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BRIEF
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An Examination of March-in Rights and Drug Products with Government-Interest Patents

This issue brief explores the potential impact and decisional factors of exercising march-in rights by analyzing characteristics of small molecule drugs that reference government-interest patents.

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KEY POINTS

- March-in authority allows the federal government to grant licenses on privately owned patents for inventions developed with federal funding (provided certain statutory requirements are met), and it was designed to ensure that the benefits of the American taxpayers' investment in research and development are reasonably accessible to the public.
- To date, no agency has initiated march-in proceedings, but march-in may help reduce the prices of certain drugs.
- This issue brief identifies 39 unique small molecule drugs, comprised of 63 drug products, that reference at least one government-interest patent in the Food and Drug Administration's publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (commonly known as the Orange Book) as of February 2024. These include 13 small molecule drug products that exclusively reference[a] government-interest patents.
- Using sales data for small molecule drug products with government-interest patents, we estimate hypothetical cost savings of approximately $12.0 billion if generic competition could be introduced for small molecule drug products that reference government-interest patents in either August 2024 or at the end of exclusivity as opposed to waiting for the end of patent protection. For the set of small molecule drug products that exclusively reference government-interest patents, the savings are estimated at approximately $0.2 billion. Sensitivity analyses suggest that cost savings are lower the longer it takes to complete the march-in process.

BACKGROUND

This issue brief explores some potential impacts of exercising march-in rights and the factors involved in choosing to exercise them by examining characteristics of small molecule drug products[b] that reference

[a] In this context, "reference" means that these patents are listed in the Orange Book entry for a given drug product. Generally, patents must be submitted for listing in the Orange Book if they are drug substance, drug product, or method of use patents. See 21 U.S.C. § 355(b)(1)(A)(viii).

[b] The unit of analysis in this issue brief is small molecule drug product (i.e., a specific strength, dosage form, and route of administration of a small molecule drug).

government-interest patents, which are patents that claim an invention made with federal funding as defined in the Bayh-Dole Act. We first provide an introduction to march-in rights and summarize some of the relevant literature. We then present an original analysis to answer two questions:

1. Which drug products have patents that are government interest and may therefore be eligible for march-in?
2. How do the characteristics of these drug products (e.g., sales, volume, pricing, and exclusivity) and the patents they reference (including any non-government interest patents) inform our understanding of the decisional factors and potential impact of exercising march-in rights?

Our work contributes to the literature on march-in rights by identifying small molecule drug products that reference government-interest patents that are not expired, abandoned, or otherwise held invalid by court or agency of appropriate jurisdiction and analyzing the characteristics of these products and their patents, such as patent and exclusivity expiration dates, and sales and price data. We highlight characteristics of these products that speak to the decisional factors of exercising march-in rights and estimate hypothetical cost savings if generic competition were to be introduced for these products.

What are March-In Rights?

The Bayh-Dole Act grants businesses and non-profits, including universities, the right to control their inventions developed using federal funding.[1] The Act recognizes the interest of the government in ensuring that their investments serve the public well. The term "march-in rights" refers to the right of the federal government to issue additional licenses for these inventions under certain circumstances.[c] The federal agency that provided funding to develop the invention may choose to initiate march-in proceedings if at least one of the following criteria are met:

- A contractor has not taken "effective steps to achieve practical application" of the invention, including making the invention available to the public on reasonable terms;
- To alleviate unmet health or safety needs;
- Greater access is needed by companies to comply with other federal regulations; or
- A contractor did not obtain or waive an agreement, or is not abiding by domestic manufacturing requirements, required by section 204 of the Bayh-Dole Act. [d]

For a federal agency to initiate march-in proceedings for a subject invention claimed in a patent resulting from federally funded research, it would need to notify the contractor in writing of its rationale and offer an informal consultation to explain the issue and discuss any alternatives. Then, the agency would inform the contractor of its decision on whether to proceed with formal march-in proceedings. If the contractor chooses to do so, the contractor may prepare counter arguments and supply additional information, which triggers agency fact-finding if the information provided raises a dispute over material facts. Finally, the contractor may appeal the final decision by an agency to march-in on an invention, potentially resulting in lengthy legal proceedings.[2]

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[c] Through march-in, the government can require funding recipients (or their assignees and licensees) to grant additional patent licenses—authorizing third parties to use the government-funded patents—or issue such licenses itself.

[d] Section 204 of the Bayh-Dole Act states that a contractor with the title to a subject invention must not grant exclusive right to use or sell the invention in the United States unless any products embodying the subject invention or produced through use of the subject invention will be manufactured substantially in the United States.

Relevant Literature

Since march-in rights have never been exercised, there is little direct evidence on the impacts that might occur should they be used in an effort to address high drug prices. Much of the relevant literature explores the preconditions for their utilization and anticipates the impacts that might occur should they be exercised.

One study on march-in rights interviewed subject matter experts to examine the five march-in petitions that had been filed with NIH at that time. The authors found that those who supported applying march-in rights to address high drug prices asserted that high prices could restrict access for some people and lead to health disparities, while others suggested that prohibitively high drug prices were secondary concerns better addressed via other avenues.[3]

Researchers have also noted the limitations on the power of march-in rights to reduce product prices.[4] For example, drugs are often covered by multiple patents, some of which may not have been developed with government support. Since march-in rights apply only to those patents claiming inventions that utilized government funds, march-in would not be sufficient to enable generic competition. Generic manufacturers interested in licensing federally funded patents through the exercise of march-in would have to contend with non-government funded patents before they could bring a product with both types of patents to market. Indeed, the creation of "patent thickets" – whereby a drug manufacturer will surround their product with multiple overlapping patents – is a strategy that is sometimes used to deter and delay competition.[5] Researchers have also pointed out that march-in proceedings can be elaborate and are likely to be lengthy.[4] The regulations entail several steps an agency must take before it can decide to exercise march-in rights, and agency march-in decisions are held in abeyance pending the outcome of appeals in the federal court system.[6] Potentially lengthy march-in proceedings relative to remaining patent life were also mentioned in NIH's most recent decision on the Xtandi petition and are cited in the NIST Draft Framework as a potential consideration for those wishing to pursue march-in.[2,7]

One study that incorporated quantitative data reviewed all approved new molecular entities (NMEs)[e] with and without public-sector support from 1988 to 2005.[8] Results suggest that the economic impact of march-in rights would be limited, due to the relatively small number of drugs for which government funding played a direct role. The group published an updated study in 2024 that examined the potential of exercising march-in rights, finding that fewer than 10 percent of NMEs referenced a government-interest patent, and only 2.5 percent of NMEs referenced only government-interest patents.[9]

While march-in rights are not a silver-bullet for curbing excessive drug prices, march-in could be paired with other government authorities to license generic competition and make drugs available to the public at a reasonable price. For example, under Section 1498 of Title 28 of the U.S. Code,[10] U.S. Government agencies can manufacture or use inventions covered by any United States patent, regardless of the patent holder, when the manufacture or use is "by or for the United States." Patent holders cannot enjoin this use and are limited to seeking reasonable compensation by suing the government in the Court of Federal Claims. Alternatively, the patent holder may negotiate compensation directly with the Government.[3,11] Previously, this mechanism (commonly referred to as "Section 1498") was used by the Department of Veterans Affairs and the Department of Defense in the 1950s and 1960s to obtain lower priced generic drugs, as well as more recently by the Department of Defense and the Department of the Treasury.[12,13] Indeed, in 2001, then-HHS Secretary

[e] A New Molecular Entity (NME) is an active ingredient that contains no active moiety that has been previously approved by the FDA in an application submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), or has been previously marketed as a drug in the United States.

Tommy Thompson considered invoking Section 1498 to obtain a generic version of the antibiotic Cipro (ciprofloxacin) during the anthrax scare. Faced with this threat, the drug's manufacturer (Bayer) agreed to reduce the price by nearly 50 percent.[14] More recently, Congress established several programs under the Inflation Reduction Act of 2022 to address drug pricing in Medicare: the Medicare Drug Price Negotiation Program, the Medicare Prescription Drug Inflation Rebate Program, and the Part D Manufacturer Discount Program. Another evolving strategy by the Federal Trade Commission (FTC) is to dispute what they consider to be improper or inaccurate Orange Book listing of patents that may serve to delay generic entry to the market. FTC issued a warning statement against improper patent listings in September 2023 and as of April 2024 has named more than 300 patent listings as disputed.[15,16]

METHODS

Analysis

Our analysis evaluates the characteristics of small molecule drug products that reference government-interest patents. We first identify drug products that reference government-interest patents, including what percentage of their patents are government-interest.[f] We then examine the characteristics of these patents, including patent types and expiration dates, along with exclusivities associated with these drug products.

Finally, we document the sales, volume, and price of these drug products over time, enabling us to estimate the potential cost savings of exercising march-in rights using certain assumptions. We estimate these cost savings for two different groups of patents – those that reference exclusively government-interest patents and those that reference at least one government-interest patent – by assuming generic competition is introduced for each drug product in either August 2024 or at the expiration of all the exclusivities (whichever is later). We also assume that without generic competition average monthly sales from 2023 would extend through subsequent years. Cost savings are then generated through increased competition, lowering the price of each drug product by 25 percent[g] from August 2024 or the end of exclusivity to the expiration of patent protection.[17] An annual real discount rate of two percent is used to calculate the present value of the sum of monthly future flows of these cost savings.

Data

We utilize the Food and Drug Administration's (FDA) Orange Book to gather data on drugs, their referenced patents, and all their exclusivities. These data are publicly available and updated regularly.[h] The Orange Book contains three data files that provide information on drug products approved by the FDA under section 505 of the FD&C Act, patents, and exclusivity. We merge these three datasets at the application-product level to obtain a dataset of small molecule drug products with unexpired patents.

We identify government-interest patents based on data obtained from three sources. First, we utilize the U.S. Patent and Trademark Office (USPTO) PatentsView, which contains a list of government-interest patent numbers. Second, we collect patent numbers from NIH RePORTER, which records patents resulting from NIH-funded grants or contracts. Third, we utilize a database of government-interest patents from Gross and Sampat (2024),[18] which includes additional data on government-interest patents collected from the USPTO.

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[f] We do not include patents with a government assignee.

[g] This parameter is obtained from Conrad and Davis (2023), who find a median drug price decline of 20-30 percent in the 12 months after generic approvals. We utilize the middle point of this range, 25 percent, as our parameter. These generic approvals are not limited to first generics.

[h] The FDA Orange Book data used in this analysis were accessed on February 14th, 2024.

We then link data from these sources to the patent numbers in FDA's Orange Book to identify small molecule drug products with government-interest patents. It is important to note that this approach may not capture all small molecule drug products with government-interest patents. While government contractors are legally required to include a government-interest statement in their patents, not all do so. Indeed, previous research has noted this issue, and worked to identify additional patents with missing government-interest statements.[19]

Our final data source is IQVIA's National Sales Perspectives (NSP) database. NSP contains monthly data on sales and volume of pharmaceutical products at the national drug code (NDC) level. It represents roughly 90 percent of the pharmaceutical market and is projected to a national total. Not all products with a government-interest patent are captured in the NSP database; for example, some products are not commercially available or are diagnostic agents. For available drug products, we calculate average price by dividing sales by volume.

Limitations

Our analysis includes a number of limitations. First, it is limited to small molecule drugs, which are listed in the Orange Book.[i] Second, FDA's Orange Book may not contain all patents for a given small molecule drug product because only certain types of patents may be listed in the Orange Book.[20,21] Third, our analysis is not able to definitively identify the total universe of government-interest patents. Fourth, our work focuses on counts of patents and their basic characteristics and is unable to state definitively how important a particular patent may be for development of a given drug or dosing regimen.

Finally, our estimate of potential cost savings due to exercising march-in rights carries a number of assumptions and should be considered informative but preliminary. First, before the government could grant a license to any government-interest patent, it would need to assess whether the statute authorizes march-in. As noted, march-in is only authorized if one of four statutory criteria are met. We have not evaluated whether those statutory criteria would apply to any of the patents in our analysis. In addition, we assume that generic competition is introduced in either August 2024 or at the expiration of all exclusivities (whichever is later), which may be earlier than feasible. March-in is likely to take some time to effectuate due to the expected lengthy administrative process and the potential for litigation to delay a final decision. [2,4,7] As a result, our estimate of cost savings may be higher than an estimate that accounts for a longer period of time spent on march-in rights proceedings and time needed for manufacturers to produce and market competitors. To mitigate this limitation, we present sensitivity analyses that estimate cost savings if generic competition were to be introduced at later dates. Additionally, although we use the latest exclusivity dates in our calculations, multiple types of exclusivities exist, and it might be possible to introduce generic competition before all exclusivities expire. Over time, savings from introducing competition to eligible drugs may also be compromised by changes in standards of care or additional competition in the drug market, such as alternative formulations.

Our cost savings estimate includes a number of other notable considerations. We assume that a generic manufacturer is interested in licensing each of the patents and that march-in would be sufficient to introduce generic competition even for products with non-government interest patents (e.g., after exclusivities no longer block generic approval). We also assume that generic competition will reduce the price of the branded competitor in our sample by 25 percent, which may not be consistent across products. For instance, new generic competition for high-priced large-market products may generate more savings than for smaller-market products, and first generics may generate larger impacts to price than subsequent generics. Additionally, we

[i] Our analysis does not include biologics due to the incomplete listing of patent information in FDA's Purple Book. More information about the scope of patents listed in the Purple Book is available at https://purplebooksearch.fda.gov/patent-list.

assume that the trend in 2023 sales would extend to future years absent generic competition, that patent protections would be effective for each product until their relevant patents expire, and that price changes due to generic competition do not affect demand. Our analysis necessarily evaluates a snapshot of the drugs in our sample, which may change in the future. Lastly, we are only able to estimate cost savings for the drug products for which we have sales data, which may lead to underestimated total cost savings.

FINDINGS

Summary statistics for drug products with at least one government-interest patent are shown in Table 1, organized into two samples: one for products that reference only government-interest patents, and one for products that reference a mix of government-interest and non-government-interest patents.

In total, we identify 39 unique small molecule drugs, comprised of 63 drug products, with 218 unique patents.[j] Thirteen of these products exclusively reference government-interest patents, while the remaining 50 drug products reference a mix of government-interest and non-government-interest patents. Those that exclusively reference government-interest patents have a substantially lower mean total number of patents (mean=2.5) than those with a mix of government-interest and non-government-interest patents (mean=6.8). For the former group, the median exclusivity and patent expiration dates occur in 2026 and 2027, respectively; but for the latter group, the median exclusivity end date is also in 2026, and the median longest patent expiration date is much later—in 2037.

Table 1. Summary statistics for drug products that reference government-interest patents

	All Government-Interest Patents	Mix of Government-Interest and Non-Government-Interest Patents
Total Number of Patents (mean)	2.5	6.8
Number of Government-Interest Patents (mean)	2.5	3.0
Exclusivity End Date (median)	11/17/2026	11/17/2026
Final Patent Expiration Date (median)	04/30/2027	06/08/2037
Number of Products	13	50

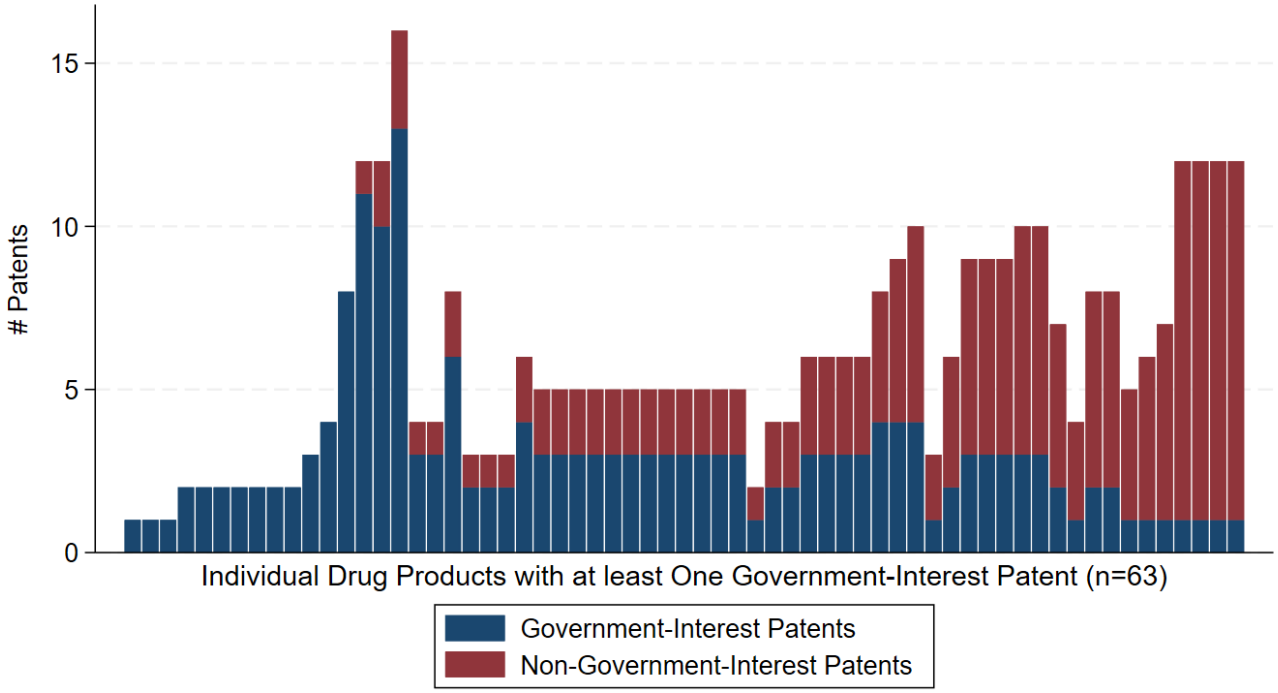
Note: This table provides summary statistics for drug products that reference government-interest patents. The data are organized into two separate samples – one for products that exclusively reference government-interest patents, and one for products that reference a mix of government-interest and non-government-interest patents. The exclusivity end date for each drug product is obtained by identifying latest exclusivity end dates in FDA's Orange Book. The final patent end date for each product was obtained by identifying the latest end date of all patents referenced by an individual product in FDA's Orange Book. The data were obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, and Gross and Sampat (2024).[18]

Figure 1 displays the number and type of patents for each of the 63 individual drug products in the Orange Book in February 2024 that references at least one government-interest patent. Each drug product is represented by a single bar. The y-axis records the total number of patents for each drug product, and drug products are sorted left to right by the percentage of total patents that are government-interest. For instance, the drug product furthest to the left references one patent, which is a government-interest patent, and the

[j] "Drug product," our primary unit of analysis, is defined at the level of ingredient-strength-dosage form-route of administration. "Drug" is defined at the ingredient level.

product furthest to the right references a total of 12 patents, only one of which is a government-interest patent (the remaining 11 are non-government-interest patents).

Figure 1. Number of patents for drug products referencing at least one government-interest patent

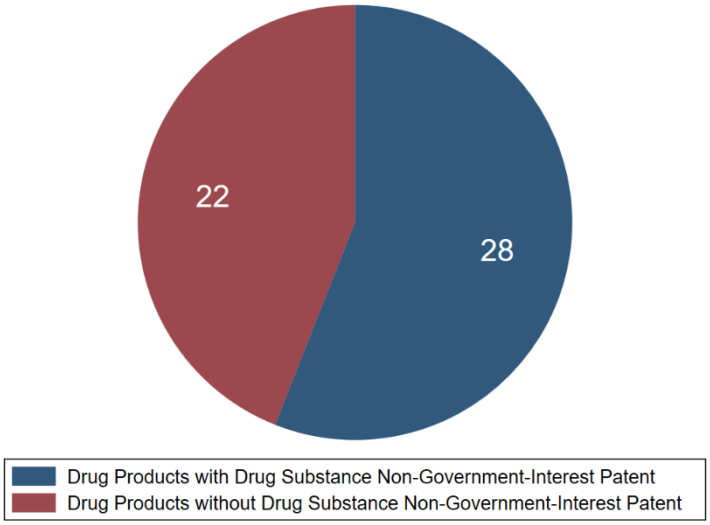


Note: This figure presents the number of government-interest and non-government-interest patents listed in the Orange Book for each drug product that references at least one government-interest patent (n= 63). Each bar along the x-axis represents a unique drug product. The y-axis depicts the number of patents listed for each drug product, categorized by whether the patents are government-interest or non-government interest. The drug products are organized from left to right along the x-axis by the percent of their patents that are government-interest, where those furthest to the left have the highest percent of patents that are government interest (100%), and those furthest to the right have the lowest (8.3%). Data were obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, and Gross and Sampat (2024).[18]

Figure 1 highlights two important points. First, it illustrates the number of drug products that reference at least one government-interest patent, 63 products. We categorize these products separately because, while the government could march in on any government-interest patents that meet the statutory criteria, generic manufacturers would have to contend separately with any non-government-interest patents. These drug products may be categorized into 13 products that exclusively reference government-interest patents and 50 products that reference a mix of government-interest and non-government interest patents. Second, it shows that, for drug products that reference a mix of patents, on average most patents are non-government interest (3.8 non-government interest vs. 3.0 government-interest). There are a number of drug products that reference a small number of non-government-interest patents (seven reference only one non-government-interest patent), but in general, among mixed-patent drug products, the majority of patents are non-government-interest. Over half of these products have at least 50 percent of the patents they reference as non-government interest patents (28 of the 50 products).

Figure 2 examines drug products that reference non-government-interest patents in more detail by identifying whether or not they reference a non-government-interest patent that is also a drug substance patent.[k] Drug substance patents cover a drug's active ingredient and are generally considered to be the most difficult type of patent to design around for competing manufacturers.[19] For the 50 products that reference a mix of both government-interest and non-government-interest patents, 28 (56%) reference a non-government-interest drug substance patent. In terms of the entire sample of patents, drug substance patents represent 36 percent of government-interest patents and 25 percent of non-government-interest patents. Indeed, of the 218 unique patents in our sample, 30 percent are drug substance patents.

Figure 2. Number of drug products with a mix of government-interest and non-government-interest patents that reference a drug substance non-government-interest patent

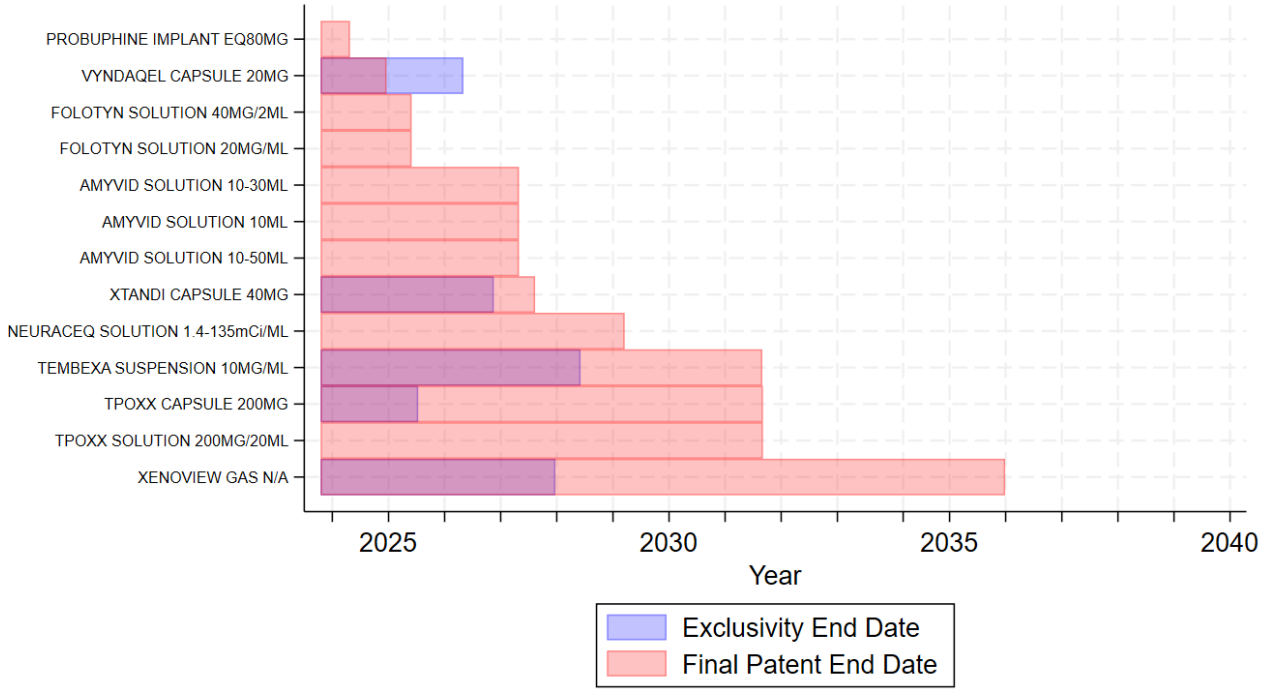


Note: This figure presents the 50 drug products that reference a mix government-interest and non-government interest patents. It categorizes these products into those that reference a *drug substance* non-government-interest patents and those that do not reference a *drug substance* non-government-interest patent. Data were obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, and Gross and Sampat (2024).[18]

Exclusivity and patent expiration dates for government-interest patents are important considerations for evaluating the potential impact of exercising march-in rights. Exclusivities introduce certain time-limited prohibitions on the introduction of competitor drugs separately from any remaining patents and so could restrict generic competition even if an agency were able to issue licenses on all patents for a given product. We examine the exclusivity timing and patent expiration dates for products in our sample. For each product, we identify the latest end date of all exclusivities and the final patent end date. Figure 3 illustrates the distribution of these dates for each of the 13 products that reference only government-interest patents. As of February 2024, five of the products are still under exclusivity, which expires for all the products prior to 2029. A majority of the final patent end dates occur prior to 2029, as well. For the two largest-market products, Xtandi and Vyndaqel, both the exclusivity end dates and final patent end dates occur prior to 2028. For Vyndaqel in particular, exclusivity expires later than patent expiration, which suggest the usefulness of using march-in rights to promote generic competition in this case may be limited. Figure A1 in the appendix displays the exclusivity and final patent end dates for all 63 products that reference at least one government-interest patent.

[k] We categorize drug substance patents as those that are flagged as such in FDA's Orange Book.

Figure 3. Exclusivity and patent coverage for drug products that reference only government-interest patents

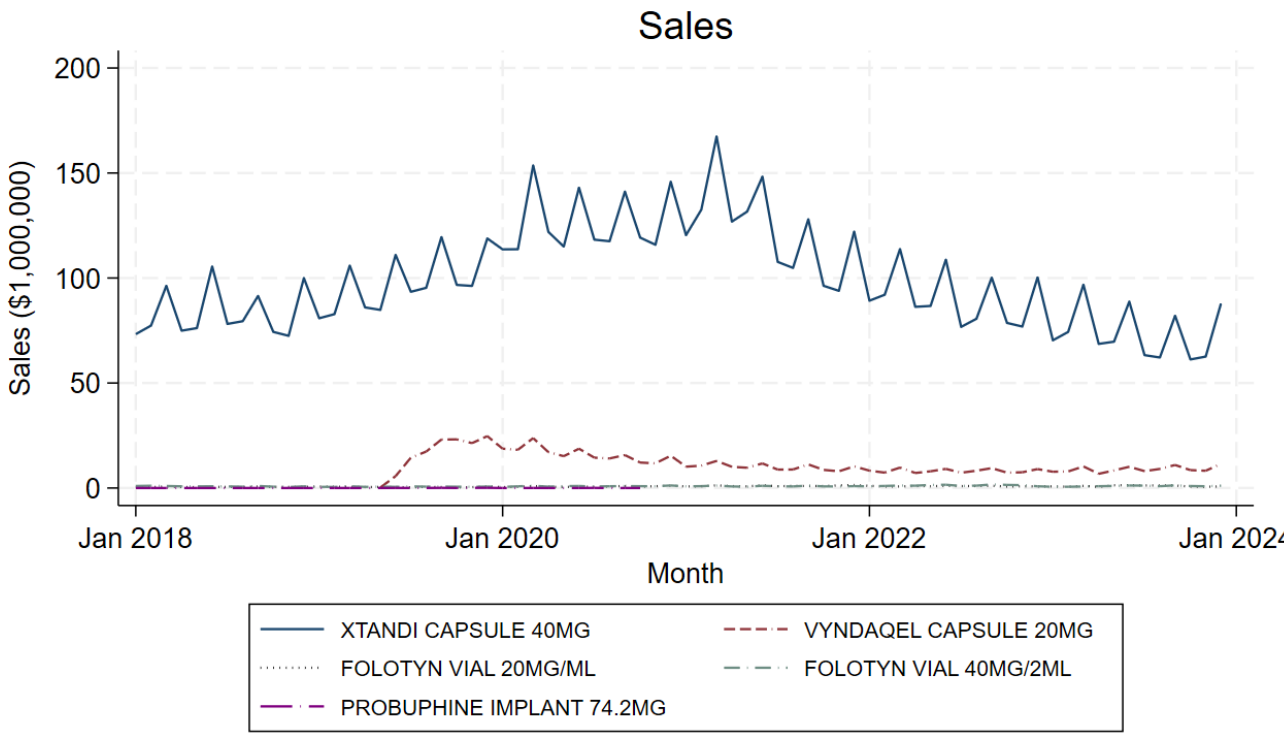


Note: This figure presents the exclusivity and patent coverage for products that reference only government-interest patents. Each bar represents a unique drug product. The exclusivity end date for each drug product is obtained by identifying latest exclusivity end dates in FDA's Orange Book. The final patent end date for each product was obtained by identifying the latest end date of all patents referenced by an individual product in FDA's Orange Book. Data were obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, and Gross and Sampat (2024).[18]

Of the 63 drug products in our dataset, we identify 42 in IQVIA's NSP database by matching based on ingredient, dosage form, and strength. We present sales and price data for the five of these 42 drug products that exclusively reference government-interest patents: Xtandi (capsule; 40 MG), Vyndaqel (capsule; 20MG), Folotyn (vial; 20MG/ML and 40MG/2ML), and Probuphine (implant; 74.2MG)[I]. Figures 4 and 5 present these data for the time period January 2018 to December 2023.

[I] Probuphine was discontinued in 2020.

Figure 4. Sales of products that reference only government-interest patents



Note: This figure presents monthly sales of drug products that exclusively reference government-interest patents. Data were obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Figure 4 shows that sales of Xtandi and Vyndaqel consistently dominate those of the other products over the course of our sample, with Xtandi peaking in March 2021 with $161 million in monthly sales. Sales of other products are non-zero but are essentially negligible compared to sales of Xtandi and Vyndaqel in terms of total sales. Generic competition to Xtandi and Vyndaqel would likely have the greatest total market impact given their higher total sales.

Table 2 presents 2023 sales, volume, and average price for each of the top 15 selling drug products that reference at least one government-interest patent. Vyndamax and Erleada exhibit the highest total sales in 2023 (approximately $1193 million and $1158 million, respectively), while three different versions of Xtandi had sales totaling $888 million, $651 million, and $492 million, respectively.[m] Despite lower overall sales, other drug products listed have higher average prices per unit, such as $667 and $1370 per unit for Orserdu and Cosela, respectively. Appendix Tables A1-A5 and Figures A2-A4 provide sales and average price information for all drug products in our dataset for which these data are available, broken out by dosage form.

[m] Only one version of Xtandi – the capsule formulation – references only government-interest patents.

Table 2. Sales, volume, and average price (2023) for the top 15 selling drug products that reference at least one government-interest patent

Trade Name	Manufacturer	Dosage Form	Strength	Therapeutic Area	# Patents	# GI Patents	Sales ($ million)	Volume (1000 NSP Ext. Units)	Avg. Price ($)
VYNDAMAX	PFIZER	CAPSULE	61MG	CARDIAC AGENTS	3	2	1193.20	1952.11	611
ERLEADA	JANSSEN PHARM	TABLET	60MG	ANTINEOPLASTICS	10	4	1157.95	10750.08	108
XTANDI	ASTELLAS PHARMA US	CAPSULE	40MG	ANTINEOPLASTICS	3	3	887.88	11189.64	79
XTANDI	ASTELLAS PHARMA US	TABLET	40MG	ANTINEOPLASTICS	4	3	650.76	7314.00	89
XTANDI	ASTELLAS PHARMA US	TABLET	80MG	ANTINEOPLASTICS	4	3	492.03	2820.90	174
ZEPOSIA	BRISTOL-M SQ US PH	CAPSULE	0.92MG	NEUROLOGICAL/ NEUROMUSCULAR	5	3	394.31	1538.07	256
OLUMIANT	LILLY	TABLET	4MG	ANTIARTHRITIC	5	3	171.58	1060.62	162
OLUMIANT	LILLY	TABLET	2MG	ANTIARTHRITIC	6	3	141.58	1758.39	81
ORILISSA	ABBVIE INC.	TABLET	150MG	NON-INFLAMMATORY PELVIC DIS	9	3	133.39	3502.39	38
ERLEADA	JANSSEN PHARM	TABLET	240MG	ANTINEOPLASTICS	9	4	129.99	298.62	435
ORSERDU	STEMLINE THERA INC	TABLET	345MG	ANTINEOPLASTICS	8	2	128.61	192.87	667
VYNDAQEL	PFIZER	CAPSULE	20MG	CARDIAC AGENTS	2	2	107.69	696.55	155
LYBALVI	ALKERMES INC	TABLET	10-10MG	ANTIPSYCHOTICS	12	1	66.28	1388.28	48
LYBALVI	ALKERMES INC	TABLET	20-10MG	ANTIPSYCHOTICS	12	1	57.32	1202.25	48
COSELA	G1 THERAPEUTICS	DRY VIAL	300MG	SPECIFIC ANTAGONISTS	12	11	53.88	39.33	1370

Note: This table presents trade name, manufacturer, dosage form, strength, therapy, number of patents, number of government-interest patents, sales (2023), volume (2023) and price (2023) for the top 15 selling drug products that reference at least one government-interest patent. This table only includes drug products for which IQVIA National Sales Perspective (NSP) data were available. Therapeutic area is defined using IQVIA's USC3 classification. IQVIA's NSP Ext. Units present volume based on dosage form, such as the number of capsules, tablets, mLs, etc. Average prices for capsules, tablets and dry vials are defined as $ per capsule, tablet, or vial, respectively. Data obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Lastly, we calculate hypothetical cost savings from exercising march-in rights, if it were able to facilitate generic entry, for each drug product in our sample with observable sales data. We estimate these hypothetical cost savings by assuming they would accrue during the time between the assumed generic entry date, which is the later of August 2024 and the end of exclusivity, and the expiration of patent protections.[n] The sum of these costs savings is approximately $0.2 billion for drug products in our dataset that exclusively reference government-interest patents. If we also include drug products with a mix of government-interest and non-government-interest patents, total savings increase to $12.0 billion. The relatively small share of savings arising from products that exclusively reference government-interest patents is due to a combination of factors, including a smaller number of eligible products, shorter protections from competition, and relatively limited overall sales of the relevant products.

[n] For drug products where exclusivity expires later than patent protections, cost savings are assumed to be zero.

To take into account the potential time needed for generic competition to be introduced, we conduct a sensitivity analysis where we estimate cost savings if generic competition occurs later than August 2024. Under the assumption that generic competition is instead introduced in August 2025 or at the expiration of exclusivity (whichever is later), we re-estimate cost savings to be approximately $0.2 billion for products that exclusively reference government-interest patents, and approximately $11.7 billion for all drug products in our sample.[o] If instead generic competition is introduced in whichever is later of August 2029 or the expiration of exclusivity, we estimate there to be no cost savings for drug products that exclusively reference government interest patents, and $8.2 billion in cost savings for all other drug products in our sample.

DISCUSSION

The question of whether exercising march-in rights could be used to address high drug prices has surfaced numerous times in the decades since the passage of the Bayh-Dole Act. Although march-in rights have never been exercised, the question remains as to how and when the government would use march-in to address a drug's price in order to make the benefits of federally funded research and development reasonably available to the public.

This analysis identifies 39 unique small molecule drugs, including 63 drug products, that reference at least one government-interest patent, just 13 of which exclusively reference government-interest patents. Because of potential gaps in our datasets, there may be small-molecule drug products with government-interest patents that we were unable to identify in our analysis. However, these numbers are consistent with other recent estimates of the number of drugs that may be eligible for march-in if the patents were determined to meet the defined criteria under the statute.[9] Only two of these drug products that exclusively reference government-interest patents have substantial sales, and their exclusivities and patents both expire prior to 2028. Consequently, the estimated hypothetical cost savings of introducing generic competition for these products (in either August 2024 or at the end of exclusivity) is $0.2 billion. This estimate is necessarily based on a single point in time; however, cost savings would change in response to new drugs and patents being introduced and older patents expiring.

When we evaluate drug products that reference both government-interest and non-government-interest patents, we find that, on average, most of the patents represented are non-government-interest. If a license were to be granted for the government-interest patents through march-in proceedings, manufacturing a product with both government-interest and non-government-interest patents would require contending with the remaining non-government-interest patents. Further, more than half of the drug products in our analysis that reference both government-interest and non-government-interest patents reference at least one non-government-interest drug substance patent, which are often considered the most difficult with which to contend.[5] Therefore, patent type (drug substance vs. non-drug substance) may be a factor to consider in exercising march-in rights. While it is beyond the scope of this issue brief to identify the avenues for contending with any particular patent, this finding highlights the potential complexity in exercising march-in rights on a product with a mix of patents.

Patent expiration and exclusivity end dates can also be a factor in exercising march-in rights. Our analysis finds that drug products that exclusively reference government-interest patents tend to have earlier patent expiration dates. This short amount of time until the expiration of protection from potential competition

[o] We assume cost savings to be zero if patent protection and any existing exclusivity expire prior to our assumed generic entry date.

suggests a limited impact to exercising march-in rights, particularly given existing concerns about the time that may be required for march-in proceedings.[4,7]

There are opportunities for future empirical work to improve our understanding of march-in rights. First, a comprehensive resource for identifying government-interest patents would enable researchers to more confidently identify the universe of products that may be eligible for exercising march-in rights. Second, this and other empirical analyses of march-in rights tend to focus on small molecule drugs due to limited availability of biologics patent information. Expanded information on patents covering biologics would enable researchers to extend their analyses of march-in rights to include biologics, which are particularly costly and have composed an increasingly large share of total drug expenditures in recent years.[22]

APPENDIX

Table A1. Trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for capsules that reference at least one government-interest patent (2023)

Trade Name	Strength	Therapeutic Area	# Patents	# GI Patents	Sales ($ million)	Volume (1000 NSP Ext. Units)	Avg. Price ($ per Capsule)
VYNDAMAX	61MG	CARDIAC AGENTS	3	2	1193.20	1952.11	611
XTANDI	40MG	ANTINEOPLASTICS	3	3	887.88	11189.64	79
ZEPOSIA	0.92MG	NEUROLOGICAL/NEUROMUSCULAR	5	3	394.31	1538.07	256
VYNDAQEL	20MG	CARDIAC AGENTS	2	2	107.69	696.55	155
ORIAHNN	300-1-0.5MG[p]	NON-INFLAMMATORY PELVIC DIS	7	2	23.73	1258.94	19
ZOLINZA	100MG	ENZYME INHIBITORS	5	3	9.67	77.40	125
SOHONOS	10MG	MUSCLE RELAXANT	5	3	1.63	.53	3062
SOHONOS	2.5MG	MUSCLE RELAXANT	5	3	0.19	.24	784
SOHONOS	1.5MG	MUSCLE RELAXANT	5	3	0.07	.15	463
SOHONOS	1MG	MUSCLE RELAXANT	5	3	0.05	.15	302

Note: This table presents trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for capsules with at least one government-interest patent. Therapeutic area is defined using IQVIA's USC3 classification. IQVIA's NSP Ext. Units present volume based on dosage form, such as the number of capsules, tablets, mLs, etc. Data are obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

[p] Oriahnn contains elagolix 300mg, estradiol 1mg, and norethindrone acetate 0.5mg.

Table A2. Trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for tablets that reference at least one government-interest patent (2023)

Trade Name	Strength	Therapeutic Area	# Patents	# GI Patents	Sales ($ million)	Volume (1000 NSP Ext. Units)	Avg. Price ($ per Tablet)
ERLEADA	60MG	ANTINEOPLASTICS	10	4	1157.95	10750.08	108
XTANDI	40MG	ANTINEOPLASTICS	4	3	650.76	7314.00	89
XTANDI	80MG	ANTINEOPLASTICS	4	3	492.03	2820.90	174
OLUMIANT	4MG	ANTIARTHRITIC	5	3	171.58	1060.62	162
OLUMIANT	2MG	ANTIARTHRITIC	6	3	141.58	1758.39	81
ORILISSA	150MG	NON-INFLAMMATORY PELVIC DIS	9	3	133.39	3502.39	38
ERLEADA	240MG	ANTINEOPLASTICS	9	4	129.99	298.62	435
ORSERDU	345MG	ANTINEOPLASTICS	8	2	128.61	192.87	667
LYBALVI	10-10MG	ANTIPSYCHOTICS	12	1	66.28	1388.28	48
LYBALVI	20-10MG	ANTIPSYCHOTICS	12	1	57.32	1202.25	48
LYBALVI	5-10MG	ANTIPSYCHOTICS	12	1	48.66	1015.50	48
LYBALVI	15-10MG	ANTIPSYCHOTICS	12	1	39.51	826.47	48
ORILISSA	200MG	NON-INFLAMMATORY PELVIC DISEASE	6	3	33.66	1762.68	19
ORSERDU	86MG	ANTINEOPLASTICS	8	2	12.12	54.33	223
OLUMIANT	1MG	ANTIARTHRITIC	6	3	5.53	69.03	80

Note: This table presents trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for tablets with at least one government-interest patent. Therapeutic area is defined using IQVIA's USC3 classification. IQVIA's NSP Ext. Units present volume based on dosage form, such as the number of capsules, tablets, mLs, etc. Data are obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Table A3. Trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for wet vials that reference at least one government-interest patent (2023)

Trade Name	Strength	Therapeutic Area	# Patents	# GI Patents	Sales ($ million)	Volume (1000 NSP Ext. Units)	Avg. Price ($ per mL)
EXONDYS 51	500MG/10ML	MUSCULAR DYSTROPHY AGENT	9	3	36.04	52.98	680
FOLOTYN	20MG/ML	ANTINEO ANTIMETABOLITES	2	2	11.42	2.58	4422
FOLOTYN	40MG/2ML	ANTINEO ANTIMETABOLITES	2	2	11.31	3.04	3716
AMONDYS-45	100MG/2ML	MUSCULAR DYSTROPHY AGENT	6	1	10.89	17.52	621
XIPERE	40MG/ML	OPHTHALMIC ANTI-INFLAM	3	1	6.53	3.52	1854
PEDMARK	12.5GM/100ML	SPECIFIC ANTAGONISTS	4	1	6.44	60.10	107
EXONDYS 51	100MG/2ML	MUSCULAR DYSTROPHY AGENT	9	3	6.25	9.23	677
VYONDYS 53	100MG/2ML	MUSCULAR DYSTROPHY AGENT	8	6	4.33	6.66	650
SYFOVRE	150MG/ML	OPHTHALMIC PREPS	10	3	2.81	.13	21002
EMPAVELI	1080MG/20ML	HEMOSTATIC MODIFIERS	10	3	2.25	10.24	220

Note: This table presents trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for wet vials with at least one government-interest patent. Therapeutic area is defined using IQVIA's USC3 classification. IQVIA's NSP Ext. Units present volume based on dosage form, such as the number of capsules, tablets, mLs, etc. Data are obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Table A4. Trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for dry vials that reference at least one government-interest patent (2023)

Trade Name	Strength	Therapeutic Area	# Patents	# GI Patents	Sales ($ million)	Volume (1000 NSP Ext. Units)	Avg. Price ($ per Unit)
COSELA	300MG	SPECIFIC ANTAGONISTS	12	11	53.88	39.33	1370
VABOMERE	2GM	B-LACTAM, INCREASED ACTIVITY	7	1	21.54	112.93	191
XERAVA	50MG	ANTIINFECTANT	4	2	8.82	152.27	58
XERAVA	100MG	ANTIINFECTANT	4	2	5.26	51.53	102

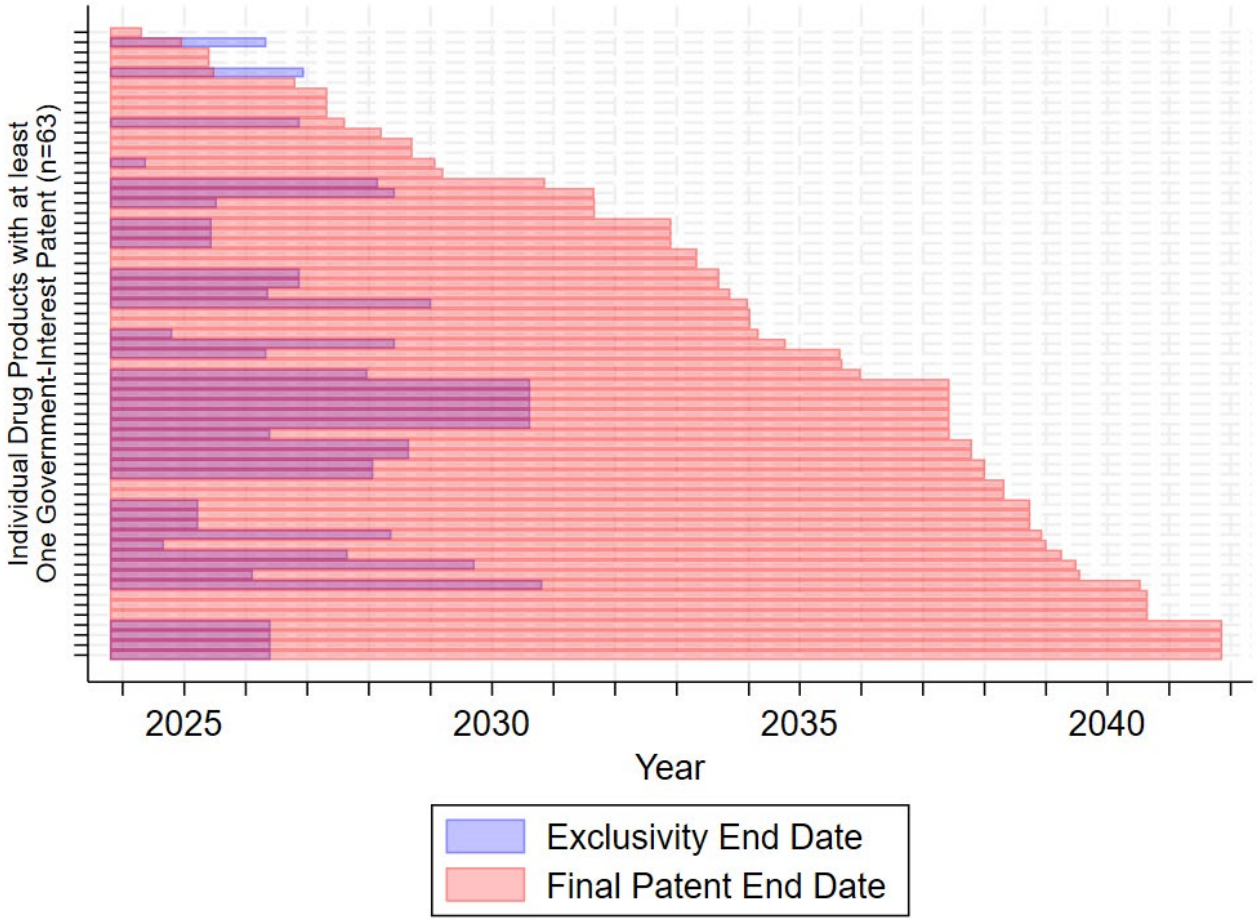
Note: This table presents trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for dry vials with at least one government-interest patent. Therapeutic area is defined using IQVIA's USC3 classification. IQVIA's NSP Ext. Units present volume based on dosage form, such as the number of capsules, tablets, mLs, etc. Data are obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Table A5. Trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for products other than capsules, tablets, wet vials, and dry vials that reference at least one government-interest patent (2023)

Trade Name	Strength	Therapeutic Area	# Patents	# GI Patents	Sales ($ million)	Volume (1000 NSP Ext. Units)	Avg. Price ($ per Unit)
EYSUVIS	0.25%	OPHTALMIC ANTI-INFLAM	16	13	32.49	559.76	58
TRUDHESA	4MG/ML	ANTI-MIGRAINE	6	4	8.60	44.00	195
ADASUVE	10MG	ANTIPSYCHOTICS	5	3	0.01	.05	148

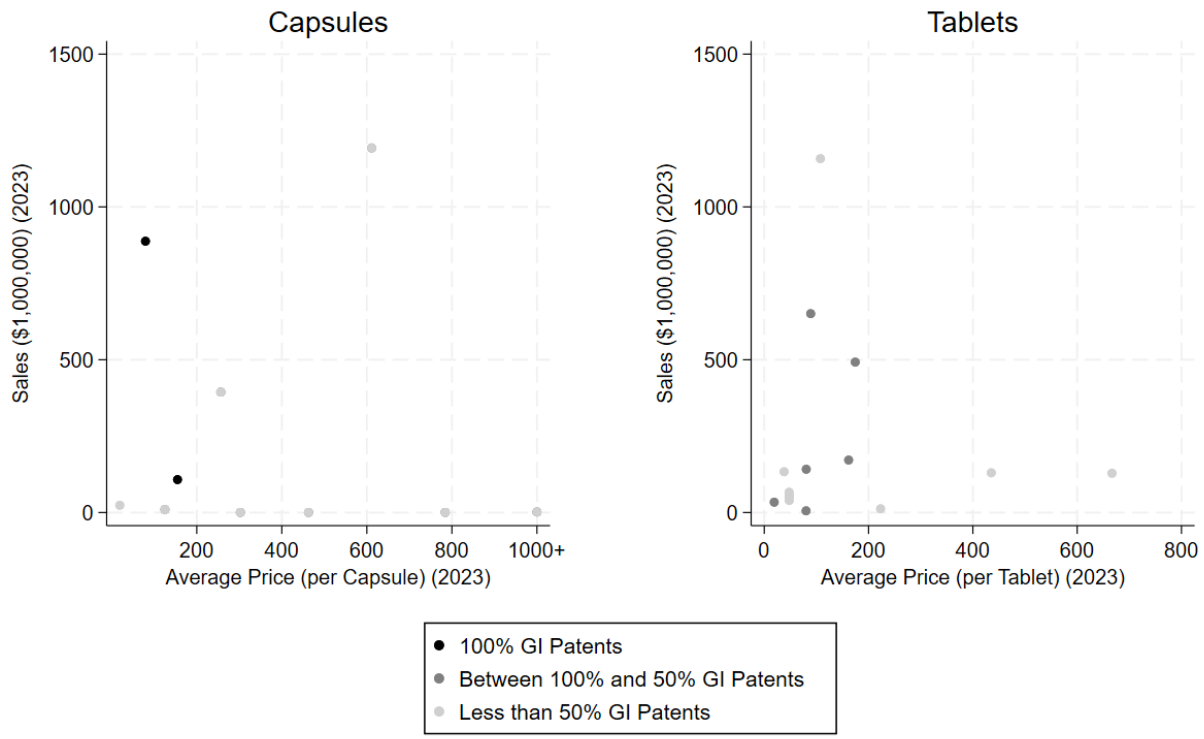
Note: This table presents trade name, strength, therapeutic area, number of patents, number of government-interest patents, sales, volume, and price for products other than capsules, tablets, wet vials, and dry vials with at least one government-interest patent. Therapeutic area is defined using IQVIA's USC3 classification. IQVIA's NSP Ext. Units present volume based on dosage form, such as the number of capsules, tablets, mLs, etc. Data are obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Figure A1. Exclusivity and patent coverage for drug products that reference at least one government-interest patent



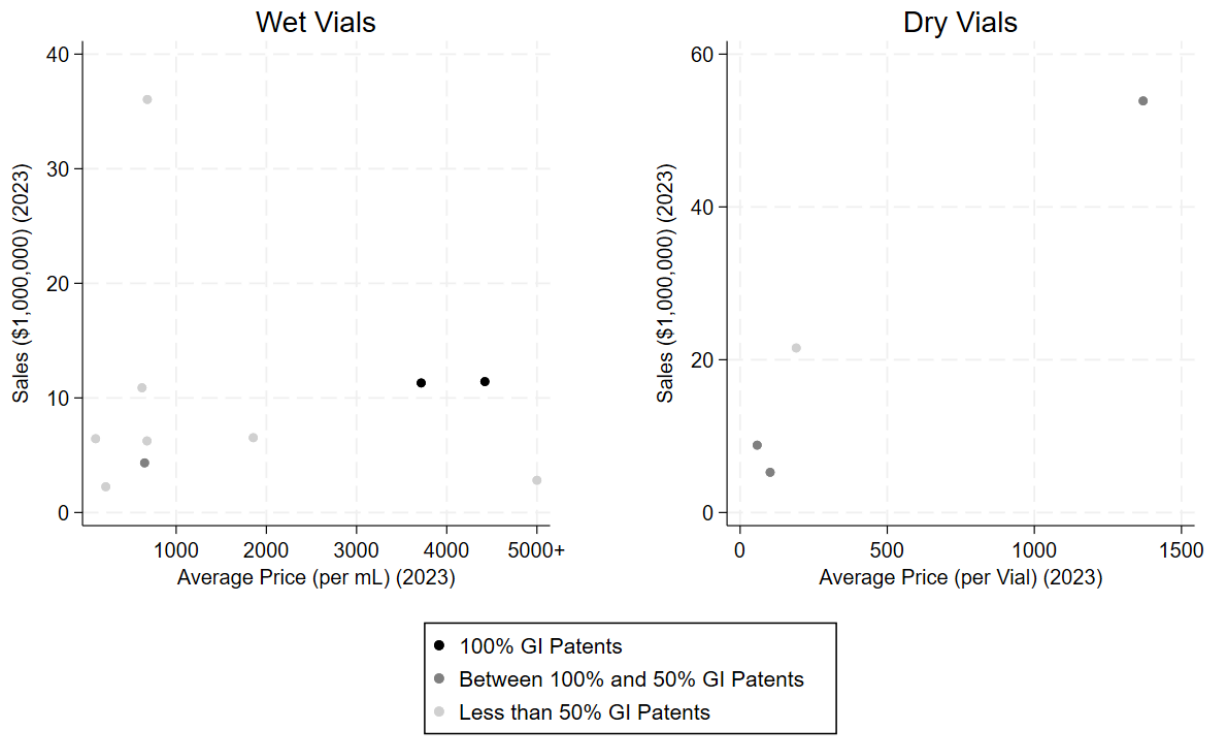
Note: This figure presents the exclusivity and patent coverage for all drug products that reference at least one government-interest patent. Each bar represents a unique drug product (n=63). The exclusivity end date for each drug product is obtained by identifying latest exclusivity end dates in FDA's Orange Book. The final patent end date for each product was obtained by identifying the latest end date of all patents referenced by an individual product in FDA's Orange Book. Data are obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, and Gross and Sampat (2024).[18]

Figure A2. Sales, price, and percent of patents that are government-interest for capsules and tablets that reference at least one government-interest patent (2023)



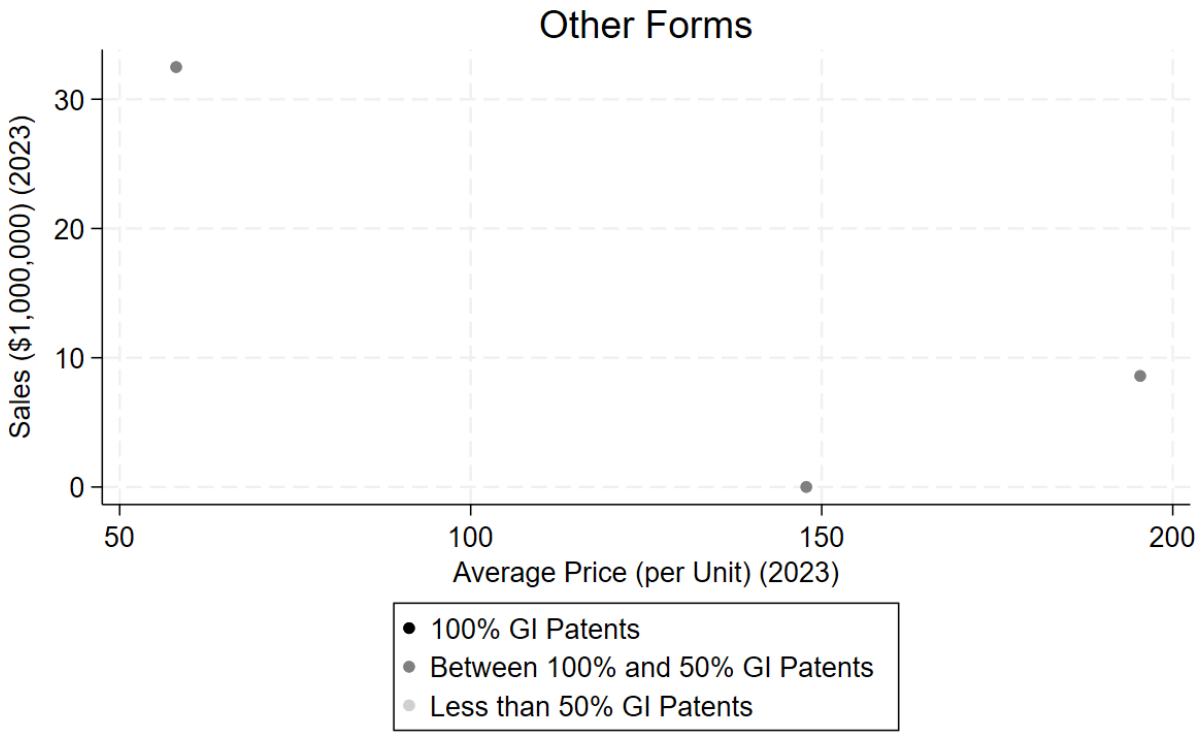
Note: This figure presents sales (2023), average prices (2023), and percent of patents that are government-interest (GI) for capsules and tablets that reference at least one government-interest patent. Since products are defined at the ingredient, dosage form, strength level, a single trade name may appear multiple times in the figure. Data were obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Figure A3. Sales, prices, and percent of patents that are government-interest for wet vials and dry vials that reference at least one government-interest patent (2023)



Note: This figure presents sales (2023), average prices (2023), and percent of patents that are government-interest (GI) for wet vials and dry vials that reference at least one government-interest patent. Since products are defined at the ingredient, dosage form, strength level, a single trade name may appear multiple times in the figure. Data were obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

Figure A4. Sales, prices, and percent of patents that are government-interest for products other than capsules, tablets, wet vials, and dry vials that reference at least one government-interest patent (2023)



Note: This figure presents sales (2023), average prices (2023), and percent of patents that are government-interest (GI) for products that reference at least one government-interest patent. These products include dosage forms other than the four presented in the above figures (capsules, tablets, wet vials, and dry vials). Data obtained from FDA's Orange Book (accessed on February 14, 2024), USPTO's list of patents with government-interest statements, NIH RePORTER, Gross and Sampat (2024),[18] and IQVIA National Sales Perspective (NSP) (accessed February 22, 2024).

REFERENCES

1. University and Small Business Patent Procedures Act of 1980. 35 US Code § 200-212.
2. Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights. National Institute of Standards and Technology. https://www.govinfo.gov/content/pkg/FR-2023-12-08/pdf/2023-26930.pdf
3. Treasure CL, Avorn J, Kesselheim AS. Do march-in rights ensure access to Medical products arising from federally funded research? A qualitative study. *The Milbank Quarterly*. 2015;93(4):761-787.
4. Cook-Deegan R, Kesselheim AS, Sarpatwari A. Updating the bayh-dole act: march-in rights and transparency. *JAMA*. 2022;327(10):923-924.
5. Darrow JJ, Mai DTC. An Orange Book Landscape: Drugs, Patents, and Generic Competition. *Food and Drug Law Journal*. 2022;77:51-65.
6. 37 CFR Part 401.6; 35 U.S.C. § 203(b).
7. Tabak, Lawrence. (March 21, 2023). [Letter to Robert Sachs and Clare Love]. Accessed at: https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/NIH_Decision_Xtandi_March-In_Request(2023).
8. Sampat BN, Lichtenberg FR. What are the respective roles of the public and private sectors in pharmaceutical innovation? *Health Affairs*. 2011;30(2):332-339.
9. Ouellette LL, Sampat BN. The Feasibility of Using Bayh-Dole March-In Rights to Lower Drug Prices: An Update. *National Bureau of Economic Research*. 2024;Working Paper 32217
10. 28 U.S.C. § 1498(a).
11. Kapczynski A, Kesselheim AS. 'Government Patent Use': A Legal Approach To Reducing Drug Spending. *Health Affairs*. 2016;35(5):791-797.
12. Brennan H, Kapczynski A, Monahan CH, Rizvi Z. A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health. *Yale JL & Tech*. 2017;18(275)
13. Cubanski J, Neuman T, True S, Freed M. *What's the latest on Medicare drug price negotiations?* 2019. https://kff.org/wp-content/uploads/2019/07/Issue-Brief-Whats-the-Latest-on-Medicare-Drug-Price-Negotiations.pdf
14. Bradsher K, Andrews EL. A nation challenged: Cipro; US says Bayer will cut cost of its Anthrax drug. *The New York Times*. October 24, 2001. https://www.nytimes.com/2001/10/24/business/a-nation-challenged-cipro-us-says-bayer-will-cut-cost-of-its-anthrax-drug.html
15. U.S. Federal Trade Commission. (April 30, 2024). FTC Expands Patent Listing Challenges, Targeting More Than 300 Junk Listings for Diabetes, Weight Loss, Asthma and COPD Drugs. [Press Release]. Accessed at: https://www.ftc.gov/news-events/news/press-releases/2024/04/ftc-expands-patent-listing-challenges-targeting-more-300-junk-listings-diabetes-weight-loss-asthma.
16. Federal Trade Commission Statement Concerning Brand Drug Manufacturers' Improper Listing of Patents in the Orange Book. (September 2023). Accessed at: https://www.ftc.gov/system/files/ftc_gov/pdf/p239900orangebookpolicystatement092023.pdf.
17. Conrad R, Davis K. *Estimating Cost Savings from New Generic Drug Approvals in 2021.* September 2023. Retrieved from https://www.fda.gov/media/172608/download
18. Gross DPS, Bhaven N. *The Government Patent Register: A New Resource for Measuring U.S. Government-Funded Patenting*. NBER Working Paper No. 32136. February 2024. https://doi.org/10.7910/DVN/BDCCN9
19. Government Accountability Office. (2023). "Better Data Will Improve Understanding of Federal Contributions to Drug Development." (GAO Publication No. 23-105656). National Institutes of Health. Retrieved from www.gao.gov/assets/d23105656.pdf
20. Food, Drug, and Cosmetic Act, Section 505(b)(1)(A)(viii).
21. 21 CFR 314.53.
22. Parasrampuria S, Murphy S. Competition in Prescription Drug Markets, 2017-2022. Washington, DC: Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services. December 2023.

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