid II 1.5%	Brand	$3,214	PureTek
Pennsaid 2%	Brand	$2,309	Horizon
Diclofenac Sodium 1.5% Gel	Generic	$1,163	PureTek
Diclofenac Sodium 1.5% Gel	Generic	$221	Apotex
Zegerid 20mg	Brand	$2,630	Valeant
Zegerid 20mg OTC	OTC Brand	$19	Schering Plough
Omeprazole Sodium Bicarb 20mg	Generic	$2,367	Akron

LEGAL PRACTICES

Delay, delay, delay

Pharmaceutical Patent Reform

"Patents need to be protected, but legal is a support service, not the core business."

Waxman - Hatch Act

- An attempt to balance brand and generic rights
  - Intent was to encourage expedited approval of generic drugs.
  - Provide incentive for research for brand manufacturers.
- Granted 6 month exclusivity period to the first generic manufacturer to file (ANDA)
  - Manufacturer can recoup some of the litigation expenses of challenging the brand manufacturer's patent.
  - Offered enticement to not wait for patent expiration.
- In 1984, only 12 percent of drugs used were generic. Today, 87%-89% of the prescriptions written this year are generic.
  - 180 day exclusivity period allows brand drug-makers a "soft landing" off patent cliff.

"Pay to Delay" is a Barrier to Generics?

- Brand manufacturer pays a generic manufacturer to delay the introduction of the generic drug.
- Under these pay-off agreements, brand companies settle patent disputes by paying the generic manufacturer in exchange for a promise that it will keep its generic version off the market.

- Out of 194 patent settlement payments, 63 were made by brand drug-makers to delay entry of generic competition.

"Pay to Delay" Payments

It's legal

- Delays generic entry by 17 months.
- Most of these agreements are still in effect.
- They currently protect at least $20 billion in sales of brand-name pharmaceuticals from generic competition.
- FTC & DOJ agree the payments may constitute unlawful collusion restrictions on competition that harm consumers.
- Two 2005 appellate courts have upheld their legality.

Creates Act

PHARMA abuses REMS regulations

- Cracks down on brand drug makers who use FDA regulations to keep drug samples out of generics makers' hands
- Creates Act aims to stifle regulatory abuses that stave off generics competition.
- Generics drug-makers have said branded drug companies use the FDA's Risk Evaluation and Mitigation Strategies regulations to limit their ability to get drug samples and test generic equivalency.
- If they can't test for equivalency, they're not able to bring cheaper generics to market.
- FDA published a list of drug makers that have received complaints on the issue, including Celgene, Johnson & Johnson, Gilead Sciences, Novartis and Pfizer.

Source: Fierce Pharma, Pharma Ready to Support Generics Easing Bill, Eric Sagonowsky |May 2018

Citizen's Petitions Abused

- A Citizen's Petition is a request from the Brand drug-maker to delay action on a pending generic drug application.
- FDA said that 92% of all petitions were from Brand Manufacturers (corporations); **NOT CITIZENS.**
- Brand manufacturers routinely file these on the eve of a generic's approval, sabotaging the marketing for at least 150 days, months, if not years.

Source: Generic Pharmaceutical Association, "2016 Generic Drug Savings & Access in the United States" Report http://www.gphaonline.org

Key Takeaways

Complex+ Convoluted + Greed = Runaway costs

- Rebates- will they go away?
- Legal maneuvers (Pay to delay, Citizen Petitions, REMs abuse)
- Orphan Drug Act Abuse
- Lobbying (Congress unwilling to provide checks & balances)
- Mergers & Acquisitions to prop up share price
- Predatory Practices (re-launch of older drugs)
- Patient Assistance Adding to the Fuel
- FDA – no power or oversight on abuses or costs

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