AHIP
Guiding Greater Health

Gaming the System

HOW BIG PHARMA DRIVES ITS HIGHER REVENUES THROUGH PATENT GAMING AND EXTENDING EXCLUSIVITY

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Out-of-control drug prices impose a heavy burden on hardworking American families. For years, prescription drugs have constituted the largest segment of total health expenditures in the commercial market.[1] Pharmaceutical companies routinely hike their prices every year, often multiple times a year. They justify high drug prices by pointing to the high costs of researching and developing new drugs. In this study, we examine that justification against the revenues that pharmaceutical manufacturers bring in over the course of a prescription drug's life cycle.

While policymakers have focused their attention on drug prices, less attention has been paid to the return on investment (ROI) realized by pharmaceutical companies over a drug's lifetime and the proportion of that ROI achieved through patent gaming. This study looks at pharmaceutical companies' revenues, which combine data for both prices and sales volume for branded drugs.

Key Takeaways

- Pharmaceutical companies earned **$18.6 billion** in total worldwide revenues, on average, for a new drug; they spent around **$1.8 billion** to develop a new drug.
- The U.S. market accounts for **more than half (56%)** of total drug revenues for a typical branded drug, while it accounts for 4% of the world's population.
- While **biologics** accounted for only 27% of drugs, they accounted for **43% of total U.S. drug revenues.**
- On average, U.S. revenues for **biologic drugs** ($17 billion) were **twice as high** as revenues for traditional non-biologic drugs ($8 billion).

Methods Summary

For this study, AHIP collected data on revenues for all novel branded drug therapies approved by the U.S. Food and Drug Administration (FDA) from 2001-2010. Revenues were obtained from the drug manufacturers' financial disclosures to the U.S. Securities and Exchanges Commission (SEC), where available. Our final sample included data for half of all novel drugs approved during the study period. For each drug, we estimated its total revenues over the duration of its exclusivity (either through patent or regulatory exclusivity),[2] U.S. share of revenues, as well as other characteristics. Most drugs approved during the study period have lost their exclusivity. Consequently, we were able to get a reasonably complete picture of their total life cycle revenues. For a detailed summary of the methodology, please see the appendix.

Data on average drug research and development (R&D) costs was based on literature review.

1 https://www.ahip.org/health-care-dollar/

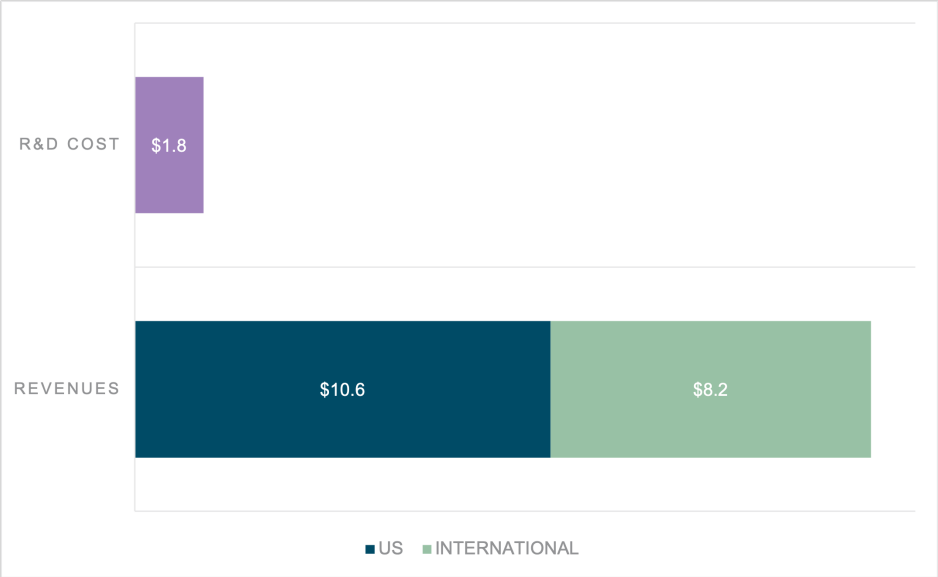
2 Patents are granted by the U.S. Patent and Trademark Office for a term of 20 years. Regulatory exclusivity is granted by the Food and Drug Administration. The length of regulatory exclusivity varies by the type of drug.

Key Findings

Average Prescription Drug Revenues Far Exceed Average Development Costs.

On average, pharmaceutical companies earned $18.6 billion in revenues for a new drug (Figure 1). Even after accounting for the expenditures on producing and marketing the drug, the high revenues leave pharmaceutical companies with substantial profit margins from each drug.

Figure 1. Average Drug Revenues vs Average R&D Costs ($ billions)



Previous studies estimated that the cost of developing and successfully bringing a new prescription drug to the market ranged between $0.5 billion and $3 billion, with the average estimate of $1.8 billion (Table 1). These estimates include the cost of risk (*i.e.*, the cost of all the failed drug candidates that a company may go through before discovering a successful drug). In addition, these estimates include the cost of capital (*i.e.*, the opportunity cost of investing capital in the drug development as opposed to earning average return on the stock market).

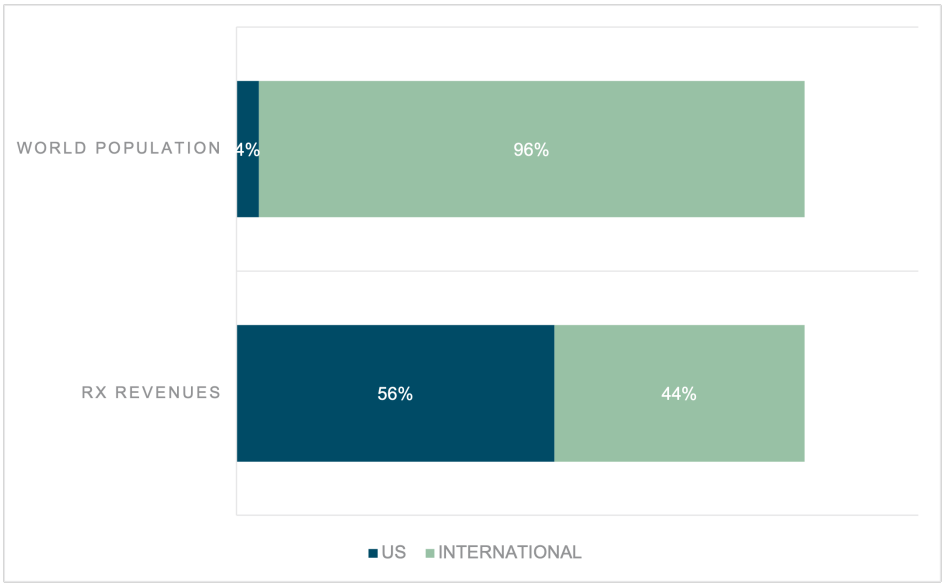
Table 1. Estimated Costs of New Drug Development

Study	Drug Development Cost Estimate 2020 $ (In Millions)
Wouters, McKee & Luyten (2020)	$993
Bedrud et al. (2020)	$2,376
Jayasundara et al. (2019)	$496
Prasad & Mailankody (2017)	$813
DiMasi et al. (2016)	$3,075
Mestre-Ferrandiz et al. (2012)	$1,886
Adams & Branter (2010)	$2,263
Paul et al. (2010)	$2,501
Adams & Branter (2006)	$1,616
DiMasi et al. (2003)	$1,495
Average	**$1,751**

U.S. Bears a Disproportionate Share of Drug Development Costs.

The U.S. market accounts for more than half (56%) of total drug revenues for a typical branded drug. Of the $18.6 billion in total life cycle revenues that pharmaceutical companies earn, on average, for each drug, they earn $10.6 billion in the U.S. market and $8.2 billion in the international markets (Figure 2). In contrast, the U.S. accounts for only 4% of the world's population.[3] Since drug revenues are used to finance new drug development, the American consumer bears a disproportionately high share of drug development costs.

Figure 2. U.S. Share of Total Drug Revenues



Longer Patents, Propelled by Anti-competitive Tactics, Drive Higher Revenues.

In general, drug manufacturers can protect their drugs from generic competition using two parallel but independent processes: patents and regulatory exclusivity. Patents are intellectual property rights granted by the U.S. Patent and Trademark Office for a term of 20 years and they apply to a wide variety of technologies beyond pharmaceuticals. A patent grants the patent holder a temporary monopoly on the patented technology and excludes others from making, using, selling, or importing the patented technology into the U.S. market. In the case of prescription drugs, patents may be granted on the active ingredient, formulation, method of use, method of production, or method of administration.

Regulatory exclusivity is an incentive provided to pharmaceutical companies by the FDA and can only be granted for pharmaceutical products. It prevents other drug manufacturers from marketing and selling a drug with the same active ingredient for a set number of years. Currently, non-biologics receive the shortest regulatory exclusivity period of 5 years. Orphan drug exclusivity is 7 years. Biologics enjoy the longest regulatory exclusivity period of 12 years.

These two methods of protection from generic competition work independently, but their impacts compound one another. A key difference between them is their timing. A drug manufacturer will typically apply for a patent during the drug development stage long before the drug's approval. Consequently, an average duration of patent protection for a newly approved drug is less than 20 years. In contrast, regulatory exclusivity starts at the time of drug approval. Thus, a drug whose patent expires soon after FDA approval may still enjoy protection from generic competition through regulatory exclusivity.

On average, longer exclusivity protection for drugs led to higher U.S. revenues. In the study sample, the average duration of exclusivity protection was 14 years (Table 2). Prescription drugs with shorter than average duration of exclusivity protection (less than 12 years) had earned, on average, around $5 billion in U.S. revenues—which accounts for half of the average U.S. drug revenues in the sample. On the other side of the spectrum, prescription drugs with longer patents (17 years or longer) earned $23 billion—more than double the average U.S. revenues. The remaining prescription drugs earned average revenues of $10 billion.

3 https://www.census.gov/popclock/

Table 2. Average Revenues by Duration of Exclusivity Protection

Exclusivity	Average US Revenue	Number of Drugs (%)
5—11 years	$5B	20%
12—16 years	$10B	64%
17—23 years	$23B	16%

Many drugs with lengthy periods of patent protection are the result of pharmaceutical companies engaging in anti-competitive tactics like patent thickets, evergreening, and pay-for-delay settlements, often used in combination with each other to prolong their monopoly on these drugs.

- **Patent thicketing** is a practice of filing numerous patents for the same drug, which increases the chances of patent infringement and, consequently, increases the cost of potential patent litigation. Patent thickets deter the makers of generics and biosimilars from entering the market.
- **Patent evergreening** is a practice of filing new patents on secondary characteristics of a drug when its original patents (typically composition of matter patents) come close to their expiration date. Later-filed patents often prevent generic versions of the drug from entering the market and effectively extend the duration of patent protection beyond the original twenty-year term.
- **Pay-for-delay settlements** often result from patent litigation between the brand drug manufacturer and the generic drug manufacturer. Under such settlements, rather than litigate the validity of all allegedly infringed patents, the generic drug manufacturer agrees to delay the launch of the generic drug version, often in exchange for payment from the brand drug manufacturer.

Examples of patent thickets and evergreening include Celgene's cancer drug Revlimid and AbbVie's immunosuppressant drug Humira—two drugs with the highest total revenues in our sample. Each company has filed for, and was granted, more than 100 patents for these drugs. Any drug manufacturer interested in producing a generic version of these drugs would have to navigate a complicated tangle of patents and would likely face costly litigation. Further, these additional patents, filed throughout the period of exclusivity, substantially extend the duration of patent protection.[4]

Beyond patent thickets and evergreening, both companies have also entered agreements with generic drug makers to delay the entry of generic versions of these drugs into the U.S. market as part of their patent litigation settlements. For example, Humira's primary patent was set to expire in 2018. Yet, AbbVie used its patent thicket and evergreening to extend Humira's patent protection until 2034.[5] It has entered into an agreement with 9 generic manufacturers to delay production and sale of biosimilars of Humira until 2023 as part of their patent litigation settlements. However, other companies trying to produce a biosimilar version of Humira may still be subject to litigation.

Biologics are Driving High Drug Expenditures.

Biologic drugs use biotechnology to make a wide variety of products derived from living organisms, either human, animal, or microorganisms. In contrast to conventional, small-molecule drugs, most biologics are complex mixtures that are not easily identified or characterized.

Until the passage of the Biologics Price Competition and Innovation Act in 2010, biologic drugs faced no competition from generic medicines. The first biosimilar drug was approved in the United States in 2015, but to date, the FDA has approved only 30 biosimilars for 10 reference biologics.[6] Of these, only 19 biosimilars for 8 reference biologic drugs have been launched for sale in the U.S. market. Biosimilars for Humira and Enbrel, two biologic drugs with highest revenues, have been delayed through patent litigation.

Given their limited competition, biologic drugs in the study sample were significantly more expensive when compared to non-biologic drugs. For example, average annual treatment cost per-patient was almost $40,000 for biologics, compared to $7,800 for traditional non-biologic drugs.[7]

4 https://www.npr.org/sections/health-shots/2018/05/17/571986468/how-a-drugmaker-gamed-the-system-to-keep-generic-competition-away; https://www.natlawreview.com/article/abbvie-s-enforcement-its-patent-thicket-humira-under-bpcia-does-not-provide

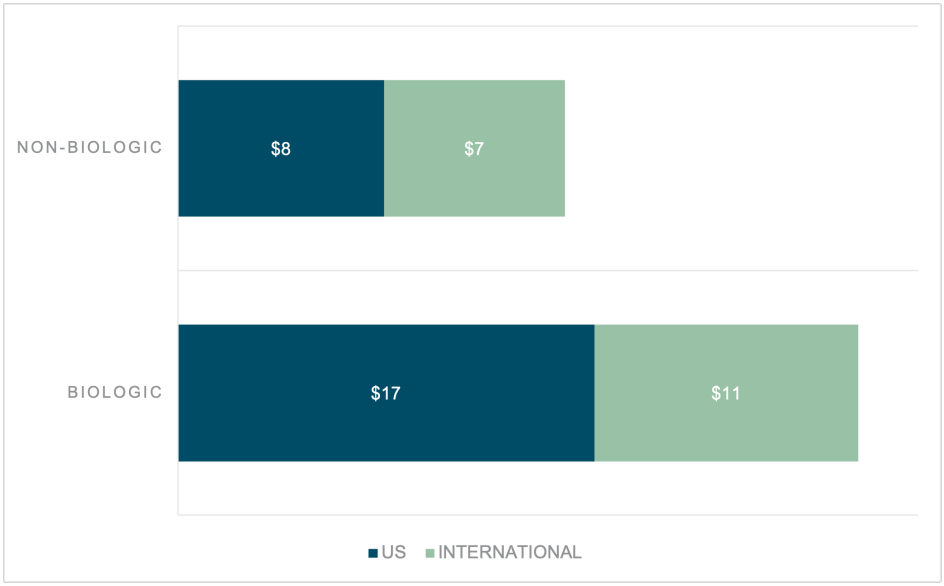
5 https://www.pharmaceutical-technology.com/comment/abbvies-successful-hard-ball-with-humira/

6 https://www.fda.gov/drugs/biosimilars/biosimilar-product-information

7 Treatment cost was calculated at launch prices. The estimates excluded orphan drugs, which tend to be very expensive and consequently distort the averages.

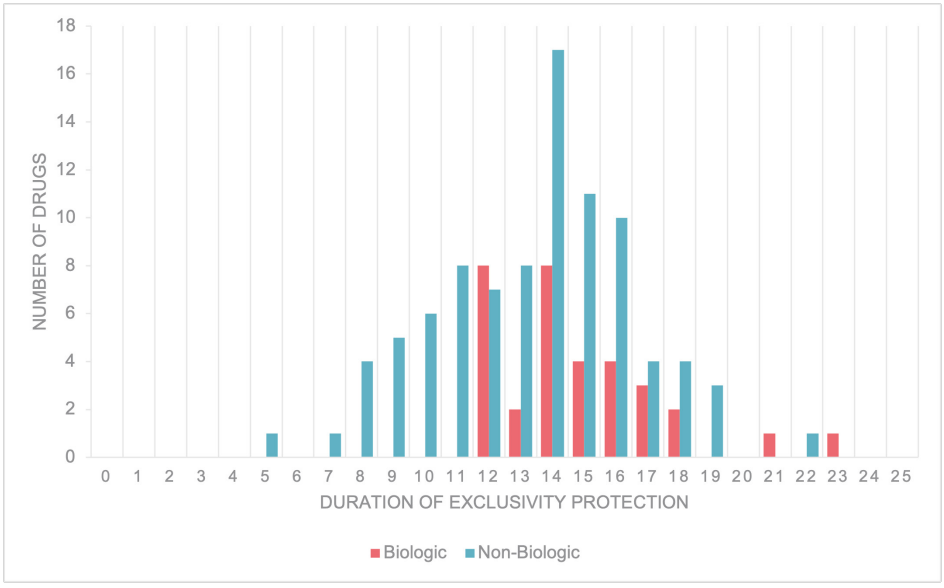
Higher per-patient treatment costs for biologics translated into higher revenues for drug manufacturers. On average, U.S. revenues for biologic drugs were twice as high as revenues for traditional non-biologic drugs, $17 billion and $8 billion respectively (Figure 3). Drug manufacturers also derived a higher share of their revenues from the U.S. market (61% compared to 53% for non-biologics). While biologics accounted for only 27% of drugs, they accounted for 43% of total U.S. drug revenues.

Figure 3. Average Revenues for Biologic and Non-biologic Drugs ($ billions)



Longer regulatory exclusivity also increased revenues for biologics. In our dataset, the long regulatory exclusivity period for biologics significantly lengthened the duration of exclusivity protection and consequently increased revenues for biologic drugs. The duration of exclusivity protection for non-biologic drugs in the sample ranged from 5 to 23 years (Figure 4). In contrast, the duration of exclusivity protection for biologics ranged from 12 to 24 years. Thus, drugs that would otherwise have shorter periods of protection from generic competition based on patents alone, had their protection period pushed up to 12 years, leading to longer exclusivity protection for biologics overall.

Figure 4. Distribution of Exclusivity Protection Duration



Policy Recommendations

Prohibit Anti-Competitive Tactics (Patent Thickets, Patent Evergreening, and Pay-For-Delay Settlements)

Patent thickets, evergreening, and pay-for-delay settlements are common anti-competitive tactics that pharmaceutical companies use to artificially extend the duration of patent protection. Pharmaceutical companies use these tactics to block cheaper generics and biosimilars from entering the market and competing with expensive brand name drugs. As in the cases of Revlimid and Humira, they artificially extend the brand name drug's monopoly pricing power beyond the time afforded by patents or regulatory exclusivity.

Prohibiting these anti-competitive tactics would increase competition in the market and give patients speedier access to more affordable drug alternatives.

AHIP supports legislation recently approved by the House and Senate Judiciary Committees that would enact these policies:

Reported out of the House Judiciary Committee on September 29, 2021:

- H.R. 2873, the Affordable Prescriptions for Patients Through Promoting Competition Act
  - Prohibits "product hopping"
- H.R. 2884, the Affordable Prescriptions for Patients Through Improvements to Patent Litigation Act
  - Improves the process to resolve patent infringement claims for biologic drugs
- H.R. 2891, the Preserve Access to Affordable Generics and Biosimilars Act
  - Prohibits "pay for delay" arrangements between a branded drug's manufacturer and the manufacturer(s) of generic drugs, biosimilars, or interchangeable biologics.

Reported out of the Senate Judiciary Committee on July 29, 2021:

- S. 1428, the Preserve Access to Affordable Generics and Biosimilars Act
  - Prohibits "pay for delay" arrangements between a branded drug's manufacturer and the manufacturer(s) of generic drugs, biosimilars, or interchangeable biologics.
- S. 1435, the Affordable Prescriptions for Patients Act
  - Prohibits "product hopping"
  - Improves the process to resolve patent infringement claims for biologic drugs

Shorten the Exclusivity Period for Biologics

As the study findings demonstrate, biologics, on average, earn higher revenues compared to non-biologic drugs. By extension, they impose higher costs on patients and health plans. In part, their higher revenues are driven by longer regulatory exclusivity periods, which substantially extended the average duration of protection from generic competition for biologics.

Shortening the biologic exclusivity from 12 years to 7 years—the exclusivity period currently offered to orphan drugs—would allow for a faster entry of biosimilar competition on the market, leading to lower prices and lower costs for consumers.

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Appendix A. METHODOLOGY

Data Collection

To construct the dataset, we identified all novel drugs approved by the FDA between January 1, 2001, and December 31, 2010, using the Novel Drugs Approval reports published by the FDA.[8] For each drug, we recorded its indications based on the earliest available FDA Label. We excluded from the list drugs that were not therapeutic, *e.g.*, birth control or diagnostic agents.

For each drug on the list, we recorded the manufacturer and the approval date. For each manufacturer on the list, we obtained their annual reports (form 10-K or 20-F) submitted by the manufacturer to the SEC.[9] For companies that were not required to submit annual reports to the SEC, we supplemented the data, where available, by annual reports published on the companies' websites.

For each drug, we strived to obtain SEC forms or annual reports for the entire period that drug was available on the U.S. market as a single source drug (from the launch date to the date of patent or exclusivity expiration). If SEC forms or annual reports were not available for the entire time period, the drugs were excluded from the dataset.

When drugs switched owners due to company mergers or acquisitions, we obtained SEC forms or annual reports of the new company. Where annual report was not available for specific years (*e.g.*, the last year before a company's acquisition), we used quarterly reports instead, which resulted in partial data for that year.

Out 241 therapeutic drugs approved in 2001-2010, our final sample included data for 123 drugs (51% of total).

Variables

Duration of Exclusivity: The duration of exclusivity protection was estimated as the difference between the patent or regulatory exclusivity expiration date (whichever was later) and the date of the FDA approval. In other words, we estimated the number of years that a drug was legally protected from generic competition.

In most cases, the date when the drug became open to competition was based on the date of patent expiration. We obtained the data of patent expiration from SEC forms. When multiple patents and expiration dates were indicated, we tried to discern the most relevant patent based on the discussions in the legal proceedings section. In general, we assumed the composition of matter patent to be the primary patent. In several cases, companies have reached agreements with competitors to delay the entry of generic or biosimilar versions of the drug. In these cases, the agreed-upon date was used as the date when drug became open to competition. Finally, in cases where regulatory exclusivity period exceeded the length of patent, we used the exclusivity expiration date.

Note that this date is not to be confused with the generic or biosimilar approval date. While in most cases, the generic entry shortly followed the date when drug became open to competition, it was not necessarily the case. Some drugs lacked generic competitors even after their patents have expired. In other cases, generics were approved in anticipation of the patent expiration a several years before the patent expiration date.

Total (Life Cycle) Drug Revenue: For each drug, the total drug revenue was estimated as a sum of its annual revenues. In addition, we separately calculated the total U.S. and international revenues. All revenues were adjusted for inflation to 2020 dollars.

The annual revenues for each drug were obtained from SEC forms and annual reports. Annual revenues were recorded for each year between the date of the drug approval by the FDA and the date of patent expiration or the latest SEC form available (2019 or 2020 depending on company's schedule). When drug revenues were unavailable in a particular year (typically in the years immediately after approval), the data were recorded as missing. Drugs missing data in the final years before the loss of patent were excluded from the sample.

For almost half of the drugs in the sample, the date of patent or exclusivity expiration was after the last year for which the data were available. For these drugs, the future revenues (up to 3 years) for each year prior to patent or exclusivity expiration were projected using the average annual change in revenues in the last 3 years of available data.

8 https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products

9 Available on SEC website at https://www.sec.gov/edgar/searchedgar/companysearch.html

For each drug, we further recorded the split between U.S. and international revenues. If the split by geography on drug revenue level was not reported, we used the U.S. share of total pharmaceutical sales to derive the drug's share of U.S. revenues. When drug revenues were reported in foreign currencies, they were converted to U.S. dollars using the average exchange rate reported in the annual reports.

U.S. Market Share of Brand Drug Revenues: The U.S. share of revenues earned by drug manufacturers was calculated as the sum of U.S. drug revenues divided by the sum of total drug revenues.

Biologic Drugs: Drugs were classified as biologics if they were approved based on Biologics License Application (BLA). Two exceptions were Vpriv and Increlex, which were approved based on New Drug Application (NDA). They were classified as biologics based on the description in SEC forms.

Annual Treatment Cost: For each drug we calculated the annual per-patient treatment cost as the product of drug price at launch and the estimated annual drug utilization. The drug utilization was estimated based on the dosage and duration indicated on the drug label. For more details on annual treatment cost estimation methodology, see our previous report, "The Rise of Orphan Drugs."[10]

Inflation Rate: We used the prescription drugs component of the Consumer Price Index reported by the Bureau of Labor Statistics.[11]

Data Limitations

The total revenue estimates for most drugs likely underestimate the actual revenues for following reasons:

1. Most companies break out drug specific revenues in their reports for only the most successful drugs. Newly launched drugs are unlikely to reach that level, and consequently be included in reports, until several years after their launch. Thus, many drugs in the dataset have missing data for the early years.
2. Many drugs are jointly marketed by multiple companies. Frequently, these agreements divide the market geographically between companies, which makes tracing revenues across all markets challenging. The drugs were included in the dataset even if the data for some international markets were unavailable.
3. Many drugs continue to earn revenues even after generic entry. Furthermore, several drugs did not face generic competition even after the patent expiration. These revenues were not recorded in the dataset.
4. Due to scope limitation, this study focused exclusively on the U.S. market. Consequently, international revenues were collected only for the period when the drug enjoyed patent protection in the United States. Since many companies launch their drugs in non-U.S. markets years after the U.S. launch, the study likely underestimates the international revenues and, consequently, total revenues.
5. On the other hand, the revenue data for drugs with low revenues were less likely to be included separately in the companies' annual reports. Thus, the dataset is likely biased towards more successful drugs.

10 https://www.ahip.org/the-rise-of-orphan-drugs/
11 https://www.bls.gov/cpi/