



The Business of Pharmacy™

# Drug Manufacturer Strategies for Keeping Drug Costs High

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Prepared by Visante on behalf of PCMA

November 2021



# Executive Summary

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- › High-priced prescription drugs contribute to financial and medication access barriers for patients. Total consumer out-of-pocket prescription drug spending is projected to increase almost 40% by 2028.<sup>1</sup>
- › Manufacturers have shifted focus to drug categories with government-established monopoly opportunities, which lead to higher prices for drugs in those categories. 80% of drugs approved in 2017 were specialty and orphan drugs, up from 40% in 2001.<sup>2</sup> Average prices for specialty and orphan drugs have doubled over the past 12 years, now with average launch prices of more than \$200,000 per patient per year.<sup>3</sup>
- › Pharmaceutical manufacturers use many strategies to keep prices and profits high, including:
  - I. Pricing practices that lead to anticompetitive market dynamics.
  - II. Delaying generic/biosimilar competition by abusing the patent system.
  - III. Extending market exclusivity periods.
  - IV. Promotion of higher-cost drugs with payments to physicians and patient coupons.

1. Visante analysis of CMS National Health Expenditure Data.

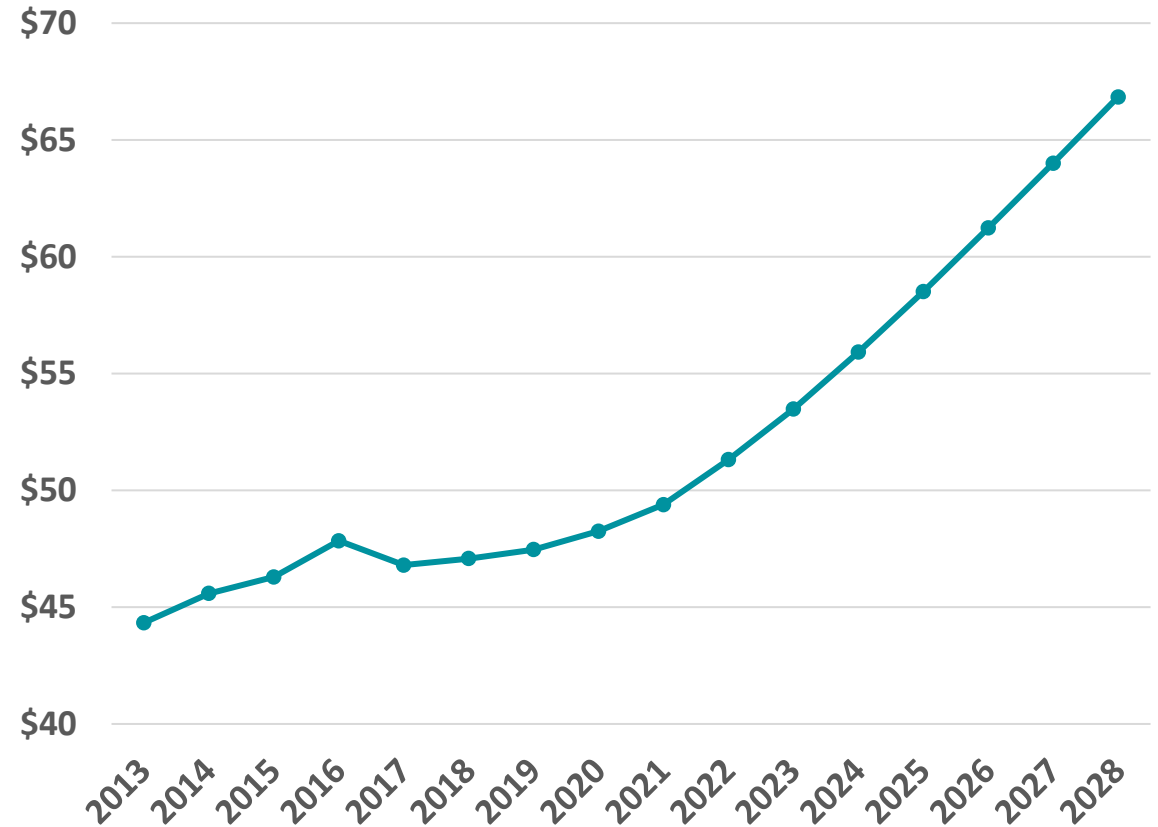
2. American Health Insurance Plans. *The Rise of Orphan Drugs*. September 2019.

3. Visante analysis of AHIP data.

# High-Priced Drugs Hurt Patients' Wallets and Health

- › Total prescription drug spending has increased by an average of 5.5% annually since 2014.<sup>1</sup>
- › Fueled by drug list price increases, total consumer out-of-pocket prescription drug spending is projected to increase almost 40% by 2028.<sup>1</sup>
- › High-priced prescription drugs contribute to financial and medication access barriers for patients.
  - A recent survey demonstrated the most cited reason for non-adherence was difficulty affording the medication.<sup>2</sup>
  - One analysis estimated a prescription abandonment rate of 0.6% for every out-of-pocket dollar.<sup>2</sup>
- › Poor adherence has been shown to result in poor health outcomes and increased health care costs.<sup>3</sup>

Consumer Out-of-Pocket Rx Expenditures Projected to Increase Almost 40% 2020-28



1. Visante analysis of CMS National Health Expenditure Data.  
2. CoverMyMeds. [Medication Access Report](#). 2020.  
3. World Health Organization. [Adherence to Long-Term Therapies](#). 2003.

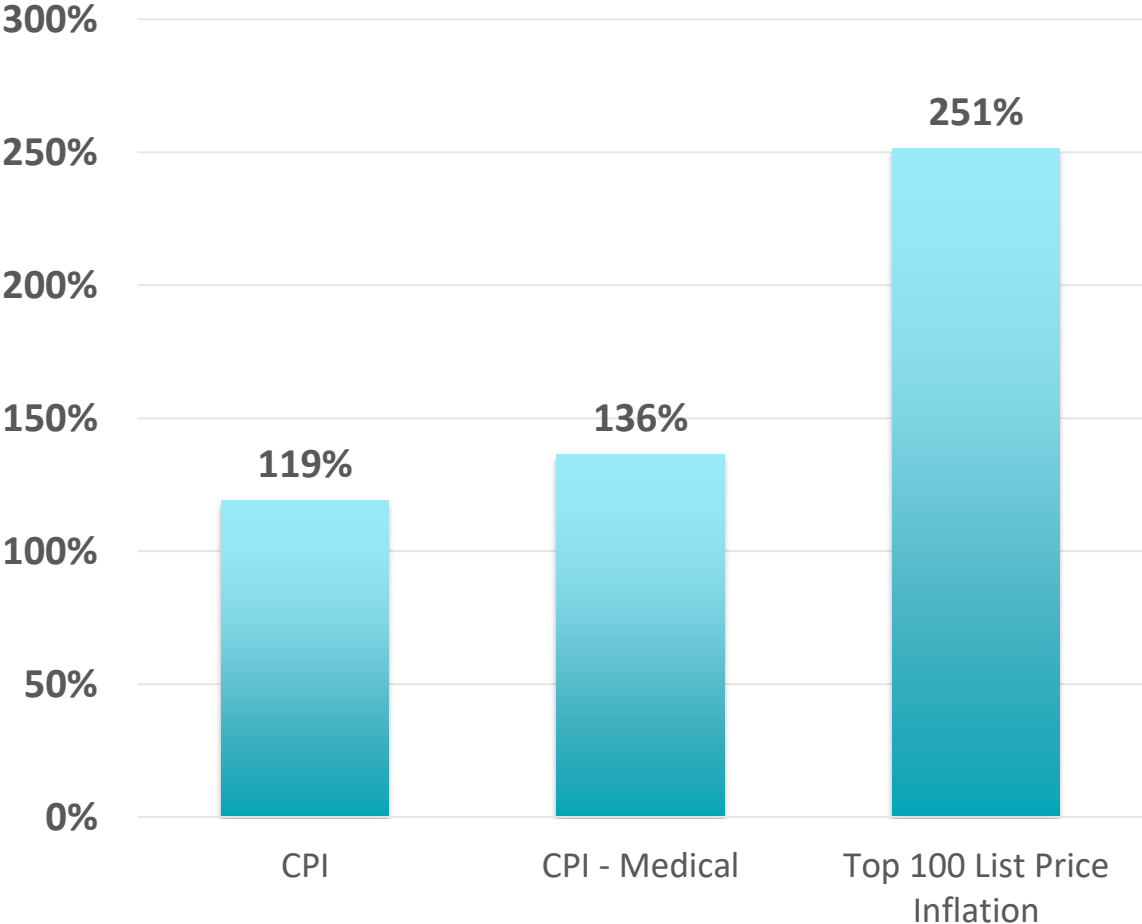
# Prices for Top-100 Brand Drugs Have Increased Much Faster Than CPI

List prices for brand-name drugs increased more than 2.5x, which was much greater than the Consumer Price Index.

### Methodology

- > We examined unit-price inflation for the “Top 100 Drugs” by US sales during the 10-year period 2010-2019. 183 different brand-name drugs were included in this sample, with 696 different strengths/dosage forms. Unit-price inflation was calculated separately for each drug/strength/dosage-form.
- > We calculated weighted average unit-price inflation using total annual Wholesale Acquisition Cost (WAC) sales for the drug/strength/dosage-form each year.
- > We compared drug price inflation to the Consumer Price Index (CPI) and Consumer Price Index – Medical (CPI – Medical) reported by US Bureau of Labor Statistics.

### Inflation for Top 100 Drugs (2009-2019)



Source: Visante analysis data from SSR Health and [US Bureau of Labor Statistics](#)

# High-Priced Prescription Drugs Are a Primary Driver of Drug Costs

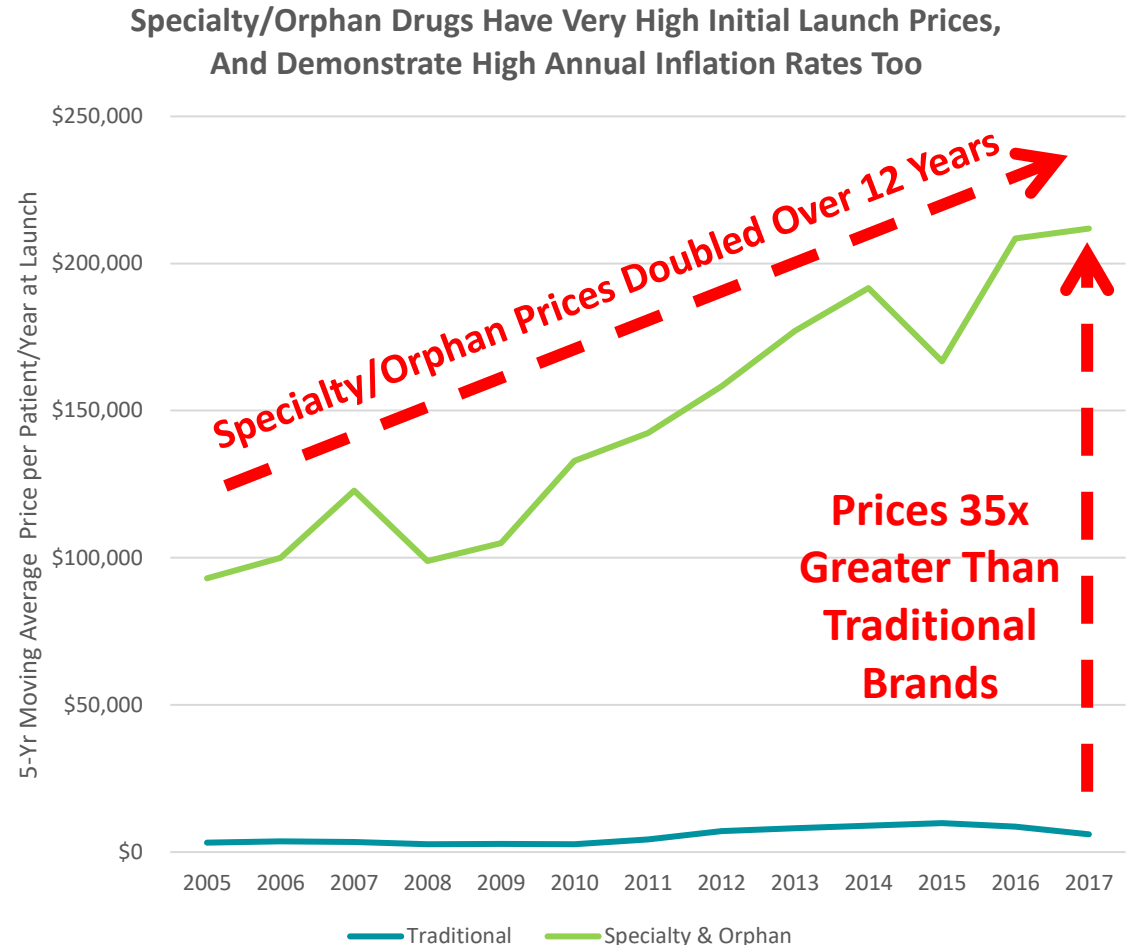
*Specialty and orphan drugs are driving increases in drug expenditures, much more than traditional brand drugs*

- Using data published by AHIP, we calculated the five-year moving average of the annual per-patient price for new prescription drugs at launch between 2001 and 2017.<sup>1</sup>
- The following drug types were included in the assessment:
  - Traditional: Brand drugs not classified as specialty or orphan.
  - Specialty: Brand drugs classified as “specialty” in publicly available drug formularies from major insurers.\*
  - Orphan: Brand drugs approved by the US Food and Drug Administration (FDA) under the orphan drug designation.<sup>2</sup>
- The average launch prices (i.e., list price during first year on the market) of specialty and orphan drugs have significantly outpaced traditional drugs.
- Manufacturers shifted their focus to these high-priced drug categories, as 80% of drug approvals in 2017 were specialty and orphan drugs compared to 40% in 2001.<sup>2</sup>

\*Major insurers included: Aetna, Cigna, BCBSA

1. Visante analysis of America's Health Insurance Plans (AHIP) data.

2. American Health Insurance Plans. *The Rise of Orphan Drugs*. September 2019.





# Pharma Strategies for High Drug Prices

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# Pharma Uses Many Strategies to Keep Prices and Profits High

*Pharmaceutical manufacturers utilize many different strategies to disrupt competition and keep prices high. Below are seven different strategies that have been identified, broken down into four different categories.*

Increase revenue using marketing and promotional ploys

Exploit regulatory pathways to extend exclusivity

Expand profits through anticompetitive pricing

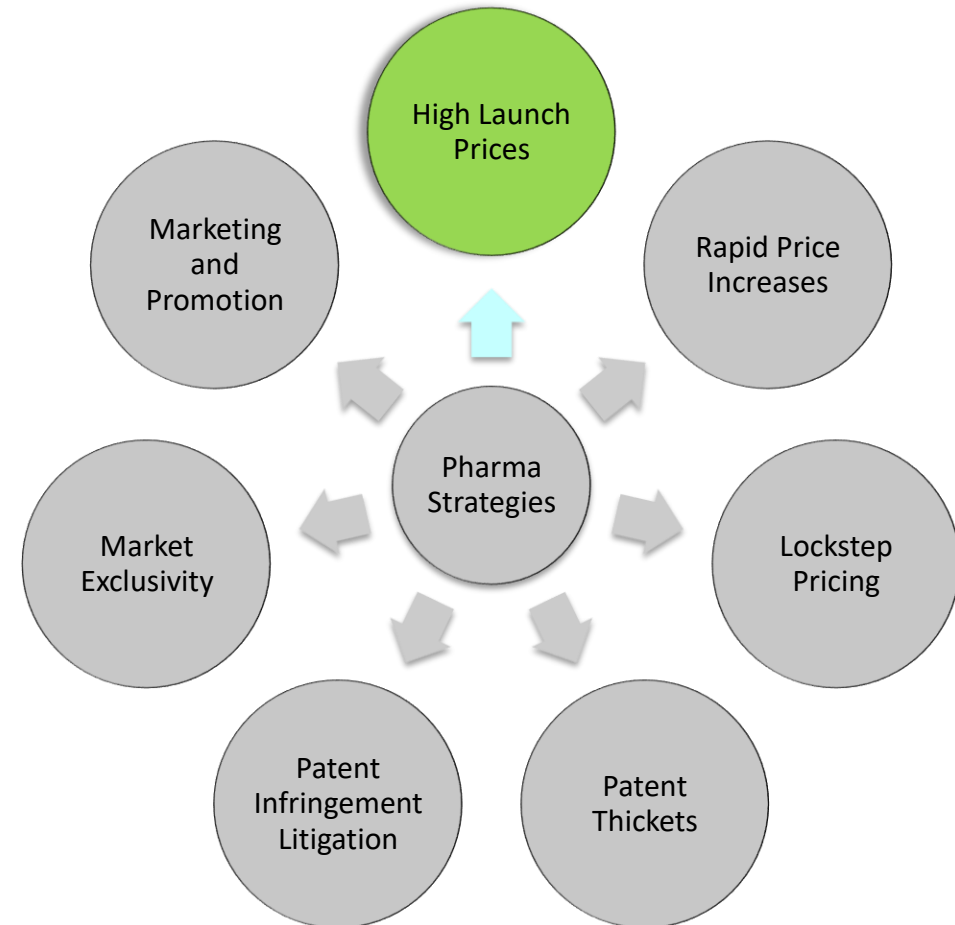
Delay generic and biosimilar competition by abusing U.S. Patent System



# Anticompetitive Pricing: High Launch Prices

## *Launch prices for new drugs are set high to reap high profits*

- › Specialty, orphan, and chemotherapeutic drugs are prime examples of extreme pricing following a new drug approval.
- › Manufacturers claim high launch prices are needed to recoup development costs. However, studies show only about 17% of total spending in most large drug companies is related to research and development costs.<sup>1</sup>
- › While there is no unilateral process for establishing a drug's list price, it is generally based upon one of the following two concepts:
  - **“What the market will bear.”**
    - › Typically, novel drugs, blockbuster drugs, first-in-class drugs, orphan drugs, drugs without significant competition.
  - **“Priced similarly to its competitors”**
    - › Typically, drugs entering a category with multiple existing therapies.<sup>2</sup>



1. Kodjak, A. (2019, January 7) *Prescription Drug Costs Driven By Manufacturer Price Hikes, Not Innovation*. NPR. Accessed December 2020.

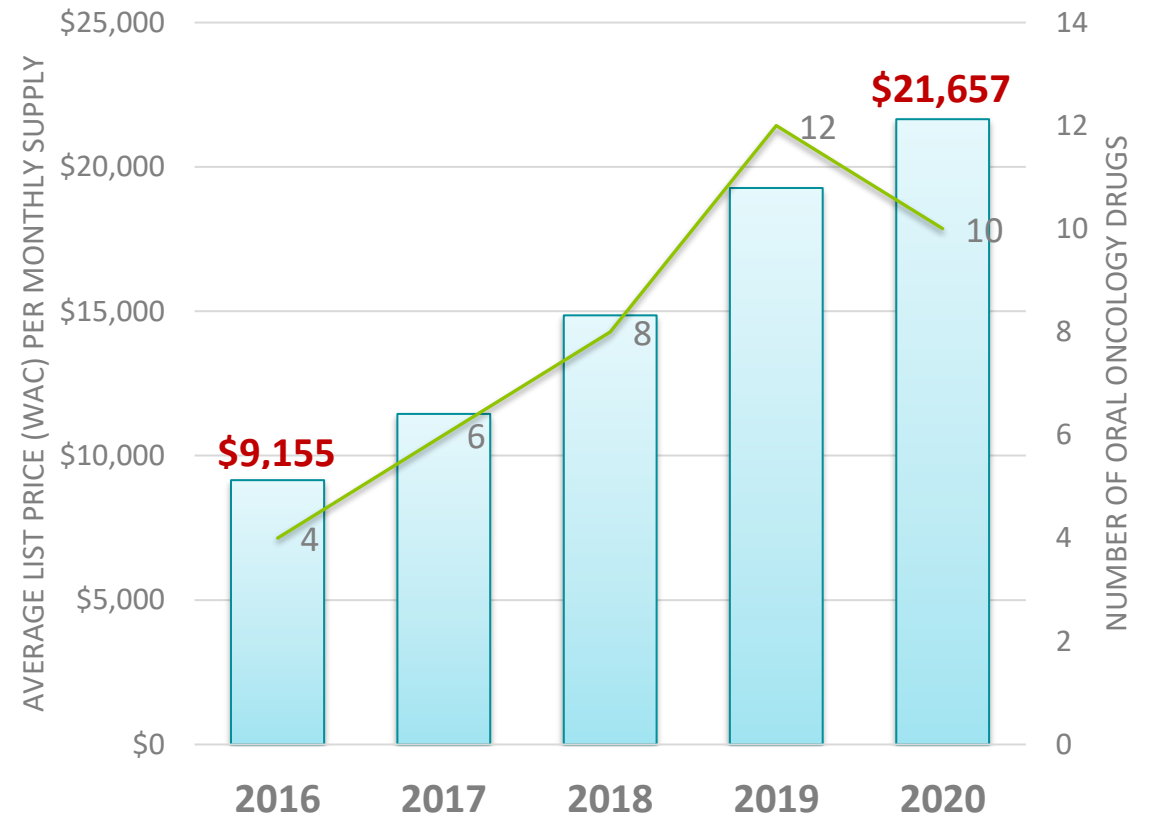
2. Entis, L. (2019, April 9). *Why Does Medicine Cost So Much? Here's How Drug Prices Are Set*. Time. Accessed May 2021.



# Average Launch Price for New Cancer Drugs More Than Doubled Between 2016-2020

- Manufacturer launch prices for cancer drugs have increased dramatically during the past five years.
- Visante analyzed list prices (i.e., Wholesale Acquisition Cost, or WAC) for 40 new oral cancer drugs launched between 2016 and 2020. Average list price for a month's supply was calculated based on FDA approved dosing.
- In 2016, the average list price for a month's supply of the four new oral cancer drugs was \$9,155. In 2020, the average list price for a month's supply of the ten new oral cancer drugs was \$21,657, an increase of 137%.

## Huge Increases In Launch Prices For New Oral Oncology Drugs



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Date range of prices referenced: April 4, 2016 – May 19, 2020. Date information accessed from AnalySource: November 13, 2020.

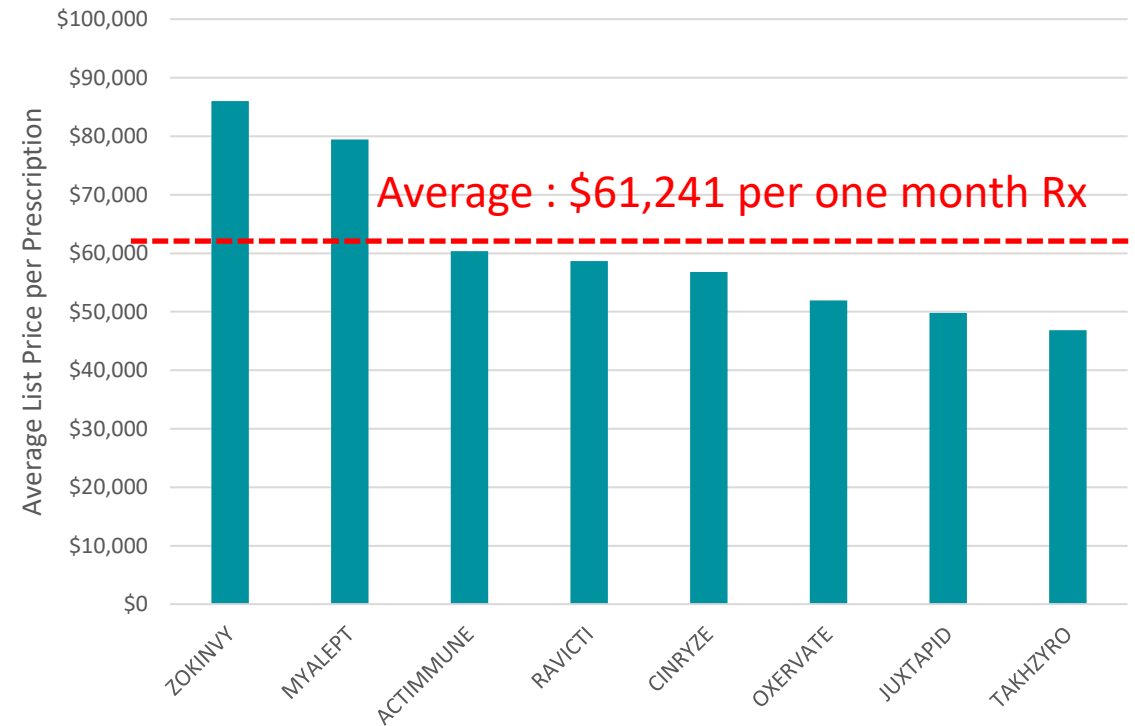
Notes: List prices are wholesale acquisition cost (WAC), which represents the manufacturer's published catalog or list price for a drug product to wholesalers and may not represent actual transactional prices. For more information on methodology see First Databank <http://www.fdbhealth.com/policies/drug-pricing-policy/>.

# Orphan Drugs Are Among the Most Expensive on the Market

## *Eight of the top-ten most expensive retail drugs have orphan designations*

- › Visante estimated list prices per prescription for self-administered (outpatient) drugs on GoodRx’s list of “The 20 Most Expensive Prescription Drugs in the U.S.A.”<sup>1</sup>
- › The average list price for a month’s prescription was calculated based on FDA-approved dosing.
- › Because of the orphan drug designation, we assumed no rebates were included. Therefore, the estimated list price is what’s being paid and there is not a much lower net price.
- › Overall, 16 drugs with orphan designations are in the top twenty, including eight in the top ten.<sup>1</sup>
- › The average list price per month’s prescription is \$61,241.<sup>2</sup>

### Orphan Drugs Are The Most Expensive<sup>2</sup>



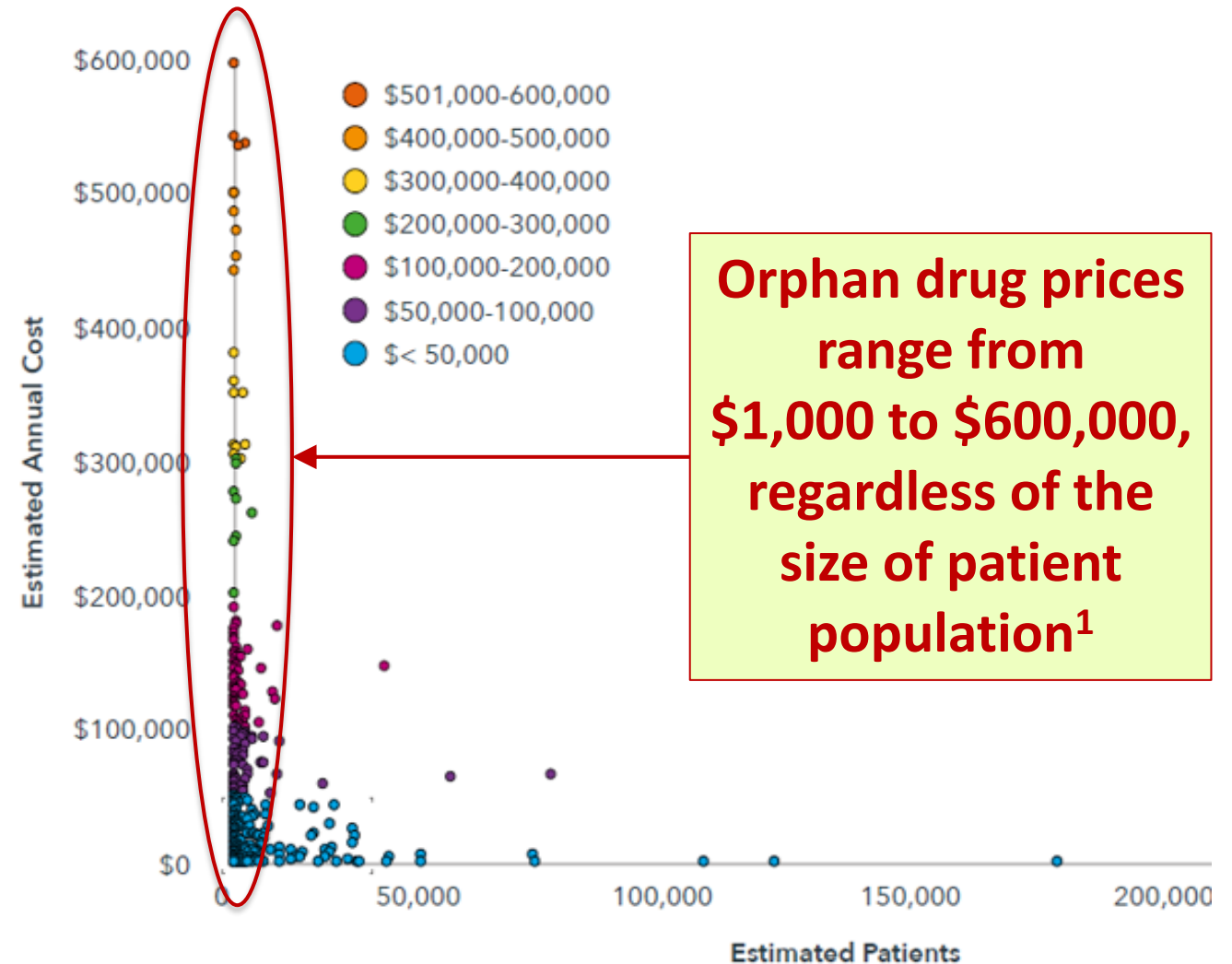
Eight Orphan Drugs in the Top Ten Most Expensive Drugs List

1. Chase, L. (2021, February 8) [The 20 Most Expensive Prescription Drugs in the U.S.A.](#) GoodRx. Accessed June 2021.

2. Visante analysis of AnalySource® — Reprinted with permission by First Databank, Inc. See Slide 9 for details. All rights reserved © (2021). Date range of prices referenced: January 1, 2020 – February 1, 2021. Date information accessed from AnalySource: June 6, 2021.

# Prices For Orphan Drugs Are Not Related to Patient Population Size

- › Manufacturers often claim that high prices for orphan drugs are required because of small patient populations.
- › But there appears to be no correlation between orphan drug prices and the size of patient populations.
- › Orphan drug prices along the y-axis range from less than \$1,000 to over \$500,000, all with treatment populations of less than 10,000 patients.<sup>1</sup>



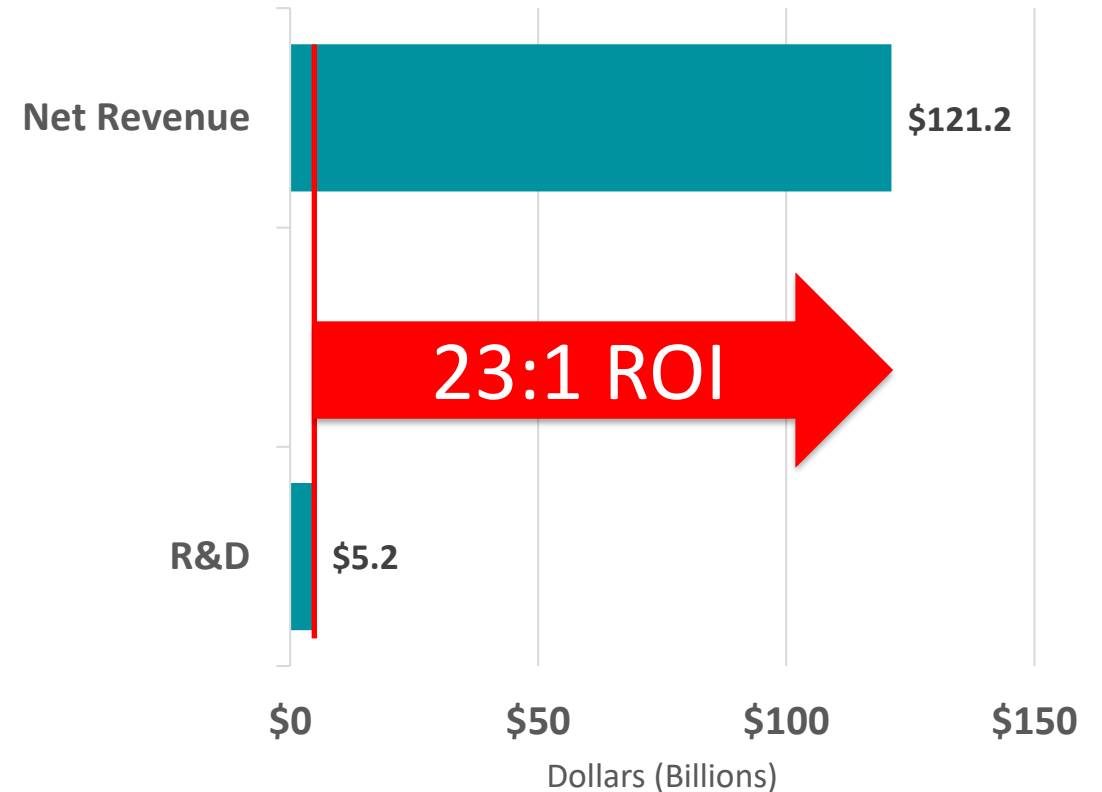
1. IQVIA. Orphan Drugs in the United States. October 2017.

# Research and Development Does Not Drive High Prices

## *AbbVie earned 23 times more than it spent on R&D for Humira*

- › AbbVie spent a total of \$5.19 billion on “Humira Research & Development (R&D)” between 2009 and 2018—approximately 4.2% of the company’s Humira worldwide net revenue over that period.<sup>1</sup>
- › In other words, the Return On Investment (ROI) to the manufacturers was 23:1 (i.e., revenues of \$121.2 billion / R&D investment of only \$5.2 billion).
- › Since Humira had already been on the market for seven years, this R&D money was used primarily on so-called “enhancements” to raise barriers to biosimilar competition.<sup>1</sup>

Humira Net Revenue Far Exceeds R&D Costs



1. U.S. House of Representatives Committee on Oversight and Reform. [Drug Pricing Investigation AbbVie—Humira and Imbruvica](#). May 2021.

# Manufacturers Do Not Try to Compete With Lower Prices

- In most competitive markets, new competitors would normally compete with lower prices. But when new brand drugs enter the market, the price is often set equal to or higher than a similar existing product.
- We estimated the list price per prescription on select drug products within three categories of orphan/specialty drugs:
  - Hereditary Angioedema (HAE)
  - Gastrointestinal Stromal Tumors (GIST)
  - Gaucher’s Disease
- In each category, the launch price of a new drug product was within five percent of the price of a similar drug for the treatment of the same disease.<sup>1</sup>
- While these examples showed launch prices for new drugs within five percent of an existing drug, one group indicated launch prices for cancer drugs are often 10-20% higher than the most recent similar drug on the market.<sup>2</sup>

## New “Competitor” Enters Market With Launch Price Equal To or Greater Than Existing Drug



1. Visante analysis of AnalySource® — Reprinted with permission by First Databank, Inc. See Slide 9 for details. All rights reserved © (2021). Date range of prices referenced: January 5, 2004 – January 10, 2020. Date information accessed from AnalySource: November 19, 2020.

2. Abboud et al. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. *Blood*. 2013 May30; 121(22): 4439-4442. doi: 10.1182/blood-2013-03-490003.

# Anticompetitive Pricing: Unchecked Price Increases

## *Manufacturers rapidly increase prices*

- › Over the past five years, price increases on branded drugs added \$21 billion to manufacturers' net sales growth.<sup>1</sup>
- › Price increases do not appear to be driven by innovation. In many cases, price increases help meet shareholder earnings goals or meet/exceed revenue targets for executive bonuses.<sup>2</sup>
- › Extreme price increases are not limited to newer drugs:
  - H.P. Acthar Gel (corticotropin) was approved by the FDA in 1952.
  - Its price has increased by more than a factor of 1,000 between 2001 (\$40/vial) and 2018 (\$39,000/vial).<sup>3</sup>



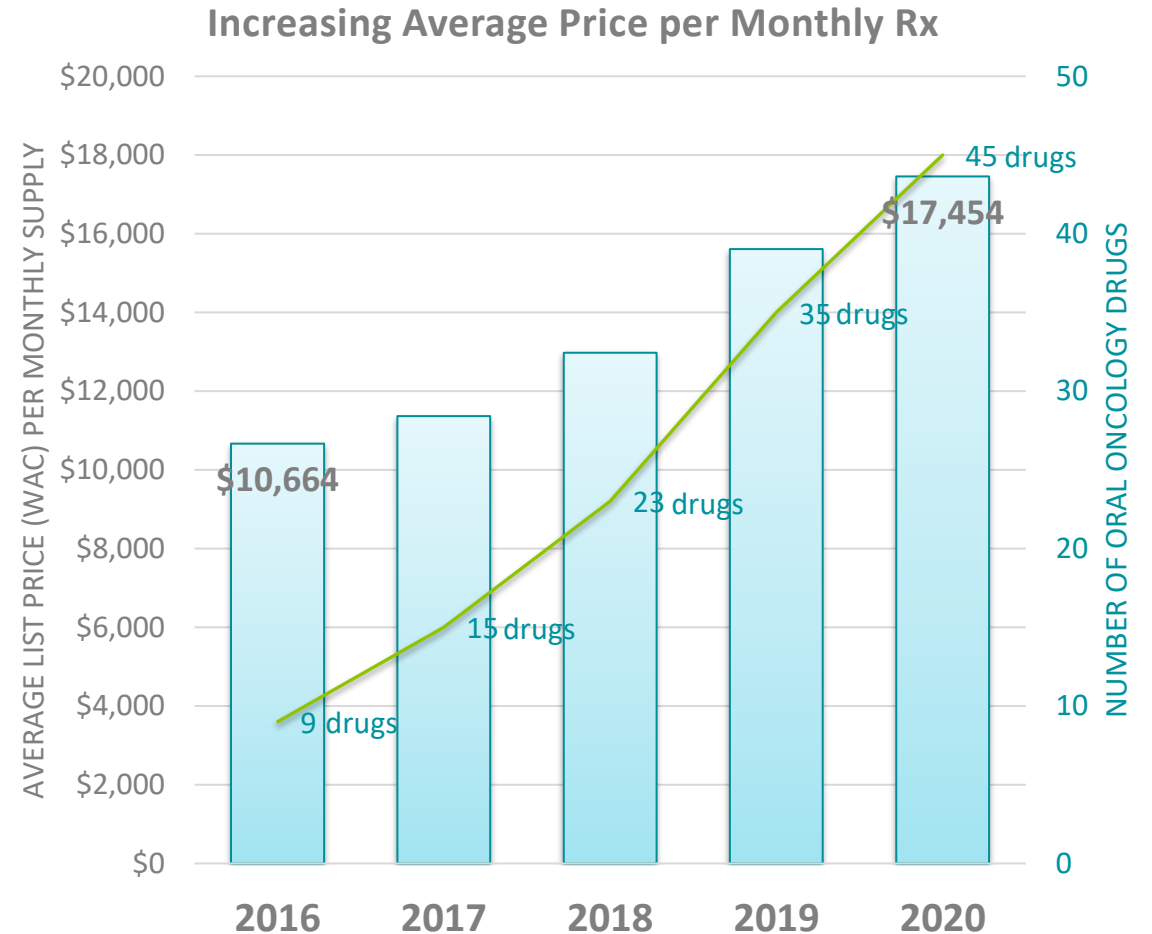
1. IQVIA. Medicine Spending and Affordability in the United States. 2020.

2. Committee on Oversight and Reform, U.S. House of Representatives. [Drug Pricing Investigation Celgene and Bristol Myers Squibb—Revlimid](#). 2020.

3. Dearment, A (2019, Aug 12). [Humana sues drug maker Mallinckrodt over alleged price gouging](#). *Med City News*. <https://medcitynews.com/>

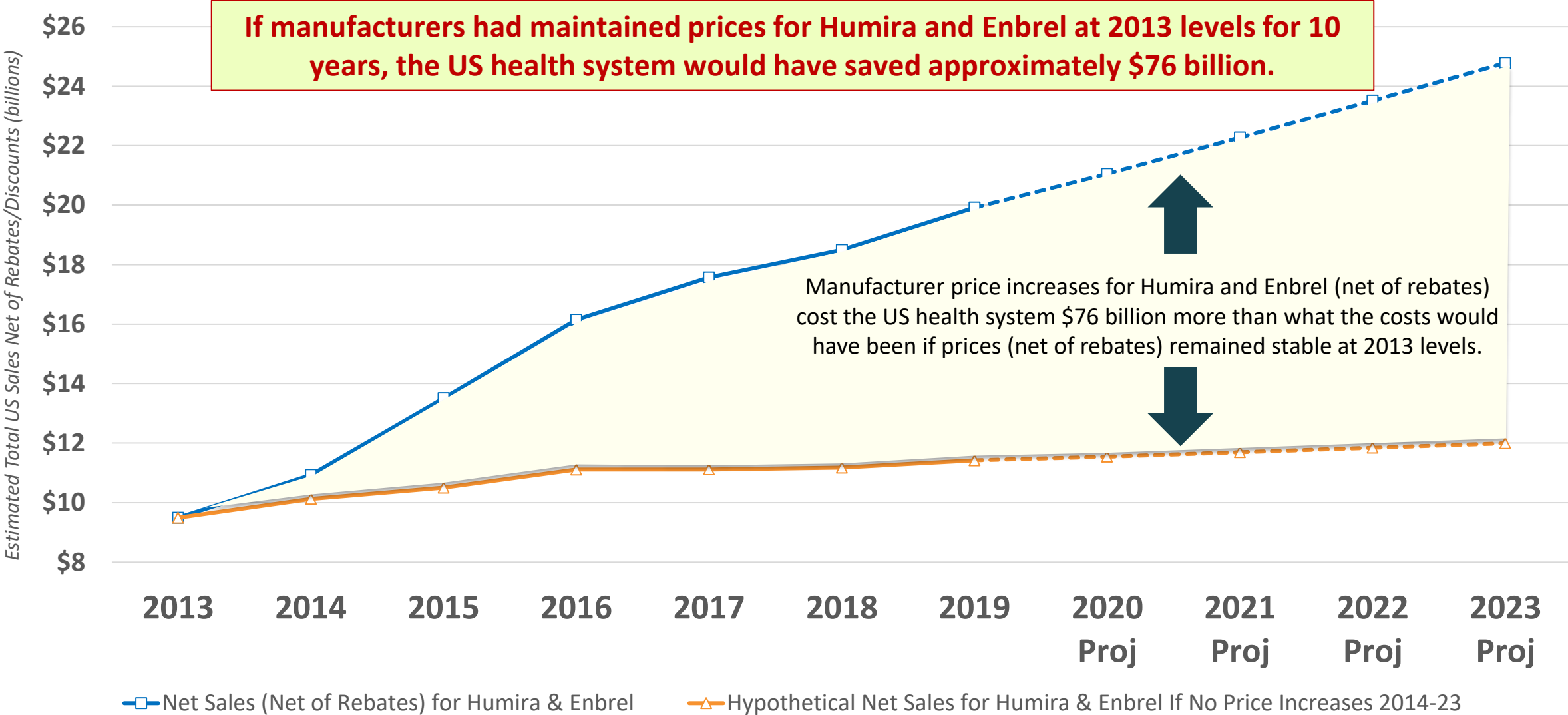
# Average Rx Prices for Oral Cancer Drugs Increased 64% From 2016 To 2020

- Manufacturers' list prices for cancer drugs have increased dramatically during the past five years.
- Visante analyzed list prices (i.e., Wholesale Acquisition Cost, or WAC) for 45 oral cancer drugs on the market in 2020. Average list price for a month's supply prescription was calculated based on FDA-approved dosing.
- In 2016, the average list price for a month's supply of the nine oral cancer drugs then on the market was \$10,664. In 2020, the average list price for a month's supply of the 45 oral cancer drugs then on the market was \$17,454, an increase of 64%.



Source: Visante analysis of AnalySource® — Reprinted with permission by First Databank, Inc. See Slide 9 for details. All rights reserved © (2021). ■ Average Price per Monthly Rx —□— Number of Drugs  
Date range of prices referenced: April 4, 2016 – May 19, 2020. Date information accessed from AnalySource: November 13, 2020.  
Oral drugs used to treat cancer, administered orally, not injection.

# Humira/Enbrel Price Increases Add \$76 Billion in Costs to US Health System Over 10 Years



■ Net Sales (Net of Rebates) for Humira & Enbrel     
 ▲ Hypothetical Net Sales for Humira & Enbrel If No Price Increases 2014-23



# Anticompetitive Pricing: Lockstep (Shadow) Pricing

## *Prices of competitor drugs increase in lockstep*

- › Oligopolies allow manufacturers to raise prices in concert with the competition, instead of competing with lower prices.

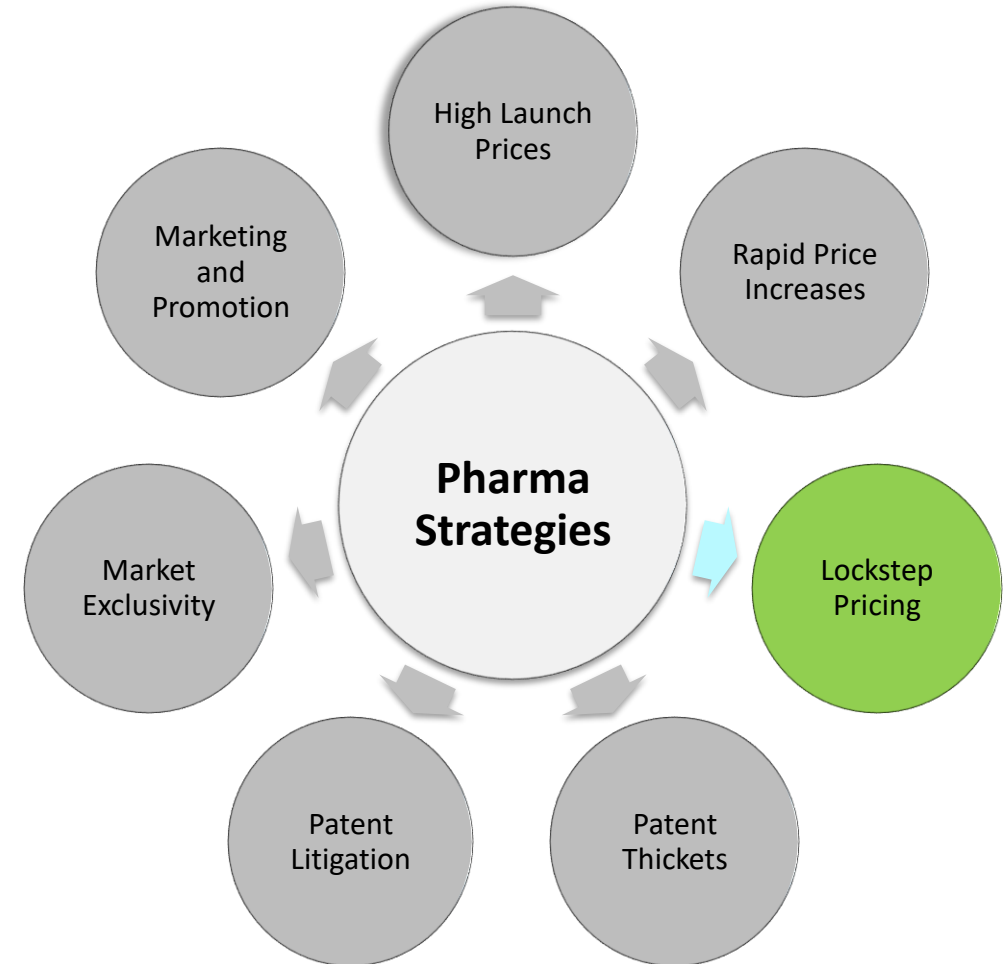
**“Rather than seeking to undercut its competitors’ pricing, from 2014 on Novo Nordisk engaged in a cat-and-mouse strategy of pricing [on insulin products] that followed Sanofi’s price increases closely, sometimes mirroring them within days or even hours.”**

*-United States Senate, Finance Committee*

- › Lockstep (shadow) pricing is no secret and manufacturers don’t try to hide it.

**“We all look at each other and keep pace with each other. Honestly, there is no science to it.”**

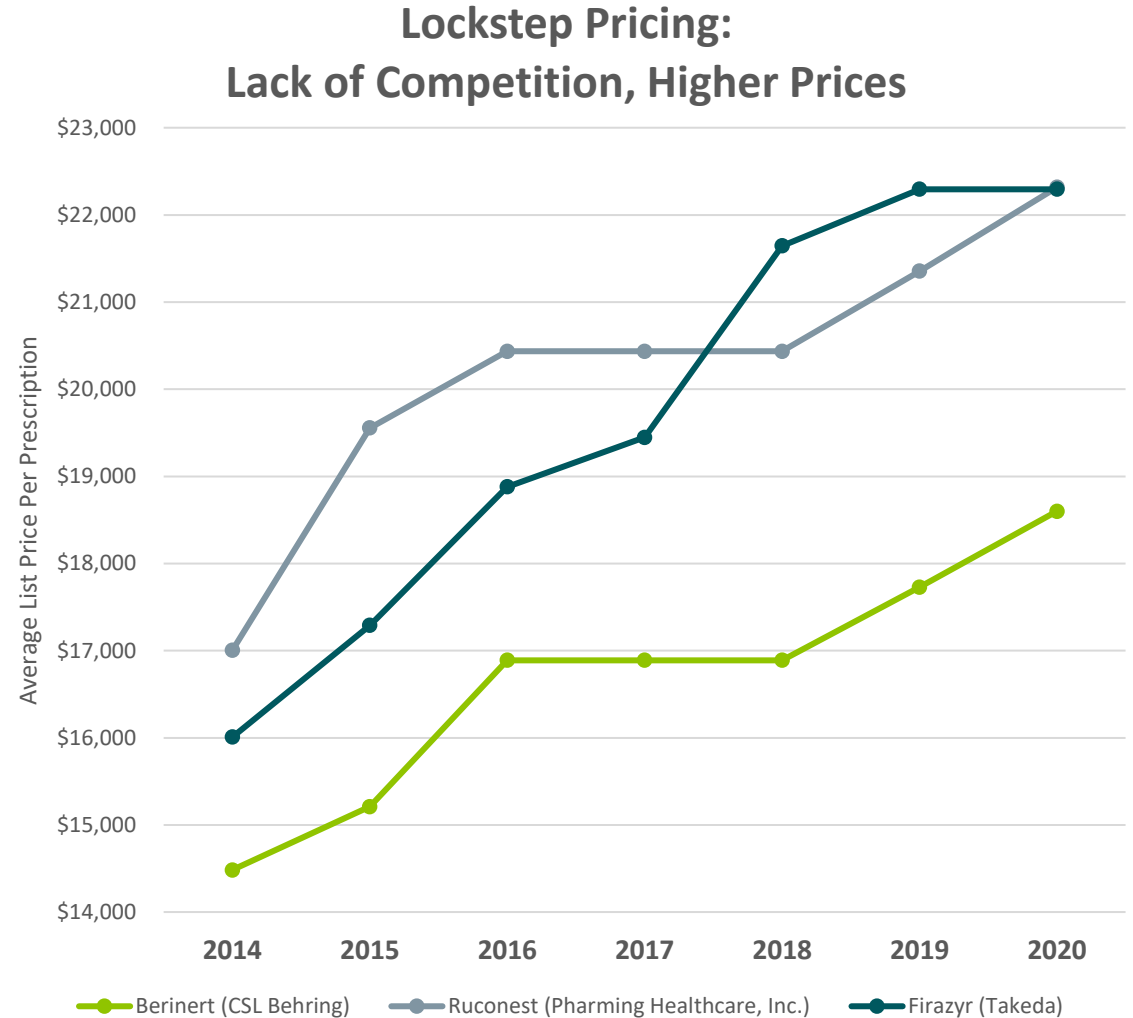
*-Anonymous Director of Drug Development*



Sources: Rockoff, J (2015, December 9). How Pfizer Set the Cost of Its New Drug at \$9,850 a Month. *Wall Street Journal*. <https://www.wsj.com/>  
United States Senate, Senate Finance Committee (2021, January 14). *Insulin: Examining the Factors Driving the Rising Cost of a Century Old Drug*.

# Pharma Oligopolies Raise Prices In Lockstep, Avoiding Competition

- › We evaluated the average list price of three self-administered drugs used to treat acute hereditary angioedema (HAE) attacks.
- › Three manufacturers exhibited lockstep pricing over the course of five years. During that span, the average list price per prescription increased by over 30%.



Source: Visante analysis of AnalySource® — Reprinted with permission by First Databank, Inc. See Slide 9 for details.

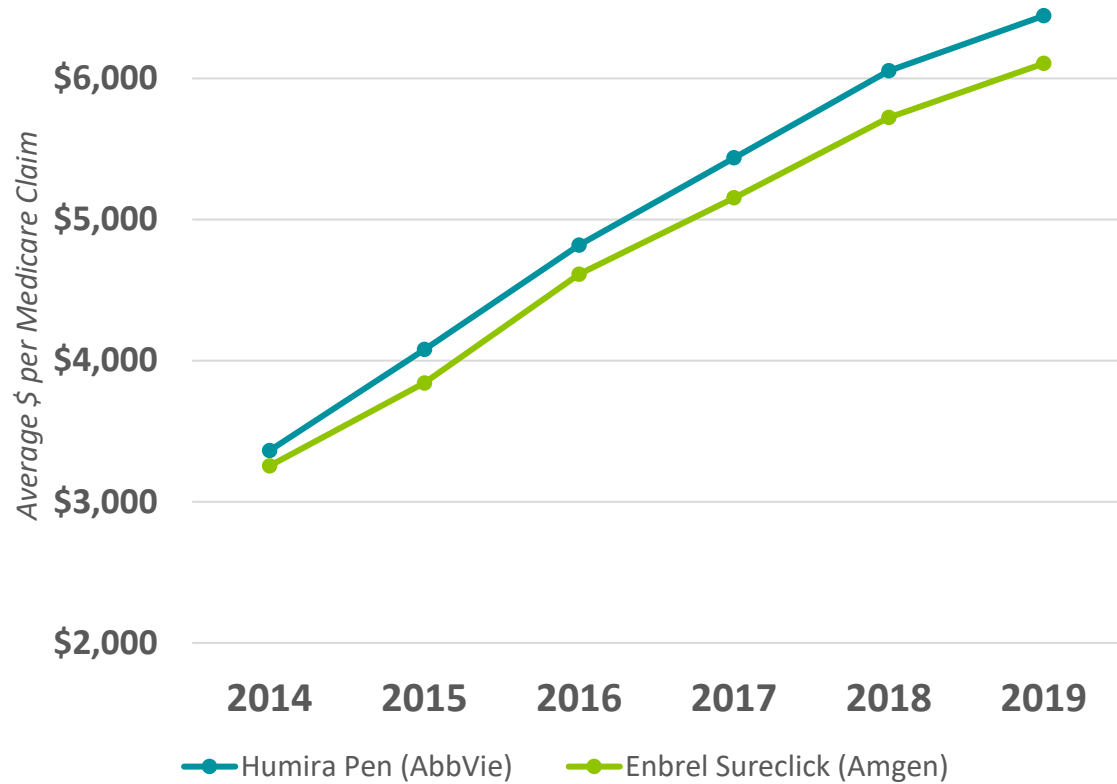
All rights reserved © (2021), database dates between October 29, 2009 and January 3, 2020.

Date range of prices referenced: October 1, 2013 – April 6, 2020. Date information accessed from AnalySource: November 19, 2020.

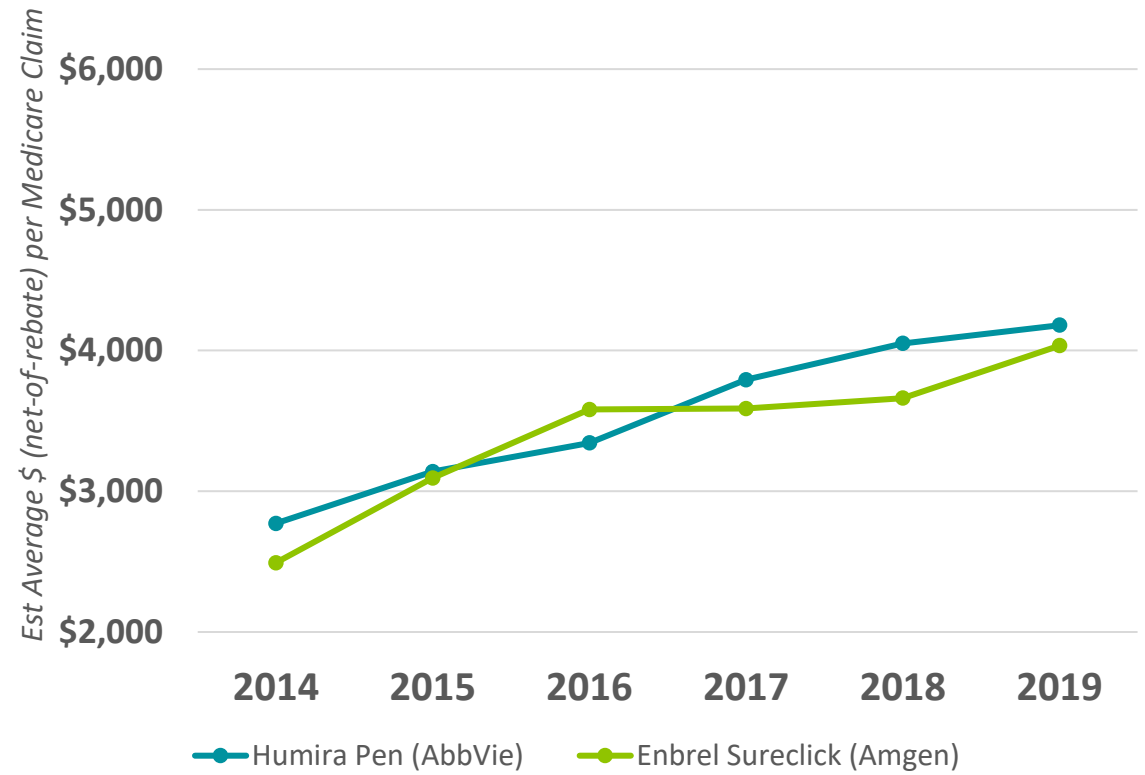
# Prices for Two Competitors Increase in Lockstep

**Both LIST PRICES and NET PRICES (i.e., net-of-rebates/discounts) increase in lockstep**

### Average List Price per Prescription



### Average Net-of-Rebate Price per Prescription



Source: Visante analysis of data from SSR Health

# Manufacturers Delay Competition by Abusing Regulatory Pathways

## Abuse Patent and Other Market Exclusivity Systems to Block Generic/Biosimilar Competition

- › Patents are property rights granted by the United States Patent and Trademark Office and provide 20 years of protection from the date the application is filed.<sup>1</sup>
  - In addition to patenting the drug molecule itself, patents can be obtained for other aspects of the drug such as the manufacturing process, different formulations, delivery devices, and new indications.<sup>2,3</sup>
- › Market exclusivity rights are statutorily granted by the FDA upon approval of a drug that provide the brand drug with protection from generic competition.
  - The length of exclusivity varies by drug and type. For example: new chemical entity (5 years), orphan drug (7 years), biologic (12 years), new clinical investigation\*(3 years), pediatric\*\*(6 months).<sup>1</sup>
  - Exclusivity can be extended by obtaining different market exclusivity rights.
- › Manufacturers use authorized generics and citizen petitions to fend-off competition.

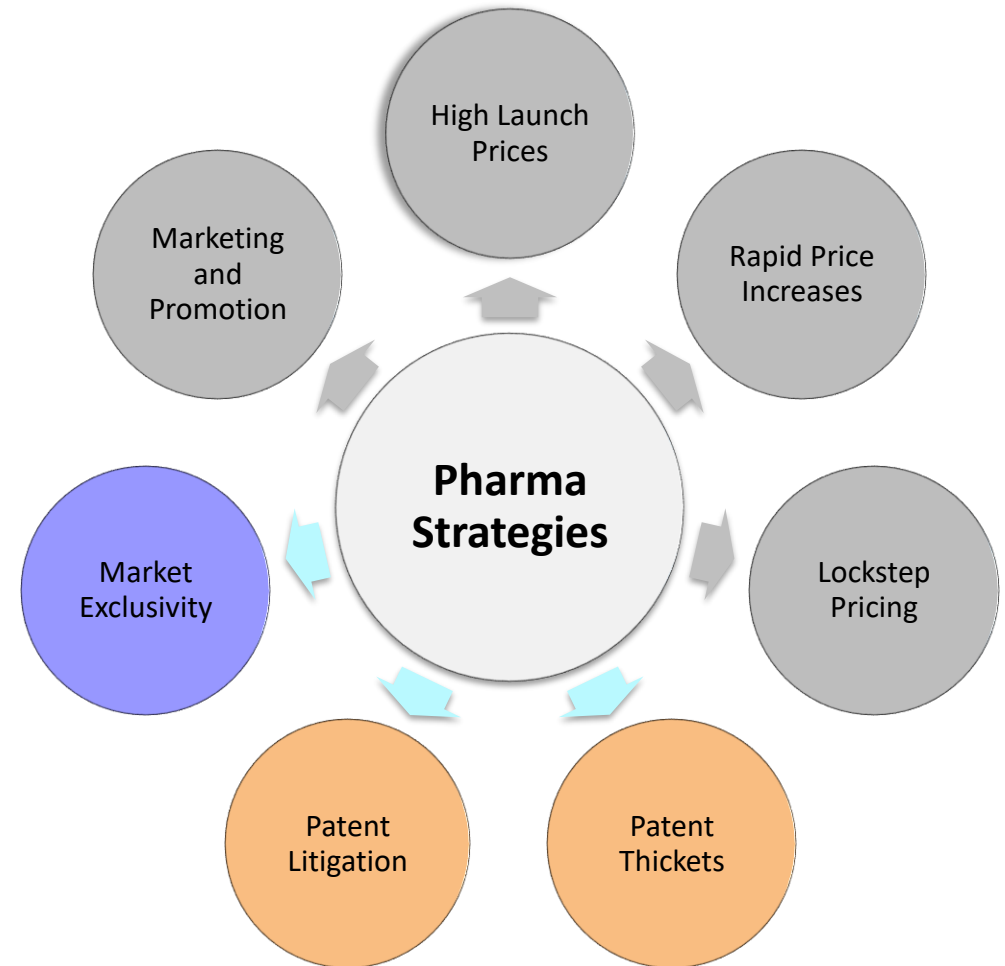
\*An example of new clinical investigation is a new indication or dosage form.

\*\*Pediatric exclusivity is added to existing patents/exclusivity

1. "Frequently Asked Questions on Patents and Exclusivity." FDA, Feb 2020. <https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity> Accessed May 2021

2. Congressional Research Service . *Drug Pricing and Pharmaceutical Patenting Practices*. February 11,2020

3. Berger et al, *How Drug Life-Cycle Management Patent Strategies May Impact Formulary Management*. AJMC January 20, 2017.



# Patent System Abuse: Patent Thickets

## *Delaying generic/biosimilar competition with patent thickets*

- › Drug manufacturers utilize a variety of patent strategies to extend their patent protection beyond the initial 20-year period.
- › One strategy is to create “patent thickets” by filing additional patents on the same drug after the drug is approved by the FDA.<sup>1</sup>
- › Oftentimes, these patents are filed as the drug nears the end of the original patent protection period.<sup>1,2</sup>
- › Dense patent thickets encourage large price hikes and can block generic or biosimilar competition for years or decades.<sup>2</sup>



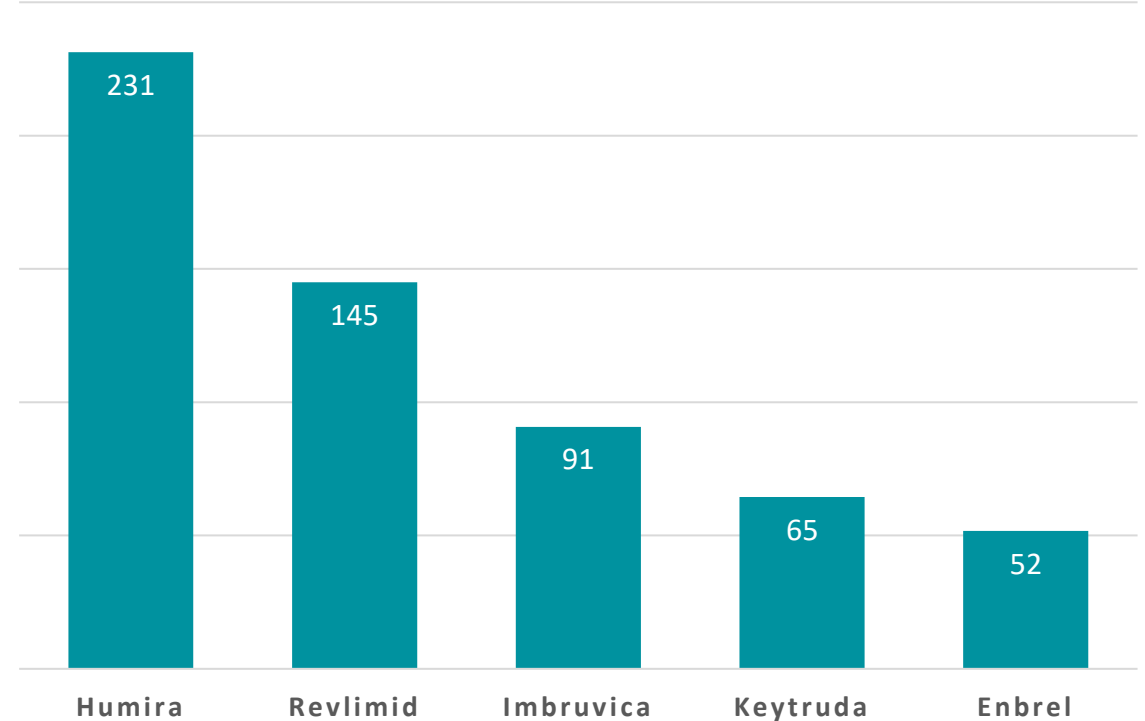
1. Congressional Research Service . *Drug Pricing and Pharmaceutical Patenting Practices*. February 11,2020

2. I-MAK. Overpatented, Overpriced - How excessive pharmaceutical patenting is extending monopolies and driving up drug prices. Retrieved December 2020 from <https://www.i-mak.org/overpatented/>

# Patent Thickets Are Commonly Used Strategy To Delay Competition

- Manufacturers of five top-selling drugs built dense patent thickets around their product with over 70% of the patents filed after the drug received FDA approval.<sup>1,2</sup>
- Oftentimes, patent thickets are amassed by obtaining “secondary patents” (i.e., patents on features other than the drug itself) representing incremental improvements such as:
  - Delivery devices (e.g., injectable pens);
  - Alternative dosage forms (e.g., granules vs. tablets);
  - Other chemicals related to the drug (e.g., salts, coloring agents).<sup>3,4</sup>

## 584 Patent Applications Filed after FDA Approval on Five Top-Selling Drugs<sup>1,2</sup>



Number of Patent Applications After FDA Approval

1. Visante analysis of I-MAK data.

2. I-MAK. Overpatented, Overpriced - How excessive pharmaceutical patenting is extending monopolies and driving up drug prices. Retrieved December 2020 from <https://www.i-mak.org/overpatented/>

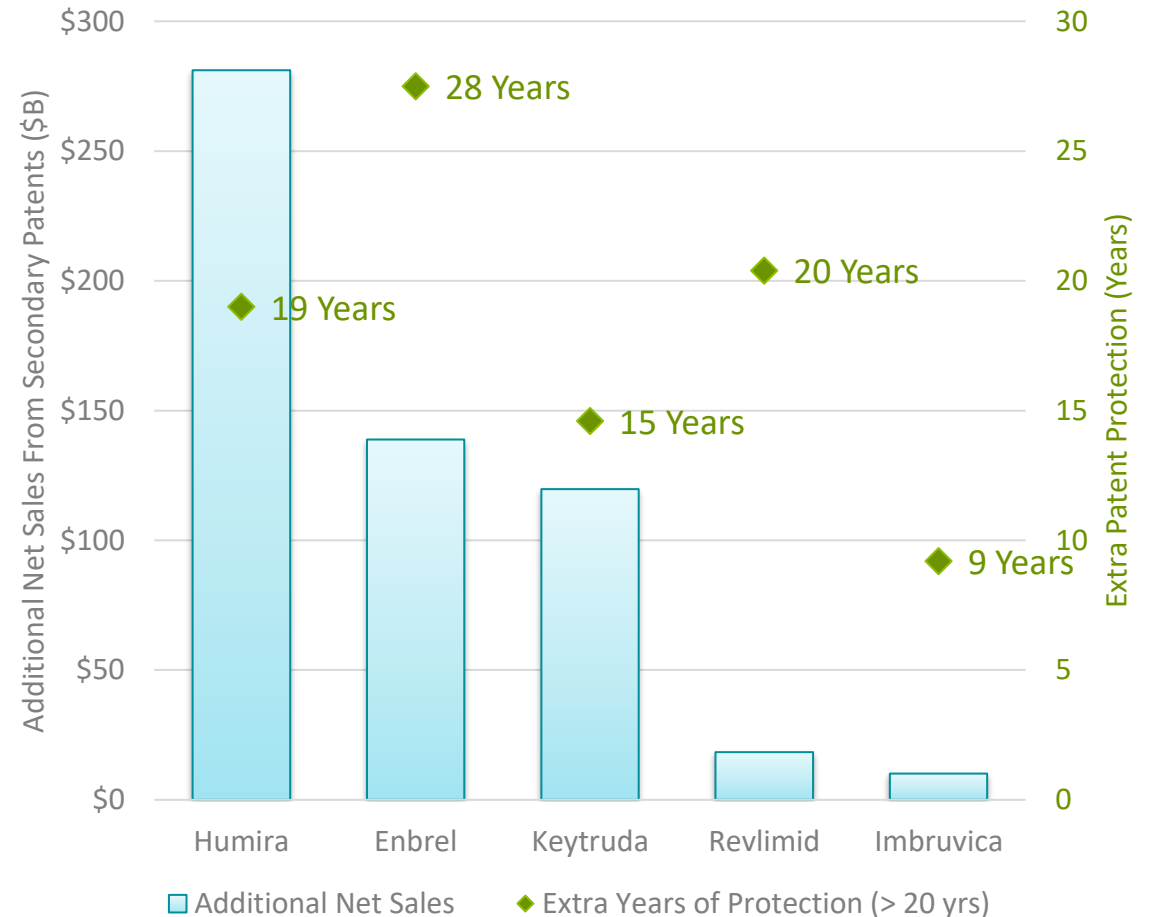
3. Congressional Research Service . *Drug Pricing and Pharmaceutical Patenting Practices*. February 11, 2020

4. Nawrat, P (2019, November 11) *From evergreening to thicketing: exploring the manipulation of pharma patents*. Pharmaceutical technology. <https://www.pharmaceutical-technology.com/>

# Additional Patents For Only Five Drugs Add \$500 Billion

- > Visante estimated the impact of patent thickets for five drugs: Humira, Enbrel, Keytruda, Revlimid, Imbruvica.
- > We used data published by I-MAK<sup>1</sup> on patents issued, extended protection beyond the initial 20-year period, and annual net sales.
- > Patent thickets for Humira alone account for more than \$280 billion in additional manufacturer sales. The total additional sales associated with secondary patents exceeds \$500 billion for the five drugs.<sup>2</sup>

Secondary Patents Add More Than \$500 Billion



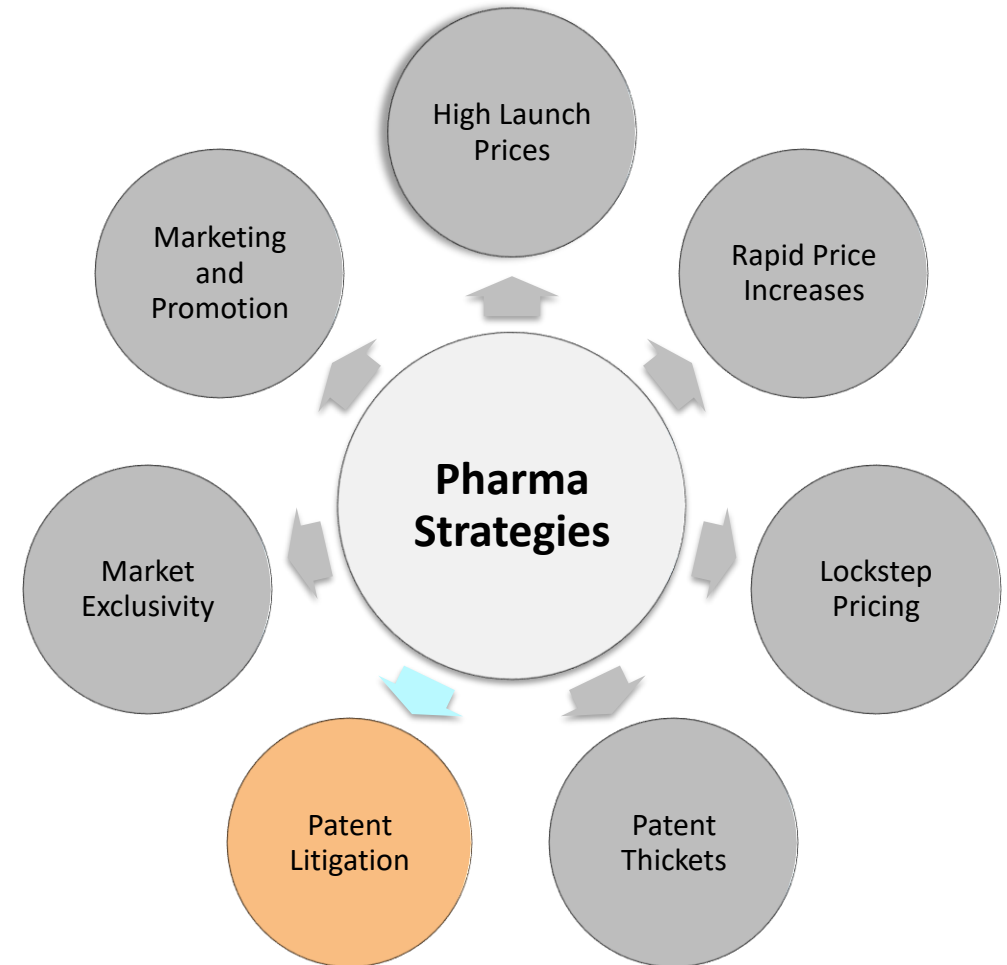
1.I-MAK. Overpatented, Overpriced - How excessive pharmaceutical patenting is extending monopolies and driving up drug prices. Retrieved December 2020 from <https://www.i-mak.org/overpatented/>

2.Total additional sales calculated by multiplying annual US net sales x number of extra years patent protection.

# Patent System Abuse: Patent Infringement Litigation

**Patent litigation costs consumers \$3.5 billion annually.**

- > Before a generic/biosimilar can be approved, the patents on the brand product must either be expired, or the generic manufacturer must certify that they didn't infringe on any of the patents.<sup>1</sup>
- > Brand manufacturers use patent infringement lawsuits to block generics/biosimilars from coming to the market. The lawsuit often triggers an automatic 30-month stay of approval to allow time to litigate patent issues. Therefore, the brand manufacturer may achieve up to an additional 30 to 45 months of effective exclusivity due to the initial hearing process and potential appeal process.<sup>1,2</sup>
- > Historically, brand manufacturers have offered generic/biosimilar manufacturers settlements that pay them to avoid bringing lower-cost alternatives to the market (pay-for-delay). Studies have shown these deals cost consumers and taxpayers \$3.5 billion in higher drug costs every year.<sup>3</sup>



1. Brennan Z (2016, August 17). Patents vs. Market Exclusivity: Why Does it Take so Long to Bring Generics to Market? RAPS: Regulatory Focus. Accessed May 21, 2021.

2. Berger et al. How Drug Life-Cycle Management Patent Strategies May Impact Formulary Management. AJMC. January 20, 2017

3. Pay-for-delay: When Drug Companies agree not to compete. Federal Trade Commission, 2019-20.



# Patent Infringement Settlements On The Rise

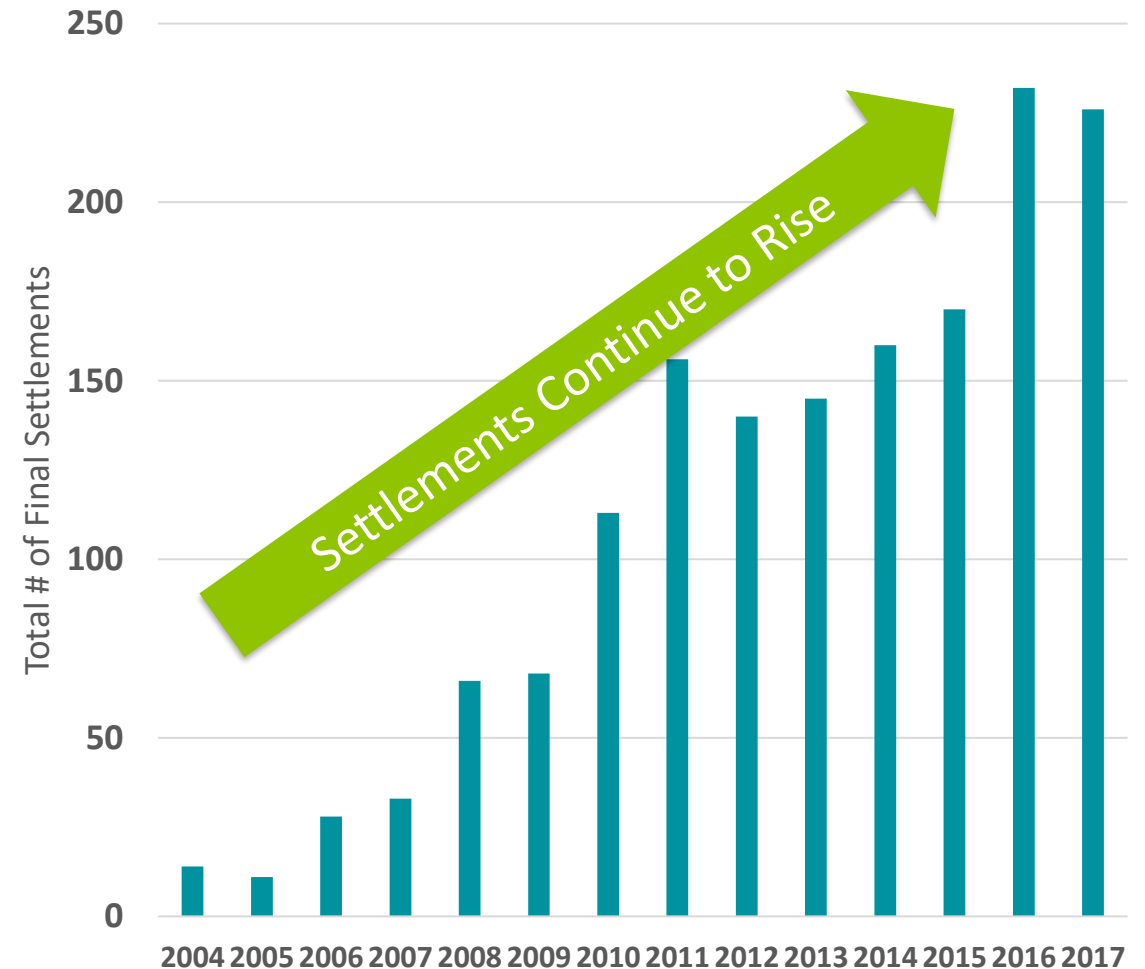
## Settlements are not slowing down

- › While pay-for-delay settlements have come under antitrust scrutiny, brand manufacturers continue to find ways of settling cases to extend their monopoly.
- › Despite increased scrutiny, brand manufacturers are reaching more settlements with generic/biosimilar manufacturers than ever before.<sup>1</sup>
- › With pay-for-delay settlements being subject to antitrust liability, brand manufacturers have gotten creative and found other ways to settle such as:
  - Licensing the patents to generic/biosimilar manufacturers.
  - Granting an exclusive license to one generic/biosimilar manufacturer, creating a duopoly.
  - Agreeing not to release an authorized generic/biosimilar.
  - Staggering market entry with multiple generic/biosimilar manufacturers.<sup>2</sup>

1. Federal Trade Commission. [Agreements Filed With the Federal Trade Commission Under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003: Overview of Agreements Filed In Fiscal Year 2017: A Report By the Bureau of Competition](#). December 2020.

2. Baumna, V. (2020, February 10). [Pharma Pay-For-Delay Deals Called 'Cost of Doing Business'](#). Bloomberg Law. Accessed Dec 2020.

Increasing Number of Final Patent Settlements<sup>1</sup>

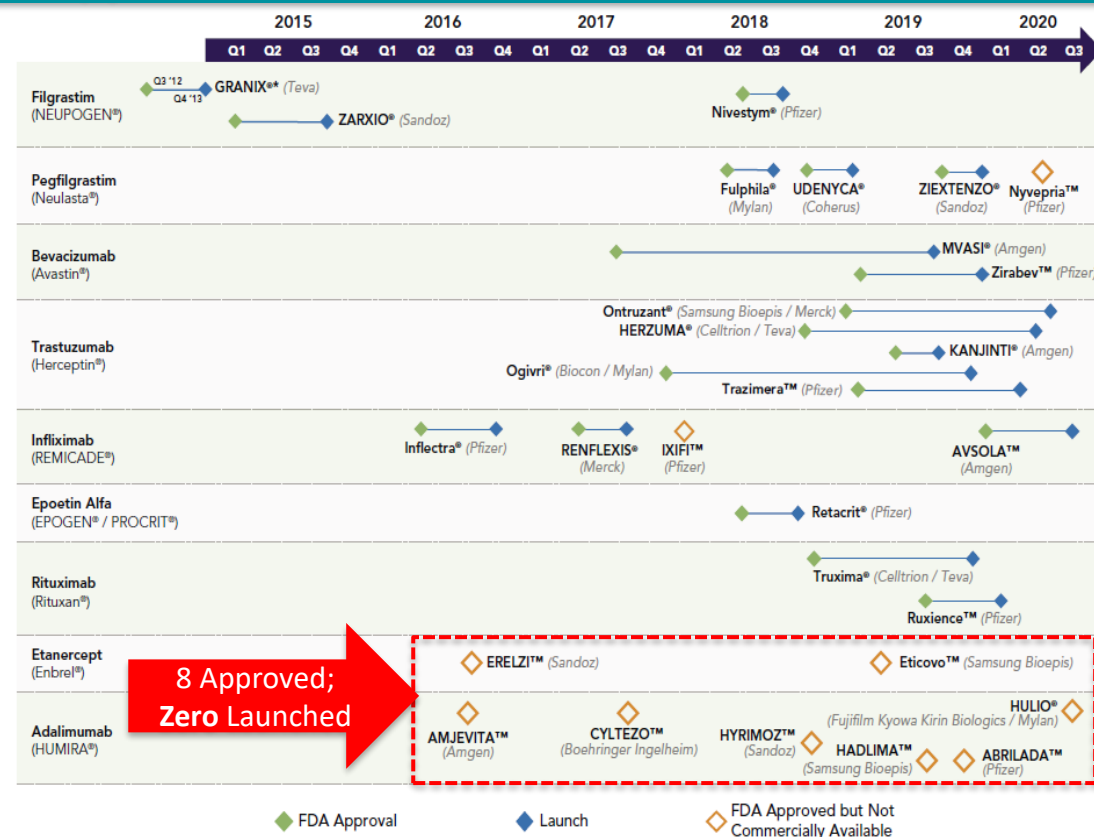


# Patent Litigation and Settlements Delay Biosimilar Launches

- As of April 2021, 29 biosimilars have been approved but just 20 (69%) have launched.<sup>1</sup>
- For the 20 biosimilars that launched, the average time from approval to launch was approximately 3.5 quarters.<sup>2</sup>
- Together, Enbrel and Humira have eight biosimilars approved (earliest in 2016), but none have launched as a result of patent litigation and settlements.
  - AbbVie settled with multiple generic manufacturers to delay any biosimilar launches until 2023.<sup>3</sup>
  - Amgen was successful in upholding its patents that protect Enbrel from competition with Sandoz's biosimilar, Erelzi. Erelzi is prohibited from launching until Enbrel's patents expire in 2029.<sup>4</sup>

1. McGowan, Jesse, Biehn. U.S. Biosimilar Report. Amerisource Bergen. April 1, 2021.  
 2. Amgen Biosimilars. 2020 Biosimilar Trends Report, Amgen Biosimilars. Accessed December 2020.  
 3. Joachim, R. (2020, September 29). "Weighing The Potential Of Humira Biosimilars In The U.S. — Competitive Dynamics Analysis." *Biosimilar Development*. Accessed December 2020.  
 4. Sagonowsky, E (2021, May 17). "Sandoz's Enbrel biosim case turned away at SCOTUS, giving Amgen's blockbuster 8 more years of free rein." *Fierce Pharma*. Accessed May 2021.

## Approved and Launched Biosimilars in the US<sup>2</sup>



Key: FDA – Food and Drug Administration.  
 \*GRANIX is not a biosimilar. It was approved under a full Biologics License Application, which was submitted to the FDA before enactment of the biosimilar approval pathway.

Note: Not depicted on this chart are the launch of Nyvapria (Q4 2020) and the approval (Q4 2020) and launch (Q1 2021) of Riabni.

# Extended Exclusivity: Orphan Drugs

## *Manufacturers extend exclusivity via orphan drug designations*

- › The Orphan Drug Act of 1983 was created to incentivize manufacturers to develop drugs used to treat rare diseases.<sup>1</sup>
- › In addition to a seven-year exclusivity period per indication, manufacturers may also receive a 25% tax credit for expenses incurred during clinical testing and waived New Drug Application fees (approximately \$1.5-3M).<sup>1,2</sup>
- › These incentives have led some manufacturers with highly-profitable drugs already on the market to seek out orphan designations to generate additional profits without incurring significant expenses.<sup>3</sup>
- › One study showed over 20% of drugs with orphan indications also have non-orphan indications. More than half received the non-orphan indication first.<sup>1</sup>



1. IQVIA. [Orphan Drugs in the United States](#). October 2018.

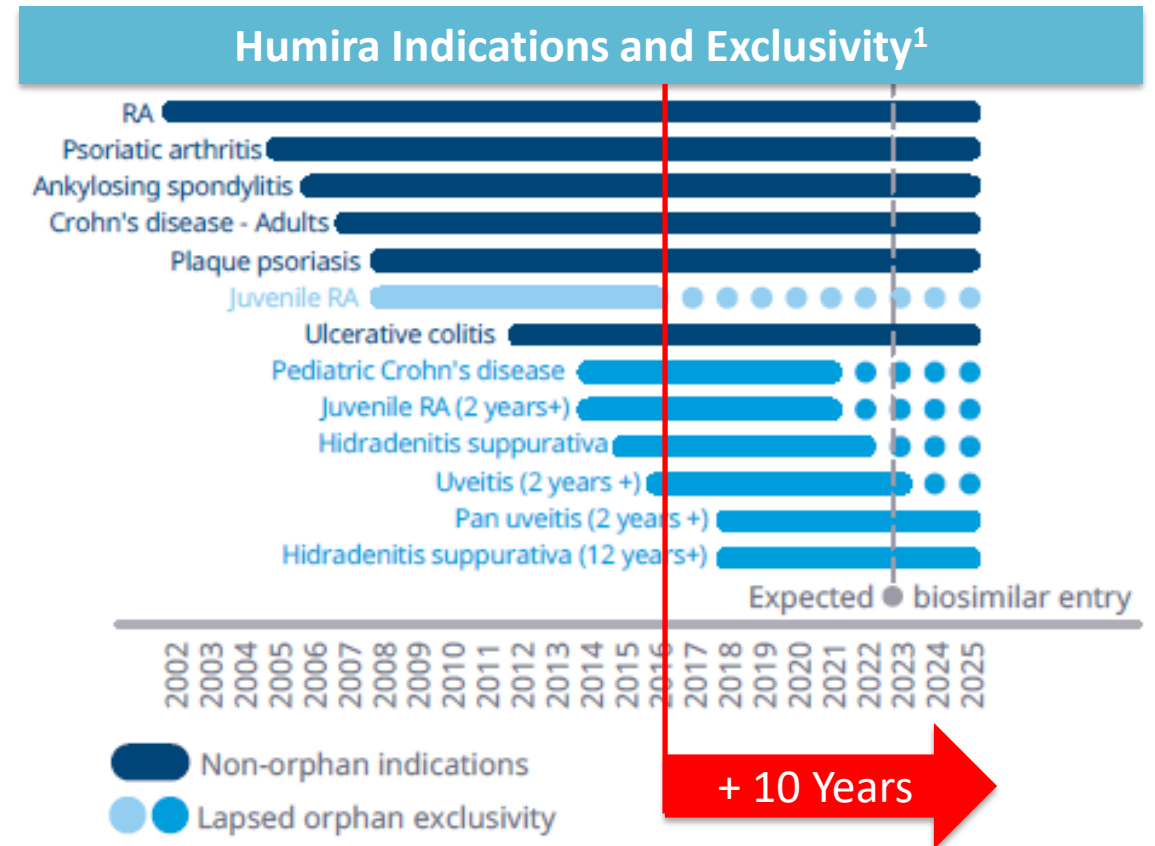
2. U.S. Food and Drug Administration. [Prescription Drug User Fee Amendments](#). Accessed December 2020.

3. Ferreri, D (2020, June 25). [Orphan Drug Exclusivity Keeps Biosimilars Off the Market, Study Says](#). AJMC, 2020. Accessed December 2020.

# Extended Exclusivity: Non-Orphan Drugs with Orphan Indications

## *Humira used orphan designations to extend exclusivity by 10 years*

- > Approximately 68% of drugs with three or more orphan designations also have non-orphan indications.<sup>1</sup>
- > Some manufacturers of drugs with non-orphan indications seek multiple orphan designations by strategically staggering applications to obtain overlapping exclusivity periods.
- > For example, Humira has:
  - six non-orphan designations, five of which were approved before the first orphan designation; and
  - eight orphan designations granted between 2008 and 2018, extending exclusivity by 10 years.<sup>1</sup>



1. IQVIA. Orphan Drugs in the United States. December 2020.

# Abuse of Regulatory Pathways to Delay Competition

## *Use authorized generics and citizen petitions to stave off competition*

### Authorized Generics

- › An authorized generic is the exact same drug product as the branded product but marketed with a generic label.<sup>1</sup>
- › Brand manufacturers use an authorized generics strategy to slow market share decline following loss of exclusivity, avoid patent litigation, and maintain profits.<sup>2</sup>
- › As of April 2021, there have been 1,190 authorized generics approved by the FDA.<sup>1</sup>
- › Because authorized generics are not typically subject to rebates, they “can be as profitable as, if not more profitable than, brand-name drugs.”<sup>3</sup>
- › One study found that implementing an authorized generics strategy produces a 50:1 ROI.<sup>2</sup>

### Citizen Petitions

- › A citizen petition is intended to be a way for engaged citizens and scientists to file concerns about the safety and regulation of drugs coming to the market, but pharmaceutical companies have abused this process to delay competition from generic drug equivalents.<sup>4</sup>
- › One study found brand manufacturers frequently submitted “frivolous or questionable claims in a last-ditch effort to hold off competition.”<sup>5</sup>
- › Nearly half of all the citizen petitions filed between 2000-2012 that could have delayed generic competition were filed within a year and a half before the FDA approved the generic.<sup>5</sup>
- › One group estimated a \$1.9 billion financial cost to the American public due to four frivolous petitions delaying generic competition for 521 days in total.<sup>4</sup>

1. US Food and Drug Administration. [FDA List of Authorized Generics Drugs](#). Accessed June 2021.

2. Global News Wire. [“Drug Industry Study Finds a 5,100% ROI for Implementing Authorized Generics Strategies”](#) Dec 04, 2015.

3. Hancock J, Lupkin S. [“Drugmakers Master Rolling Out Their Own Generics To Stifle Competition”](#) Aug 5, 2019.

4. Robin C. Feldman, [The Burden on Society from Eleventh-Hour 'Citizen Petitions' Filed to Slow Generic Drugs](#), 79 Md. L. Rev. Online 1 (2020). Available at: [https://repository.uchastings.edu/faculty\\_scholarship/1779](https://repository.uchastings.edu/faculty_scholarship/1779)

5. Robin Feldman and Connie Wang, [A Citizen's Pathway Gone Astray — Delaying Competition from Generic Drugs](#), 376 New Eng. J. Med. 1499 (2017). Available at: [https://repository.uchastings.edu/faculty\\_scholarship/1558](https://repository.uchastings.edu/faculty_scholarship/1558)

# Marketing and Promotion: Coupons and Payments

## *Manufacturers promote use of higher-cost drugs using coupons and physician payments*

- › Manufacturers use coupons and copay cards to offset the higher costs of high-priced drugs, leading to greater utilization and higher overall costs.<sup>1</sup>
- › The prices for brand drugs with coupons are rising 12-13% every year, compared to 7-8% increases for brand drugs without coupons.<sup>2</sup>
- › “Most often, patients acquire drug coupons by downloading them after hearing about them through DTC advertising.”<sup>3</sup>
- › Studies have shown “that patients who receive more exposure to DTC [direct-to-consumer] advertisements tend to request advertised drugs and that the drugs are frequently prescribed despite physician reservations.”<sup>4</sup>
- › In a survey of over 450 family practice physicians, 71% indicated that “DTC ads pressures physicians to use drugs they might not ordinarily use.”<sup>5</sup>
- › Manufacturers also reward physicians more than \$2 billion a year in a variety of ways (e.g., consulting and speaker fees, travel and hotel expenses, and dining out).<sup>6</sup>
- › According to a recent study, “Physicians who receive money from a given company are more likely to prescribe that company’s more expensive drug instead of other lower cost treatment options.”<sup>7</sup>



1. Massachusetts Health Policy Commission. *Prescription Drug Coupon Study - Report to the Massachusetts Legislature*. July 2020.

2. Dafny, Ody, Schmitt. *When Discounts Raise Costs: The Effect of Copay Coupons on Generic Utilization*. The National Bureau of Economic Research. October 2016.

3. *Understand pharma discount coupons*. Medical Economics Journal, October 10, 2018 edition, Volume 95, Issue 19.

4. Robinson AR, Hohmann KB, Rifkin JJ, et al. *Direct-to-Consumer Pharmaceutical Advertising: Physician and Public Opinion and Potential Effects on the Physician-Patient Relationship*. Arch Intern Med. 2004;164(4):427-432. doi:10.1001/archinte.164.4.427

5. Lipsky MS, Taylor CA. *The opinions and experiences of family physicians regarding direct-to-consumer advertising*. J Fam Pract. 1997 Dec;45(6):495-9. PMID: 9420585.

6. *We Found Over 700 Doctors Who Were Paid More Than a Million Dollars by Drug and Medical Device Companies*. ProPublica, Ornstein et al, Oct 17 2019.

7. *Doctors Prescribe More of a Drug If They Receive Money from a Pharma Company Tied to It*. ProPublica, Hannah Fresques, Dec 20 2019.

# Coupons and Copay Cards Increase Use of Higher-Cost Drugs

## *Coupons raise overall prescription drug costs*

- › The number of branded drugs that offered coupons rose from 278 in 2012 to 701 in 2018.<sup>1</sup>
- › In 2018, an estimated 19% of commercially-insured patients in the U.S. who filled a prescription for a branded drug used a coupon at least once in the year, and the total dollar value of redeemed coupons reached \$13 billion nationwide.<sup>1</sup>
- › A study for the state of Massachusetts found that excess spending attributable to coupons for the 14 sample drugs studied totaled \$45 million per year (for the state of MA).<sup>1</sup>
- › One group estimates that “banning copay coupons would lower prescription drug costs by approximately \$1.2 billion per year.”<sup>2</sup>
- › Coupons are barred for use under federal health care programs as illegal kickbacks, as well as in some states.<sup>3</sup>

Coupons are promoted as a program to reduce patient’s out-of-pocket spending, but drug coupons also:

- 1. Drive manufacturer profits**
  - › Have been referred to as “a money tree” by providing a way for brand manufacturers to raise prices infinitely without reducing demand.<sup>4</sup>
  - › Manufacturers may earn a 20:1 ROI.<sup>5</sup>
- 2. Circumvent formulary and utilization management tools<sup>1,6</sup>**
  - › Used to increase market penetration of drugs that do not receive a favorable formulary placement.
  - › Encourage use of higher-cost drugs instead of clinically appropriate lower-cost alternatives.
- 3. Retain brand drug market share by staving off generic competition<sup>5</sup>**

1. Massachusetts Health Policy Commission. [Prescription Drug Coupon Study - Report to the Massachusetts Legislature](#). July 2020.

2. Dafny, Ody, Schmitt. [Eliminating Prescription Drug Coupon Cards](#). One Percent Steps. Accessed May 2021.

3. [How Copay Coupons Could Raise Prescription Drug Costs by \\$32 Billion over the Next Decade](#). Visante, 2011.

4. [Prescription Drug Coupons Actually Increase Healthcare Spending by Billions](#). Kellogg School of Management at Northwest University, 2017.

5. Dafny, Ody, Schmitt. [When Discounts Raise Costs: The Effect of Copay Coupons on Generic Utilization](#). The National Bureau of Economic Research. October 2016.

6. Van Nuys, Joyce, Ribero. [Prescription Drug Coupons: A One-Size-Fits-All Policy Approach Doesn't Fit The Evidence](#). Health Affairs, Feb 2018.

# Marketing and Promotion: Direct-to-Consumer Advertising

## *DTC ads for prescription drugs influence prescribing habits and drive profits*

- › Manufacturers invest heavily in DTC ads
  - Manufacturers spend approximately \$6.5 billion per year on DTC ads.<sup>1</sup>
  - There were 4.6 million DTC ads in 2016, representing a 58-fold increase since 1997.<sup>2</sup>
  - One study identified “a shift toward advertising high-cost biologics and cancer immunotherapies”<sup>2</sup>
- › DTC ads influence prescribing habits of physicians
  - Multiple studies have shown that “patients that ask physicians for medication are more likely to receive a prescription than those who do not ask”<sup>3</sup>
  - In a survey of almost 1,900 physicians, 40% responded they “often” or “sometimes” prescribed a brand-name drug when an equivalent generic was available because of a patient request for the brand name.<sup>4</sup>
- › Manufacturers’ profits increase as a result of DTC ads
  - One study estimates a \$4.20 increase in sales for every \$1 spent on DTC ads.<sup>3</sup>
  - Based on a total of \$6.5 billion spent, we estimate more the \$27 billion in additional annual sales.

1. Lexchin J, Menked DB. Can direct-to-consumer advertising of prescription drugs be effectively regulated? New Zealand Medical Association. 2019; 132(1496):59-65.

2. Schwartz LM, Woloshin S. Medical Marketing in the United States, 1997-2016. JAMA. 2019;321(1):80–96. doi:10.1001/jama.2018.19320

3. Porter, Dayna M. (2011) "Direct-to-Consumer (DTC) Pharmaceutical Marketing: Impacts and Policy Implications," SPNHA Review: Vol. 7 : Iss. 1 , Article 5. Available at: <https://scholarworks.gvsu.edu/spnhareview/vol7/iss1/5>

4. Science Daily, "Many U.S. Physicians Often Fulfill Patient Requests for Brand-Name Drugs Instead of Equivalent Generics," sciencedaily.com, Jan. 7, 2013



# Billions in Pharma Physician Payments Drive Prescribing of High-Cost Drugs

- › More than \$2 billion a year was paid by pharma companies to doctors, based on a published review of 36 studies.<sup>1</sup>
- › More than 2,500 physicians received at least half a million dollars apiece from drug makers and medical device companies in the five-year period 2014-18. And that doesn't include money for research or royalties from inventions. More than 700 of those doctors received at least \$1 million.
- › The main forms of payment were consulting and speaker fees, travel and hotel expenses, and dining out. In some cases, the incentives were actually enough to be the main source of a physician's income.<sup>1</sup>
- › According to the oncologist who led the research team investigating the impact of drug prescription coupons, *"Physicians who receive money from a given company are more likely to prescribe that company's drug instead of other treatment options. Doctors are more inclined to prescribe expensive brand-name drugs rather than the cheaper generic, with the results being a big 'return on investment' for the drug companies."*<sup>1</sup>
- › One recent "before-and-after" study indicates that physician payments increased prescribing by 4-12%. Other similar studies have found an increase in prescribing as high as 73%.<sup>2</sup>
- › Studies comparing physicians who receive payments to other physicians who do not receive payments found large differences in prescribing. In 2016, for example:
  - Doctors who received payments related to Myrbetriq, which treats overactive bladder, wrote 64% more prescriptions for the drug than those who did not.
  - Doctors who received payments related to Restasis, used to treat chronic dry eye, wrote 141% more prescriptions.<sup>3</sup>

1. [Pharma payments to physicians still deliver a big 'return on investment' in prescription growth, study finds](#). Fierce Pharma, Dec 3, 2020.

2. [Drug Firms' Payments and Physician Prescribing Behavior In Medicare Part D](#). Carey et al, National Bureau of Economic Research, March 2021.

3. [We've Been Tracking Pharma Payments to Doctors For Nearly A Decade. We Just Made A Big Breakthrough](#). ProPublica, Charles Ornstein Dec. 20, 2019.



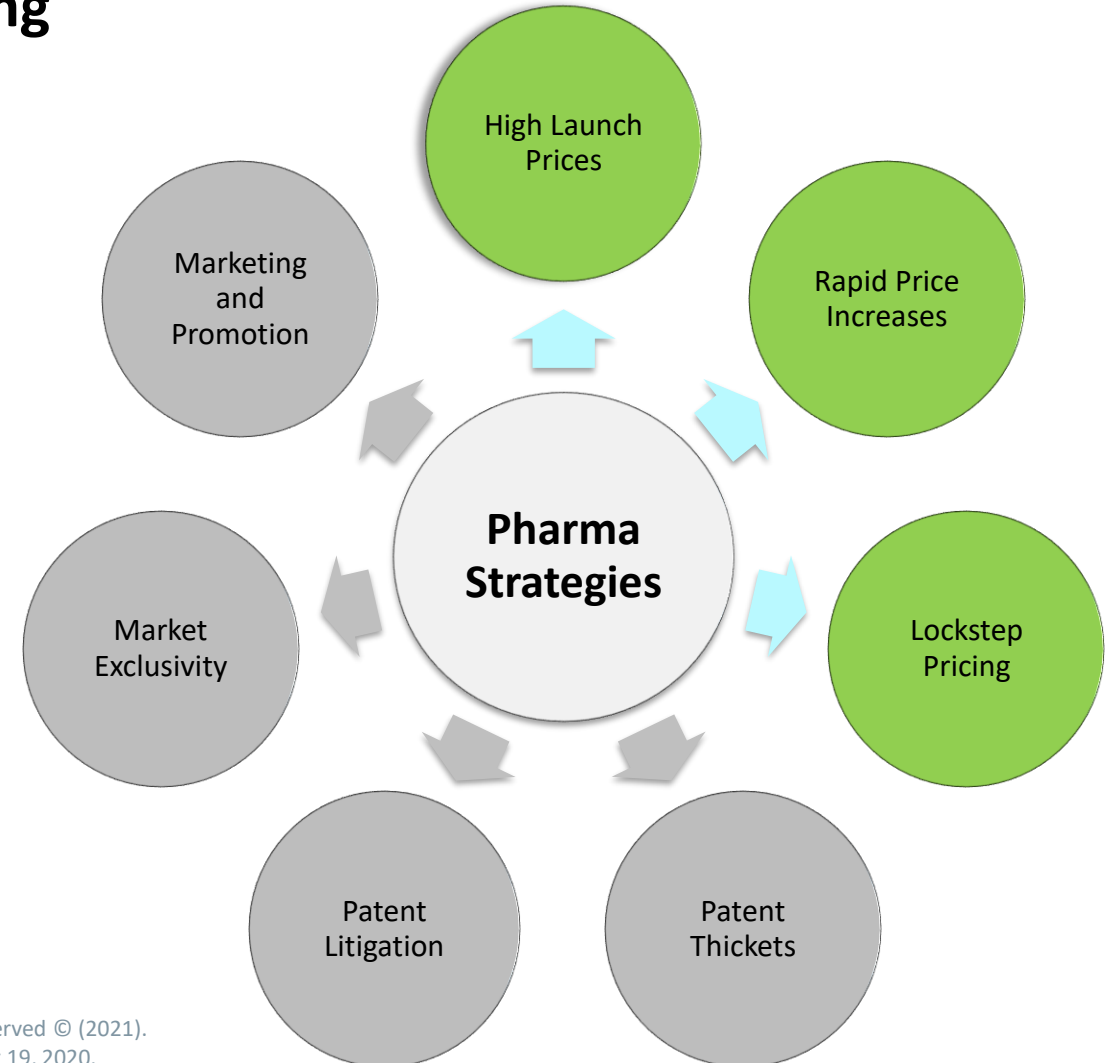
**Pricing  
Case Studies:  
Humira and Enbrel**

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# Pharma Strategies for Humira/Enbrel: Anticompetitive Pricing

## Expand profits through anticompetitive pricing




- › Humira and Enbrel launch prices were more than 15x the average price of brand name drugs at the time of launch.<sup>1,2</sup>
- › Since being launched, Enbrel and Humira have increased prices more than 25 times.<sup>2</sup>
- › Enbrel and Humira increased prices by the same percentage more than 75% of the time.<sup>2</sup>



1. Kaiser Family Foundation. Prescription Drug Trends: A Chartbook Update. November 2001.

2. Visante analysis of AnalySource® — Reprinted with permission by First Databank, Inc. See Slide 9 for details. All rights reserved © (2021). Date range of prices referenced: November 4, 1998 - July 30, 2020. Date information accessed from AnalySource: November 19, 2020.

# Enbrel and Humira Pricing Strategies

	Enbrel	Humira
 <b>Launch Price Per Prescription</b>	<b>\$880</b> (1998)	<b>\$1,096</b> (2002)
 <b>Average Annual Price Increase</b>	<b>8.90%</b>	<b>10.21%</b>
 <b>Lockstep Pricing</b>	<b>\$7.55</b> <b>Average Annual Difference in Price Per Prescription</b>	

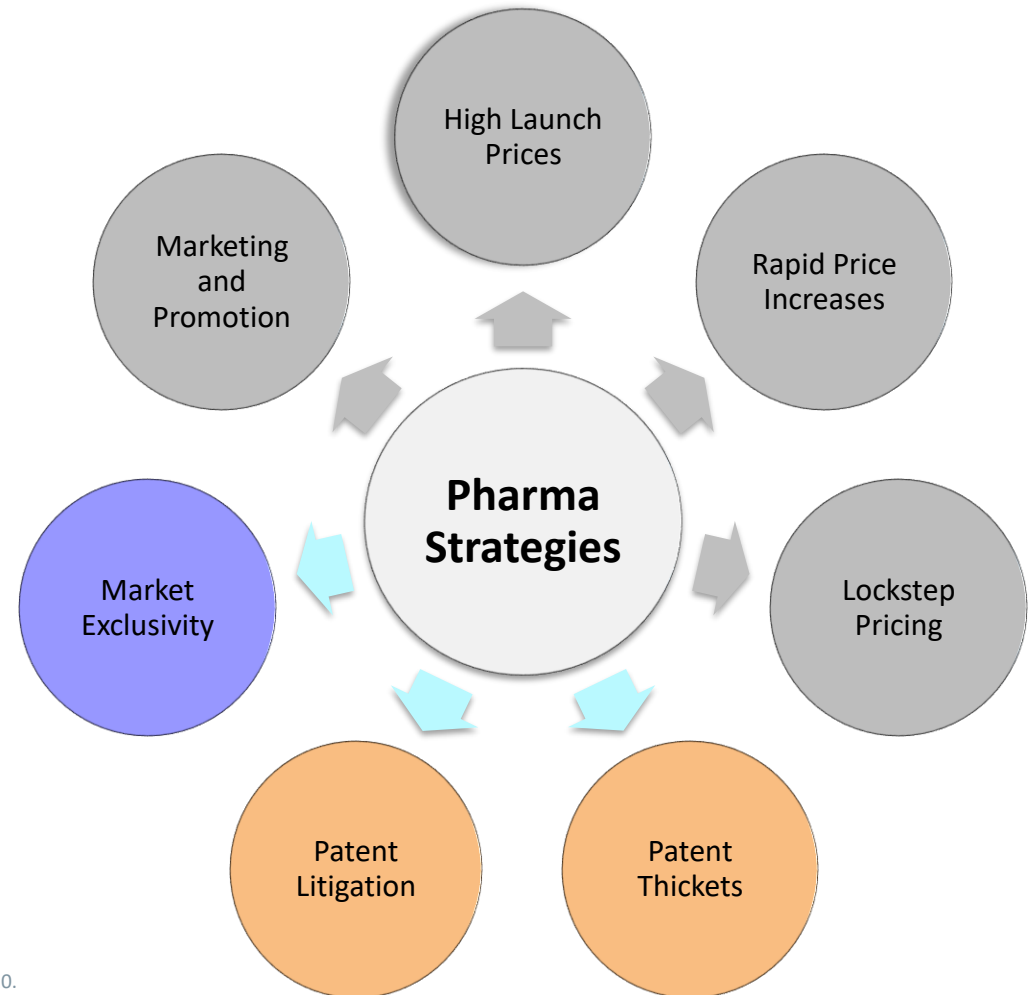
Source: Visante analysis of AnalySource® — Reprinted with permission by First Databank, Inc. See Slide 9 for details.

All rights reserved © (2021). Date range of prices referenced: November 4, 1998 - July 30, 2020. Date information accessed from AnalySource: November 19, 2020.

# Pharma Strategies for Humira/Enbrel: Extend Exclusivity

*Extend exclusivity via exploitation of orphan drug act, patent thickets, and patent litigation*

- › Over the 18+ years on the market, Humira and Enbrel have amassed over 160 patents combined to help protect their product from generic competition.<sup>1</sup>
- › Both products were granted orphan designations (nine combined) after receiving FDA approval for a non-orphan indication.<sup>2</sup>
- › While there have been eight biosimilars approved since 2016, none have launched due to patent settlements and litigation.<sup>3,4,5</sup>



1. Visante analysis of I-MAK data.

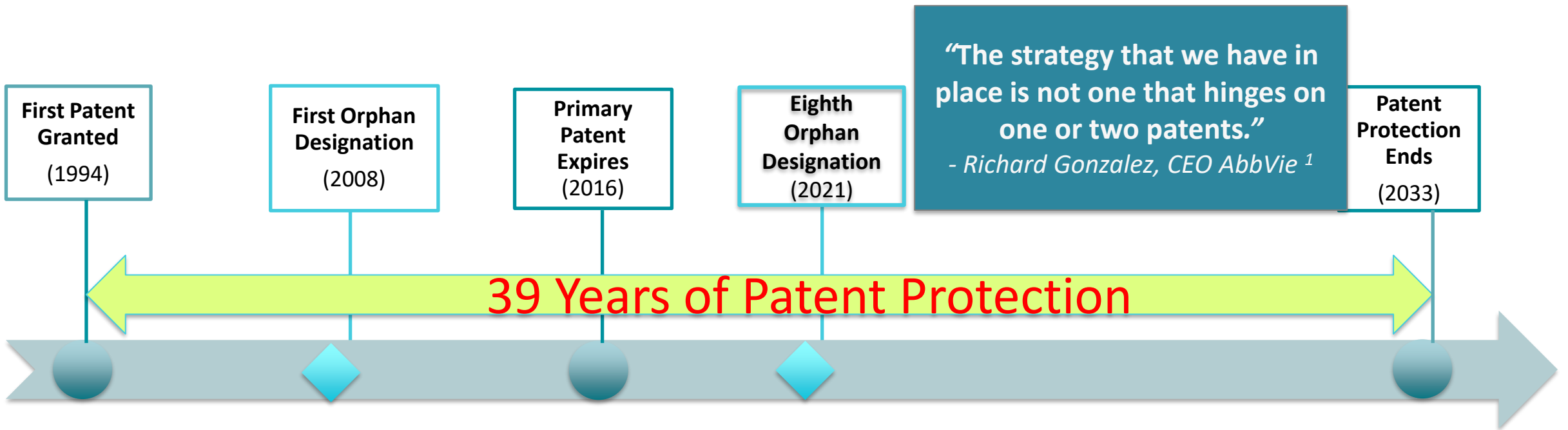
2. US Food and Drug Administration. Orphan Drug Product designation database. Accessed Dec 2020.

3. McGowan, Jesse, Biehn. U.S. Biosimilar Report. Amerisource Bergen. April 1, 2021.

4. Joachim, R.. "Weighing The Potential Of Humira Biosimilars In The U.S. — Competitive Dynamics Analysis." *Biosimilar Development*. September 29 2020.

5. Sagonowsky. Sandoz's Enbrel biosim case turned away at SCOTUS, giving Amgen's blockbuster 8 more years of free rein. *FiercePharma*, Accessed May 25 2021.

# Patent Thickets Extend Humira Expiration 17 Years (from 2016-2033)



## Humira's Massive Patent Thicket<sup>2,3</sup>

- AbbVie filed 257 total patent applications on Humira, 130 of which were granted.
- Almost half of the patents on Humira have been filed since 2014, which is two years before Humira's original patent expired.
- Humira's patent thicket extends length to 39 years.
- During this time, AbbVie also obtained eight orphan designations for Humira.

1. AbbVie's Humira: The poster child for how drug companies abuse the patent system to keep drug prices high. But only for Americans. Coalition Against Patent Abuse.

2. Humira's Patent Wall. I-MAK, 2020.

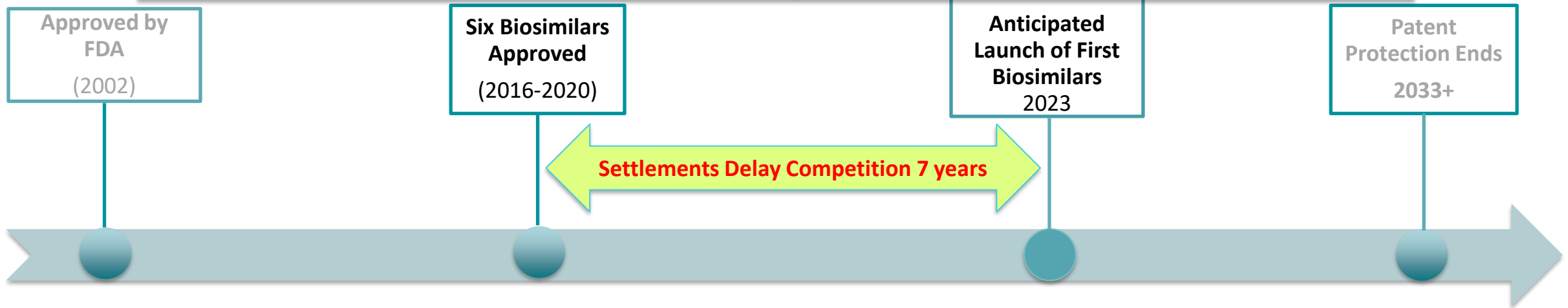
3. I-MAK. Report Finds 89% of Total U.S. Patent Applications on Humira Were Filed After FDA Approval – Pointing to a Deliberate Strategy to Delay Competition. December 2018.

4. US Food and Drug Administration. Orphan Drug Product designation database. Accessed Dec 2020.

# Patent Litigation Delays Biosimilars by Seven Years

“You’ve seen us execute very nicely with our legal strategy and the settlements around the U.S. events to delay the onset of [loss of Humira’s monopoly] into the 2022-2023 time period..”

- Richard Gonzalez, CEO AbbVie <sup>1</sup>



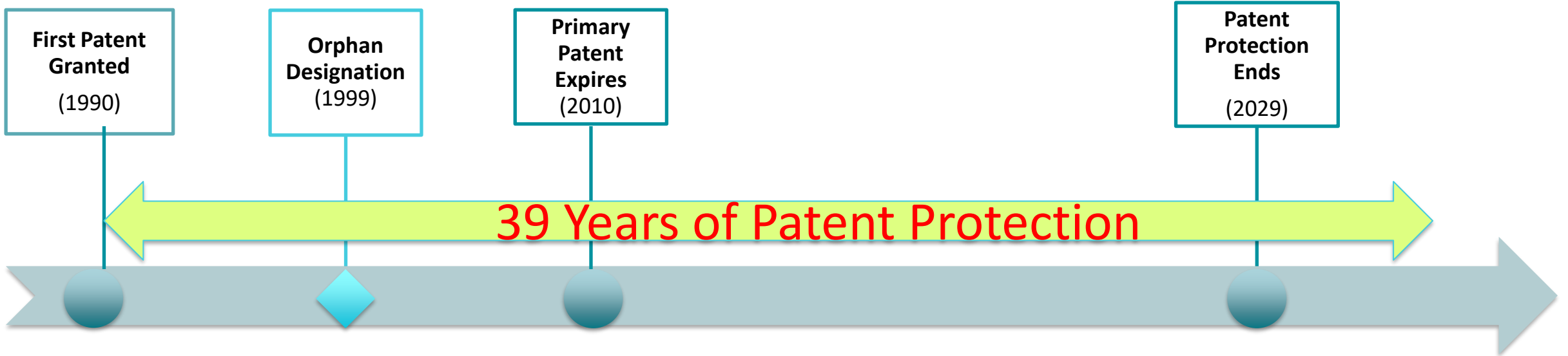
## Patent Litigation Settlements Have Extended Humira’s Market Exclusivity<sup>2</sup>

- AbbVie has entered into eight separate settlements since 2017.
- These eight settlements prevent the entry of a lower-cost competitor to the market until 2023.
- As a result, Humira gains an additional seven years without any generic competition.

1. AbbVie’s Humira: The poster child for how drug companies abuse the patent system to keep drug prices high. But only for Americans. Coalition Against Patent Abuse Biosimilars Pipeline Report. AmerisourceBergen, 2021.

2. Joachim, R. (2020, September 29). “Weighing The Potential Of Humira Biosimilars In The U.S. — Competitive Dynamics Analysis.” *Biosimilar Development*. Accessed December 2020.

# Patent Thickets Extend Enbrel Expiration 19 Years (From 2010-2029)



## Enbrel's Dense Patent Thicket <sup>1,2</sup>

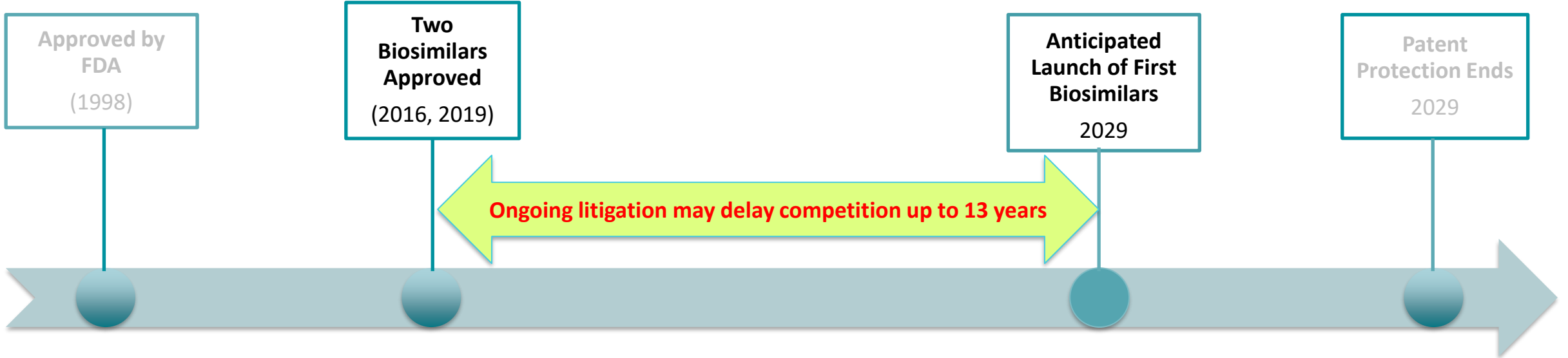
- There have been 68 total patent applications on Enbrel, 39 of which were granted.
- Over 70% of the patents filed were after the drug was approved by the FDA.
- Enbrel's patent thicket extends length to 39 years.
- During this time, Amgen also obtained one orphan designation for Enbrel.

1. I-MAK. *Overpatented, Overpriced Special Edition Enbrel*. October 2020.

2. US Food and Drug Administration. Orphan Drug Product designation database. Accessed Dec 2020.



# Patent Litigation Delays Biosimilars By Up To 13 Years



## Amgen Defends Enbrel Patents in Ongoing Litigation<sup>1,2</sup>

- Amgen has been involved in ongoing litigation with two biosimilar manufacturers (Sandoz and Samsung Bioepis).
- Amgen successfully defended their patents in the Sandoz case, and the Samsung Bioepis case will go to trial in 2023.
- While litigation continues, it is possible lower-cost competitors won't be available until 2029.

1. Sagonowsky E (2021, May 17). Sandoz's Enbrel biosim case turned away at SCOTUS, giving Amgen's blockbuster 8 more years of free rein. FiercePharma, Accessed May 25 2021.

2. US District Court, District of Delaware. Genentech v. Samsung Bioepis (1:20-cv-00859)

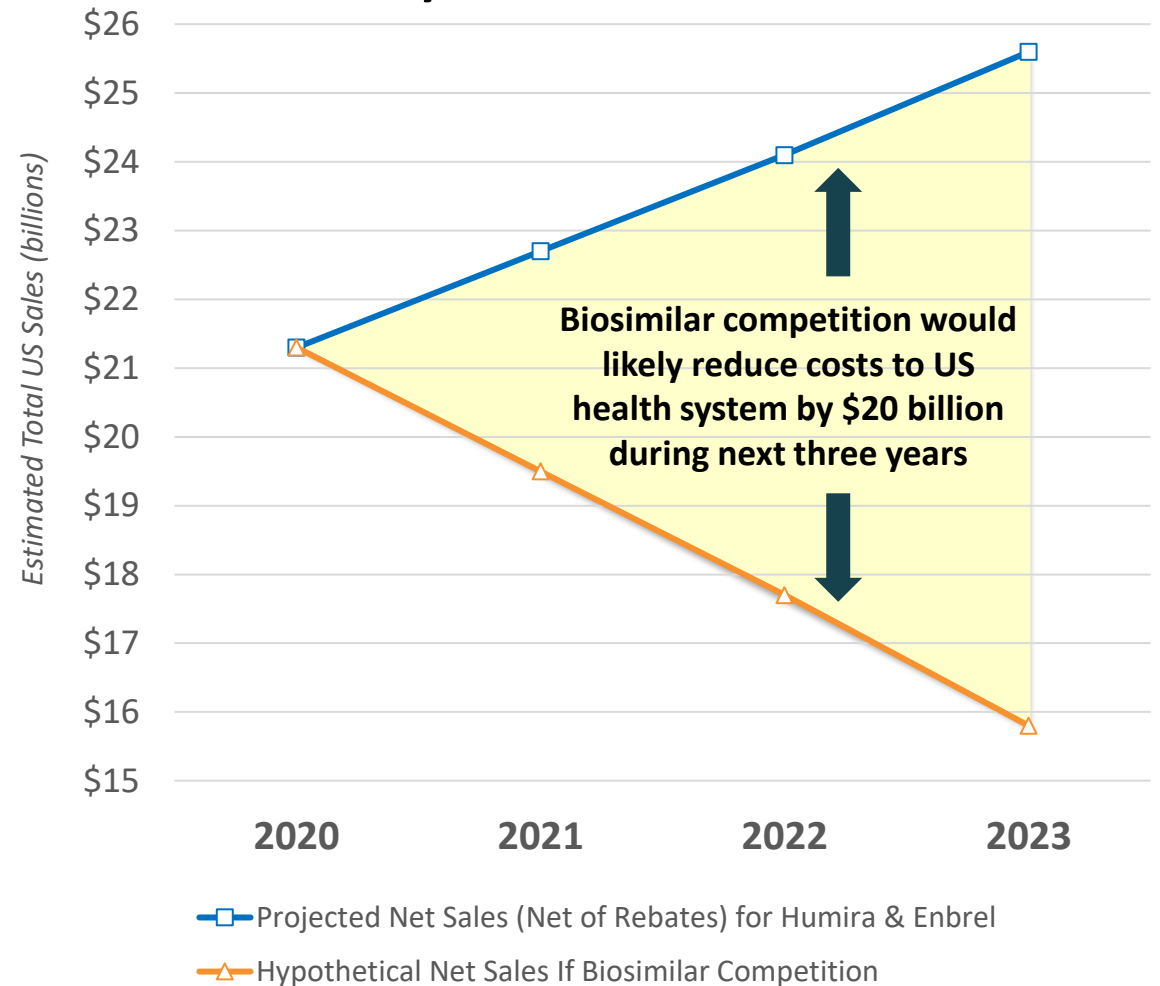
# Biosimilars for Humira and Enbrel Could Save \$20 Billion In 2021-23

- > Visante estimates that savings of \$20 billion in 2021-23 could be achieved if biosimilars to Humira and Enbrel were launched in early 2021.
- > Visante extrapolated price increases and utilization changes for 2020-23 based on historical data for Humira and Enbrel from 2017-19.<sup>1</sup>
- > Visante also projected hypothetical reduced sales based on assumptions derived from a biosimilars report published in 2020:
  - Cost savings of 10% in year 1, 20% in year 2, 30% in year-3, and 40% in year-4 and beyond.
  - Cost savings apply to both the biosimilar and the reference product.<sup>2</sup>
- > Since Enbrel protection has now been extended to 2029, Visante estimates additional Enbrel costs of another \$15 billion in years 2024-29.

1. Visante estimates based on data from SSR Health.

2. [2020 Biosimilar Trends Report](#), Amgen Biosimilars. Accessed December 2020.

## Delay of Humira/Enbrel Biosimilars Will Cost US Health System \$20 billion Over 3 Years



# Pharma Strategies for Humira/Enbrel: Marketing and Promotion

## *Increase revenue using coupons and physician payments*

### > **Coupons and Copay Cards**

- *Humira*: Patients with commercial insurance can use Humira coupons or copay cards to receive Humira prescriptions for as little as \$5 per month.<sup>1</sup>
- *Enbrel*: For patients with commercial insurance, 76% of prescriptions, including those where the Enbrel® Co-Pay Card was used, cost \$50 or less per month.<sup>2</sup>

### > **Physician Payments<sup>3</sup>**

- *Humira*: AbbVie paid more than \$12 million in 2018, and a total of \$80 million for the period 2014-18.
- *Enbrel*: Amgen paid more than \$3 million in 2018.



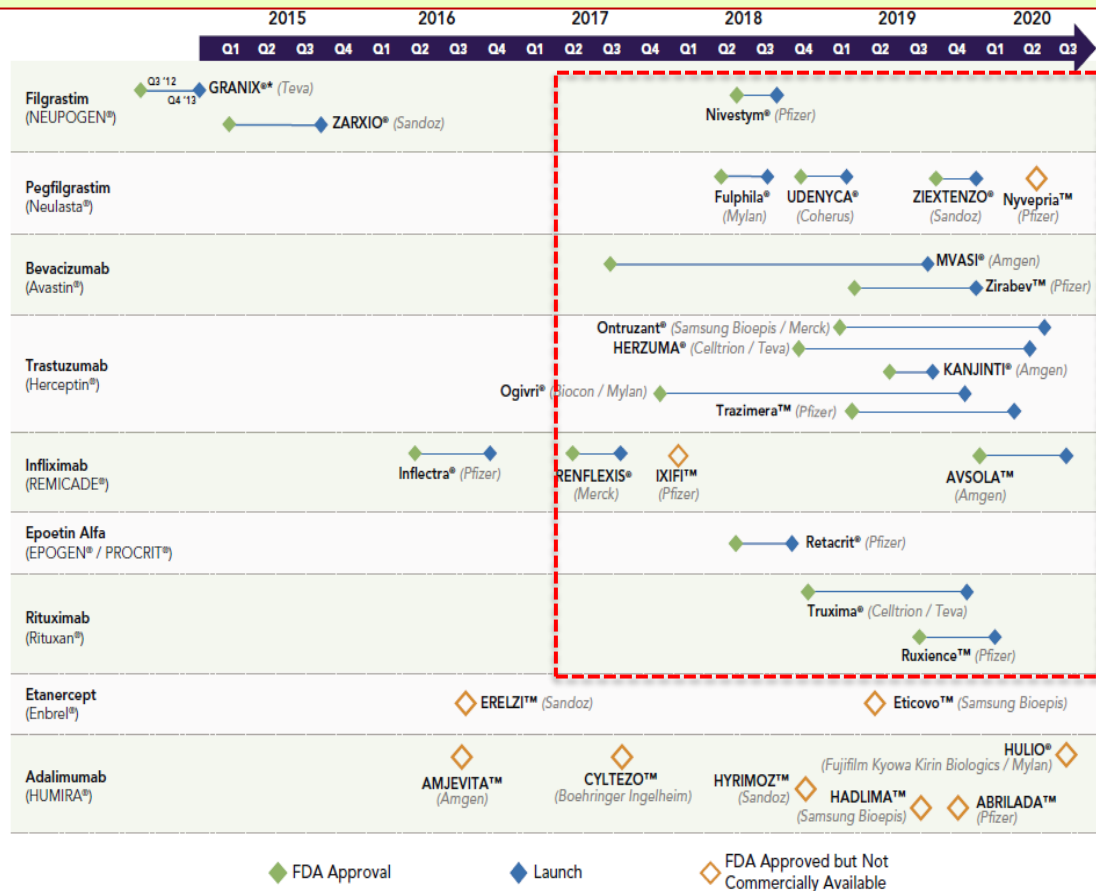
1. HUMIRA Complete Savings Card.

2. Enbrel Copay Card.

3. ProPublica Dollars for Docs.

# Reason For Optimism: More Biosimilars Approved, Launched, and Used

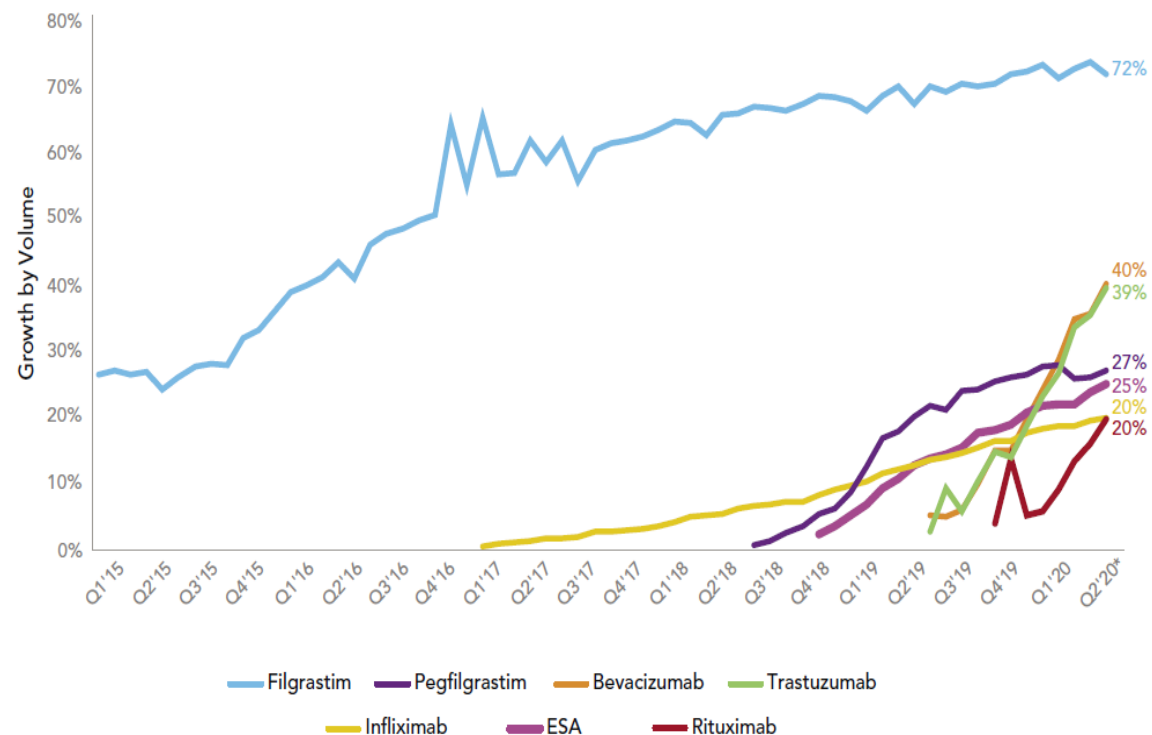
The number of biosimilars approved and launched has significantly increased in the last three years.



Key: FDA – Food and Drug Administration.  
 \*GRANIX is not a biosimilar. It was approved under a full Biologics License Application, which was submitted to the FDA before enactment of the biosimilar approval pathway.

Source: 2020 Biosimilar Trends Report, Amgen Biosimilars.

Market uptake of biosimilars is rapidly rising. As utilization increases, cost saving opportunities will increase.



\*Q2'20 sales data through July 3, 2020; monthly rollup based on 4-4-5 calendar. With a launch date of July 6, 2020, AVSOLA™ data is unavailable at time of comparison and excluded from figure.  
 Source: OBU Customer Data Pack Weekly (IQVIA DDD + Chargeback).