



January 2020

DRUG DEVELOPMENT

FDA's Priority Review Voucher Programs

GAO Highlights

Highlights of [GAO-20-251](#), a report to congressional committees

Why GAO Did This Study

Few drugs are currently available to treat certain tropical and rare pediatric diseases and to use as medical countermeasures, given their small market or potentially limited profitability. To help provide incentives for the development of such drugs, Congress created three PRV programs, which award PRVs to drug sponsors that develop drugs for tropical diseases, rare pediatric diseases, and medical countermeasures (e.g., drugs to mitigate harm from biological, chemical, radiological, or nuclear agents). FDA, an agency within the Department of Health and Human Services (HHS), administers these programs.

The 21st Century Cures Act included a provision for GAO to study the PRV programs. GAO examined the number of PRVs awarded and redeemed and the drugs for which they were awarded or redeemed, and what is known about the extent to which the PRVs provide incentives for developing drugs to meet unmet needs. GAO analyzed FDA data on awarded and redeemed PRVs for fiscal years 2009 through 2019 and other publicly available information on their transfers and sales. GAO conducted a literature review of peer-reviewed articles published from January 2009 through May 2019 that examined the PRV programs and interviewed FDA officials. GAO also interviewed seven stakeholder groups, seven academic researchers, and seven drug sponsors selected based on factors such as familiarity with PRV programs or drug development.

HHS provided technical comments on a draft of this report, which were incorporated as appropriate.

View [GAO-20-251](#). For more information, contact John E. Dicken at (202) 512-7114 or dickenj@gao.gov.

January 2020

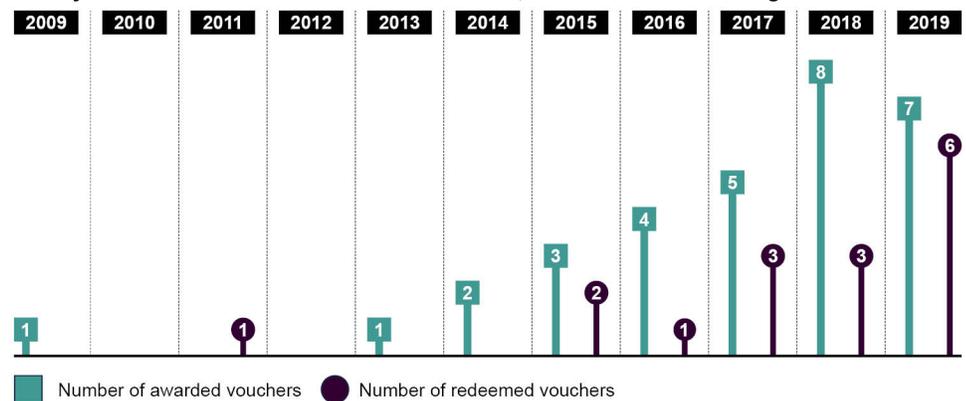
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FDA's Priority Review Voucher Programs

What GAO Found

The Food and Drug Administration (FDA) awards priority review vouchers (PRV) to drug sponsors that develop drugs for tropical diseases or rare pediatric diseases or to use as medical countermeasures. The PRV—which can be sold to another drug sponsor—may be redeemed later to receive priority review from FDA with a targeted review time of 6 months, rather than the 10-month standard review, for a drug application of the PRV holder's choice. The potential for additional revenue from either marketing a drug about 4 months sooner or from selling the PRV could provide an incentive for drug sponsors to develop drugs for these diseases or conditions. From fiscal year 2009, when the first PRV was awarded, through fiscal year 2019, FDA awarded 31 PRVs, mostly for drugs to treat rare pediatric diseases. Of the 31 PRVs awarded by FDA, 17 were sold to another drug sponsor for prices ranging from about \$67 million to \$350 million, according to available data. As of September 30, 2019, available data show that drug sponsors had redeemed 16 of the 31 PRVs to obtain a shorter FDA review time for drugs to treat conditions and diseases such as human immunodeficiency virus (HIV), type 2 diabetes, and different forms of arthritis. These drug applications may not otherwise qualify for priority review.

Priority Review Vouchers Awarded and Redeemed, Fiscal Years 2009 through 2019



Source: GAO analysis of Food and Drug Administration (FDA) data and publicly available information. | GAO-20-251

GAO found few studies that examined the PRV programs, and those that did found the programs had little or no effect on drug development. However, all seven drug sponsors GAO spoke with stated that PRVs were a factor in drug development decisions—six sponsors said they were one of a number of factors, while one sponsor said they were pivotal in its development of a drug. Some academic researchers and stakeholders expressed concerns about the PRVs as incentives for drug development, including the potential for the expected revenue from the sale of a PRV to decline as more are awarded and available for sale.

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Abbreviations

FDA	Food and Drug Administration
PRV	priority review voucher
HHS	Department of Health and Human Services
HIV	human immunodeficiency virus

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January 31, 2020

The Honorable Lamar Alexander
Chairman
The Honorable Patty Murray
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Frank Pallone, Jr.
Chairman
The Honorable Greg Walden
Republican Leader
Committee on Energy and Commerce
House of Representatives

Few drugs are available for certain tropical diseases, rare pediatric diseases, and material threat medical countermeasures (medical countermeasures), despite their potential to affect millions of people.¹ Drug sponsors—facing a lengthy and expensive drug development process—may be reluctant to develop treatments for these diseases or conditions given the small markets or potentially limited profitability for them.² Other challenges can make drug development for tropical diseases, rare pediatric diseases, and medical countermeasures more difficult than for other drugs. Specifically, tropical diseases often affect people living in low-income areas outside of the United States, making it difficult for drug sponsors to recover drug development costs; rare pediatric diseases affect a limited number of children, making it difficult to

¹Tropical diseases, such as malaria and dengue fever, disproportionately affect poor and marginalized populations. Rare pediatric diseases, such as Duchenne muscular dystrophy and certain types of cystic fibrosis, are serious and life-threatening diseases where the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years. Medical countermeasures include drugs and vaccines that can diagnose, prevent, protect from, or treat the effects of exposure to emerging infectious diseases, such as pandemic influenza, and to chemical, biological, radiological, or nuclear agents.

²A drug sponsor is the person or entity that assumes responsibility for the development of a new drug, including responsibility for complying with applicable laws and regulations. While drug development time frames and costs can vary, the drug industry estimates that, on average, a sponsor spends over a decade developing a drug at an average cost of \$2.6 billion. We use the term “drug” to refer to both chemically synthesized drugs and therapeutic biological products, such as vaccines.

identify and recruit sufficient numbers of patients to include in studies; and medical countermeasures treat high-priority threats that affect health security, making it difficult to test the drugs because exposing study volunteers to such threats would be an unethical and unacceptable risk.

To encourage the development of drugs to treat tropical diseases, treat rare pediatric diseases, and use as medical countermeasures, Congress established three priority review voucher (PRV) programs under which the Food and Drug Administration (FDA) awards a PRV to a drug sponsor upon approval of that sponsor's drug in one of these three areas.³ A drug sponsor can later redeem the PRV when submitting a future drug application to treat any disease or condition, or sell or transfer it to another drug sponsor. When redeemed, a PRV entitles a drug sponsor to priority review by FDA—which has a goal of a 6-month review, rather than the 10-month goal for a standard review. The potential for additional revenue that comes from marketing a drug approximately 4 months sooner—or the proceeds that may come from selling the PRV to another drug sponsor—could provide an incentive for drug sponsors to develop drugs for tropical diseases, rare pediatric diseases, or medical countermeasures.

The 21st Century Cures Act included a provision for us to review and report on the PRV programs.⁴ This report examines

1. the number of PRVs that have been awarded, and what is known about them and about the drugs for which they were awarded;
2. the number of PRVs that have been redeemed, and what is known about them and about the drugs for which they were redeemed; and
3. what is known about the extent to which PRV programs provide incentives for drug development to meet unmet needs.

To determine how many PRVs have been awarded and redeemed, as well as what is known about the drugs for which they were awarded or redeemed, we examined FDA information and publicly available information for all PRVs from the date of each program's inception

³To be awarded a PRV, the approved drug must meet applicable criteria for one of the three PRV programs.

⁴Pub. L. No. 114-255, § 3014, 130 Stat. 1033, 1093 (2016).

through fiscal year 2019.⁵ Publicly available information included PRV sales (including sales prices), transfers, purchases, and redemptions reported by drug sponsors in documents such as press releases and Securities and Exchange Commission filings.⁶ We compared the FDA data to FDA approval letters, press releases, and other publicly available sources and determined these data were sufficiently reliable for our purposes.

To examine what is known about the extent to which PRV programs provide incentives for drug development to meet unmet needs, we conducted a literature review of relevant articles published in peer-reviewed and other publications from January 2009 through May 2019. We reviewed these articles for information related to the PRV programs, including the extent to which PRVs are incentives for drug development and alternative incentives to the PRV programs for developing drugs for tropical diseases, rare pediatric diseases, and medical countermeasures.⁷

For all three objectives, we interviewed FDA officials; representatives from seven stakeholder groups, including trade associations, patient advocates, and organizations that partner with or provide funding to drug sponsors and are familiar with the PRV programs (hereafter, stakeholders); seven academic researchers with expertise in drug development, drug pricing, or the PRV programs (hereafter, researchers); and representatives from seven drug sponsors that have been awarded,

⁵Congress authorized the tropical disease PRV program in 2007, the rare pediatric disease PRV program in 2012, and the medical countermeasure PRV program in 2016. See Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 1102, 121 Stat. 823, 972 (2007); Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 908, 126 Stat. 993, 1094 (2012); and 21st Century Cures Act, Pub. L. No. 114-255, § 3086, 130 Stat. 1033, 1145 (2016).

⁶According to FDA, drug sponsors are not required to provide sale prices of PRVs to FDA and may choose not to publicly disclose the sale prices.

⁷We identified articles through a search of bibliographic databases, including AgeLine, MEDLINE, and Scopus, using terms such as “priority review voucher,” “rare disease,” “tropical disease,” and “incentive.” Of the 155 citations we reviewed, we determined there were 77 relevant articles. We reviewed the 77 articles for background information on the PRV programs, information on the market for selling PRVs, alternatives to the PRV programs, and studies that analyzed data on the effects the PRV programs have had on drug development. Of the 77 articles we reviewed, we identified four that analyzed data on the effect the programs have had on drug development. We reviewed the methodology of these four articles and determined they were sufficiently reliable for our purposes. In addition, we reviewed other relevant publications, such as an evaluation prepared for the Department of Health and Human Services.

purchased, or redeemed a PRV.⁸ We conducted these interviews to obtain information on (1) PRV awards and sales and insights into the characteristics of awarded PRVs and trends in PRV sales; (2) redemption data, reasons why a drug sponsor might redeem a PRV, and the effect the PRV redemptions have had on FDA resources; and (3) what is known about the extent to which PRV programs provide incentives for drug development to meet unmet needs. The perspectives of selected stakeholders, researchers, and drug sponsors are not generalizable.

We conducted this performance audit from February 2019 to January 2020 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

Priority and Standard Review

For a priority review, the Food and Drug Administration (FDA) directs its resources to applications for new drugs that prevent, diagnose, or treat a serious condition and, if approved, would provide significant improvements in safety or effectiveness compared to available drugs. A drug may also receive priority review if the drug sponsor redeems a priority review voucher, among other things. FDA's goal is to complete the review of a priority application within 6 months.

Drugs that do not receive priority review receive standard review. FDA's goal is to complete the review of a standard application within 10 months.

Source: GAO review of FDA information. | GAO-20-251

FDA, an agency within the Department of Health and Human Services (HHS), is responsible for overseeing the safety and efficacy of drugs and biological products, such as vaccines, sold in the United States.⁹ Before a drug sponsor can market a new drug, it generally must submit evidence of the drug's safety and effectiveness to FDA in a new drug application or biologics license application.¹⁰ While FDA reviews most drug applications using its standard review process, FDA's priority review designation is intended to reduce the review time needed to bring a drug to market for

⁸The stakeholders we interviewed were the Bill and Melinda Gates Foundation, Biotechnology Innovation Organization, Drugs for Neglected Diseases Initiative, Médecins Sans Frontières, Medicines for Malaria Ventures, National Organization for Rare Disorders, and Pharmaceutical Research and Manufacturers of America. The drug sponsors we interviewed or obtained information from were BioMarin, Janssen Pharmaceuticals, Medicines Development for Global Health, Novartis, Sanofi, SIGA Technologies, and Ultragenyx. These sponsors were selected based on their different experiences with the three PRV programs and their interactions (e.g., selling and purchasing) with the PRV programs. In some cases, the drug sponsors elected to respond to our questions in writing; however, similar questions were provided to all drug sponsors.

⁹Unless otherwise indicated, we use the term "drug" in this report to refer to both chemically synthesized drugs and therapeutic biological products. Biological products—which include vaccines, blood products, and proteins, among other things—are derived from living sources such as humans, animals, and microorganisms.

¹⁰Hereafter, we use the term "drug application" to refer to both new drug applications and biologics license applications submitted to FDA for review.

certain drugs that treat serious conditions.¹¹ A drug application typically receives a priority review designation if the drug would provide a significant improvement in the safety or effectiveness of the prevention, diagnosis, or treatment of a serious condition when compared to available drugs, among other things (see sidebar).¹² FDA reviews all applications to determine if they qualify for priority review.¹³

FDA is also responsible for the implementation of the three PRV programs, which are intended to encourage development of drugs for tropical diseases, rare pediatric diseases, and medical countermeasures.¹⁴ Qualifying diseases and conditions for the tropical disease PRV program and criteria for the rare pediatric disease PRV program are set forth in statute—though the list of eligible tropical diseases can be updated by order of the Secretary of HHS.¹⁵ For the medical countermeasure PRV program, HHS publishes a list of high-priority threats that qualify for a PRV, including those that the Department of Homeland Security determines to pose a material threat sufficient to

¹¹For more information on priority review and FDA's other programs intended to facilitate and expedite the development and review of new drugs that have the potential to address an unmet medical need for the treatment of serious conditions, see GAO, *Drug Safety: FDA Expedites Many Applications, But Data for Postapproval Oversight Need Improvement*, [GAO-16-192](#) (Washington, D.C.: Dec. 15, 2016).

¹²Drug applications may also be eligible for priority review if (1) the drug treats a disease designated as a qualified infectious disease, (2) it is a supplemental application for a drug that proposes a labeling change based on certain pediatric studies; or (3) it is submitted with a PRV.

¹³FDA assesses each drug application when it is submitted to determine if it qualifies for priority review; however, a drug sponsor may expressly request priority review. FDA informs the drug sponsor of a priority review designation within 60 days of the receipt of the drug application. Designation of a drug as "priority" does not alter the scientific or medical standard for approval or the quality of evidence necessary.

¹⁴We previously reported on the rare pediatric disease PRV program. See GAO, *Rare Diseases: Too Early to Gauge Effectiveness of FDA's Pediatric Voucher Program*, [GAO-16-319](#) (Washington, D.C.: Mar. 2, 2016).

¹⁵The Secretary of HHS can add to the list of tropical diseases any infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations.

affect national security.¹⁶ (See table 1 for the types of drugs eligible for a PRV.)

¹⁶To be eligible for a medical countermeasure PRV, the drug must be intended for use either to (1) prevent or treat harm from a biological, chemical, radiological, or nuclear agent identified as a material threat under 42 U.S.C. § 247d-6b(c)(2)(A)(ii) or (2) mitigate, prevent, or treat harm from a condition that may be caused by administering a drug against a biological, chemical, radiological, or nuclear agent. The Secretary of Homeland Security is responsible for identifying such agents as a material threat, and new agents that present a material threat may be identified without public announcements. According to FDA, the publicly available list of agents that have been identified as material threats can be found in the Public Health Emergency Medical Countermeasure Enterprise Strategy and Implementation Plan; the threats identified in table 1 appear in the 2017-2018 plan.

Table 1: Types of Drugs Eligible for Priority Review Voucher (PRV) Awards, by Program, Publicly Available as of September 30, 2019

Tropical disease PRV program	Rare pediatric disease PRV program	Medical countermeasure PRV program
<p>Application must be for a drug intended to prevent or treat a tropical disease. The diseases qualifying for a tropical disease PRV are the following:</p> <ul style="list-style-type: none"> • tuberculosis • malaria • blinding trachoma • Buruli ulcer • cholera • dengue/dengue haemorrhagic fever • dracunculiasis (guinea-worm disease) • fascioliasis • human African trypanosomiasis • leishmaniasis • leprosy • lymphatic filariasis • onchocerciasis • schistosomiasis • soil transmitted helminthiasis • yaws • filovirus diseases • Zika virus disease • Chagas disease • neurocysticercosis • Chikungunya virus disease • Lassa fever • rabies • cryptococcal meningitis 	<p>Application must be for a drug intended to prevent or treat a rare disease or condition that is serious or life-threatening, and the serious or life-threatening manifestations must primarily affect individuals aged from birth to 18 years.</p> <p>A rare disease or condition is any disease or condition which affects less than 200,000 persons in the United States, or affects 200,000 or more people in the United States and there is no reasonable expectation of recovering the cost of drug development and marketing from U.S. sales.</p>	<p>Application must be for a drug intended to prevent or treat harm from a biological, chemical, radiological, or nuclear agent identified as a material threat, which include the following:</p> <ul style="list-style-type: none"> • Bacillus anthracis (anthrax) • Multi-drug resistant B. anthracis (MDR anthrax) • Burkholderia mallei (glanders) • Burkholderia pseudomallei (melioidosis) • Clostridium botulinum toxin (botulism) • Ebola virus (Ebola hemorrhagic fever) • Francisella tularensis (tularemia) • Marburg virus (Marburg hemorrhagic fever) • Rickettsia prowazekii (typhus) • Variola virus (smallpox) • Yersinia pestis (plague) • acetylcholinesterase inhibitor nerve agents • cyanide salts (potassium and sodium cyanide) • hydrogen cyanide • Vesicants • radiological and nuclear threats^a

Source: GAO summary of information from the Food and Drug Administration and the Department of Health and Human Services. | GAO-20-251.

Notes: In this table, the term “drug” refers to both chemically synthesized drugs and therapeutic biological products. The tropical disease PRV program was first authorized in 2007, the rare pediatric disease PRV program was first authorized in 2012, and the medical countermeasure PRV program was first authorized in 2016.

^aA medical countermeasure application may also be for a drug intended to mitigate, prevent, or treat harm from a condition that may be caused by administering a drug against a biological, chemical, radiological, or nuclear agent. As of September 30, 2019, the list of agents included as material threats in this table are those that have been publicly identified in the 2017-2018 Public Health Emergency Medical Countermeasure Enterprise Strategy and Implementation Plan.

In order to be awarded a PRV, drug applications must meet additional criteria. For example, for all three PRV programs, the drug application must be eligible for priority review and a drug may be disqualified if its active ingredient has been previously approved by FDA in another drug application.¹⁷ If a drug application meets the eligibility criteria for one of the PRV programs, the drug sponsor can include a request for a PRV in its application, including supporting documentation demonstrating how the application meets the PRV eligibility criteria. Once FDA receives a sponsor's drug application and PRV request, it reviews the information and considers whether the drug should be approved. If FDA approves the drug application, it includes its decision regarding whether to award a PRV in its approval letter.

Once FDA awards a PRV to a drug sponsor, the sponsor can redeem the PRV with the submission of a future drug application for a drug intended to treat any disease or condition, shortening FDA's targeted review time from the 10-month standard review to 6 months, even if the drug in that future application would not qualify for priority review on its own merits. The drug sponsor also has the option of selling or transferring the PRV to another drug sponsor, which may then choose to use it or similarly sell or transfer it.¹⁸ PRVs may be transferred any number of times before they are used.¹⁹ When the drug sponsor possessing the PRV ultimately decides to redeem it, the sponsor must notify FDA at least 90 days in

¹⁷For other, program-specific requirements, see 21 U.S.C. §§ 360n(a)(4) (tropical disease product application), 360ff(a)(4) (rare pediatric disease product application), and 360bbb-4a(a)(4) (medical countermeasure product application).

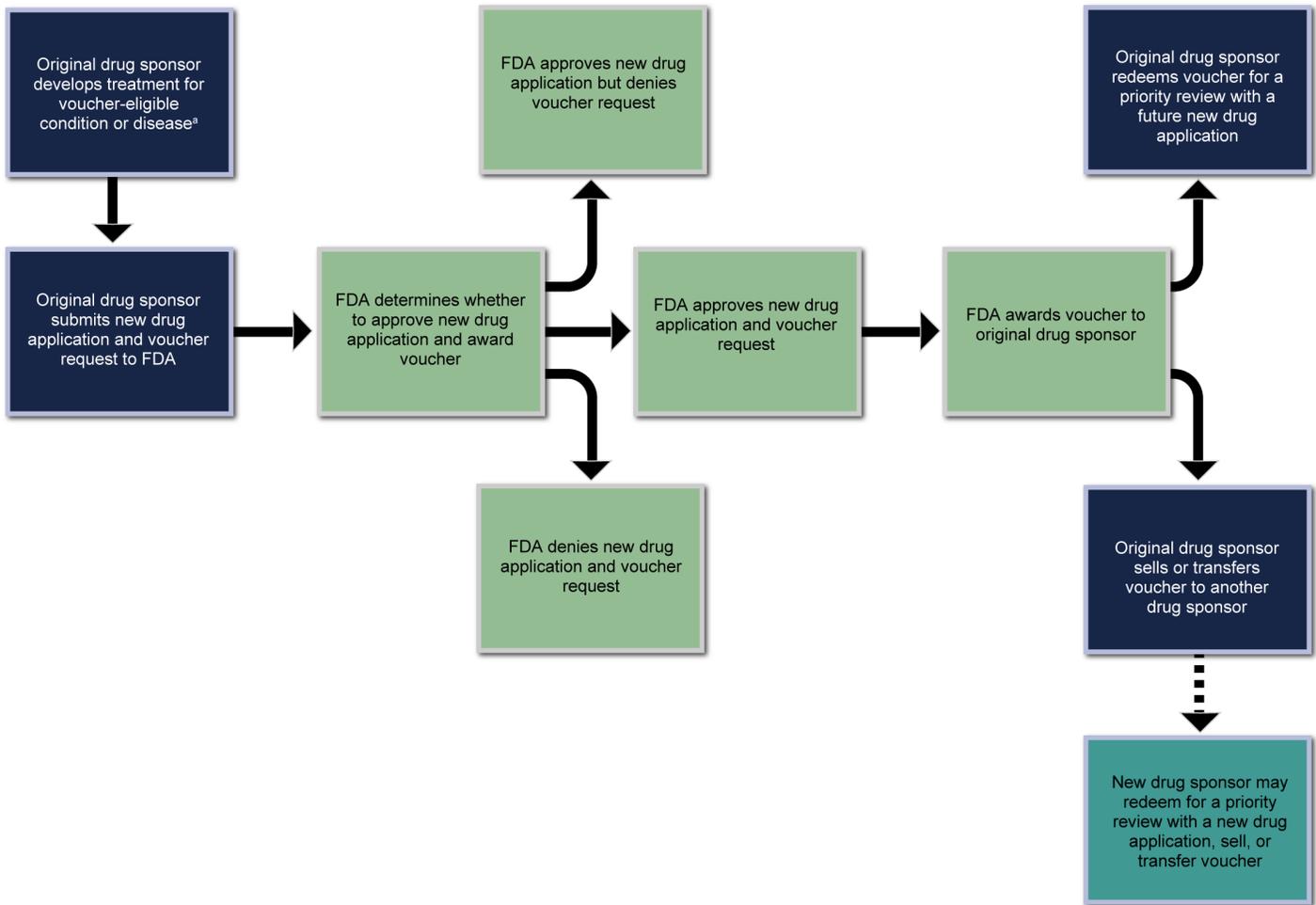
¹⁸FDA may revoke any rare pediatric disease PRV if the drug for which the PRV was awarded is not marketed in the United States within 1 year following the date of approval. 21 U.S.C. § 360ff(e)(1).

¹⁹Each person to whom a rare pediatric disease PRV is transferred must notify FDA of the change in PRV ownership within 30 days of the transfer. 21 U.S.C. § 360ff(b)(2)(B). For the tropical disease and medical countermeasure PRV programs, letters of transfer should be included when the PRV is redeemed, according to FDA guidance.

advance of submitting its drug application that is using the PRV. Figure 1 provides a general overview of the PRV programs.²⁰

²⁰For rare pediatric disease PRVs, a drug sponsor may request a rare pediatric disease designation for a drug that is still in development. In its designation request, a drug sponsor is to include information about, among other things, the drug and the rare pediatric disease for which the drug is being investigated, and the basis for concluding that the disease is rare and the serious or life-threatening manifestations primarily affect children. FDA reviews the provided information and generally informs a drug sponsor of its designation decision within 60 days of receiving the request. FDA encourages drug sponsors to request such a designation in order for the agency to have the necessary information to evaluate a drug's PRV eligibility and to ensure that drug sponsors have an adequate opportunity to provide this information before requesting a PRV. Although requesting such designation is not currently required in order to receive a rare pediatric disease PRV, after September 30, 2020, FDA may not award any rare pediatric disease PRV unless the drug is designated by September 30, 2020, and FDA has approved the drug application by September 30, 2022.

Figure 1: Overview of the FDA Priority Review Voucher (PRV) Programs



- Original drug sponsor
- FDA
- New drug sponsor

Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-251

Notes: Among other things, a drug application submitted by a drug sponsor seeking a PRV must itself be deemed eligible by FDA for a priority review.

^aEach of the three PRV programs—for tropical diseases, rare pediatric diseases, and medical countermeasures—has its own criteria for the types of drugs that are eligible for a PRV.

The drug sponsor redeeming a PRV must also pay a PRV user fee (about \$2.5 million in fiscal year 2019), in addition to other user fees required for all drug applications.²¹ Because drug applications submitted to FDA with a PRV would not otherwise qualify for priority review, PRV user fees are intended to cover FDA's additional costs incurred when reviewing new drug applications with a PRV.²² When a drug sponsor notifies FDA of its intent to redeem a PRV, its notification serves as a legally binding commitment to pay the PRV user fee.²³

Of the three PRV programs, two—the rare pediatric disease and the medical countermeasure PRV programs—are set to expire in the coming years, unless they are reauthorized by Congress. The rare pediatric disease PRV program will begin to expire on September 30, 2020, and the program will end in September 2022.²⁴ The medical countermeasure PRV program will expire on October 1, 2023. After these end dates, FDA could no longer award a PRV for a rare pediatric disease or a medical countermeasure; however, the expiration dates do not affect PRV redemptions, as drug sponsors may redeem PRVs earned at any point in the future.

²¹In fiscal year 2019, the user fee for a drug application was about \$2.6 million.

²²For the tropical disease and medical countermeasure PRV programs, the PRV user fee is to be based on the average cost incurred by FDA in the review of drug applications subject to priority review in the previous fiscal year. For the rare pediatric disease PRV program, the PRV user fee is to be based on the difference between the average cost incurred by FDA in the review of drug applications subject to and not subject to priority in the previous fiscal year.

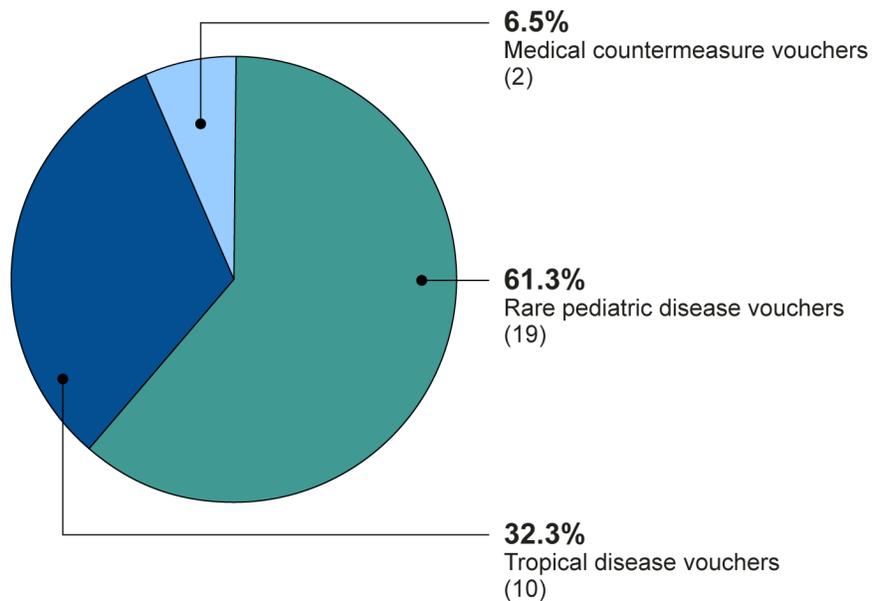
²³According to FDA, for the rare pediatric disease, tropical disease, and medical countermeasure PRV programs, drug sponsors may transfer their PRVs after notification is provided to FDA, if the sponsors have not yet submitted the drug application described in the notification letter. For the redemption of rare pediatric disease PRVs, user fees are paid by the drug sponsor when it notifies FDA that it intends to redeem a PRV. For the redemption of tropical disease and medical countermeasure PRVs, user fees are paid when the new drug application is submitted.

²⁴FDA may not award any rare pediatric disease PRVs after September 30, 2020, unless the drug has received a rare pediatric disease designation by that date, and FDA has approved the drug application by September 30, 2022.

Most of the 31 PRVs Awarded by FDA Were for Drugs to Treat Rare Pediatric Diseases

As of September 30, 2019, FDA awarded 31 PRVs across the three PRV programs, with the majority being awarded through the rare pediatric disease PRV program (see fig. 2). According to FDA, all PRVs were awarded for drugs that met unmet medical needs. The 31 PRVs were awarded to 26 different drug sponsors; three sponsors were awarded two PRVs each and one sponsor was awarded three PRVs. FDA awarded the 31 PRVs for drugs that treat 27 different diseases. For five diseases—malaria, tuberculosis, smallpox, spinal muscular atrophy, and Duchenne muscular dystrophy—FDA awarded PRVs to two different drugs for their treatment, and FDA awarded one PRV for a drug that prevents two different diseases.²⁵ (See appendix I for more information about the drugs for which FDA awarded PRVs.)

Figure 2: Priority Review Vouchers (PRV) Awarded by FDA by Program Type, as of September 30, 2019



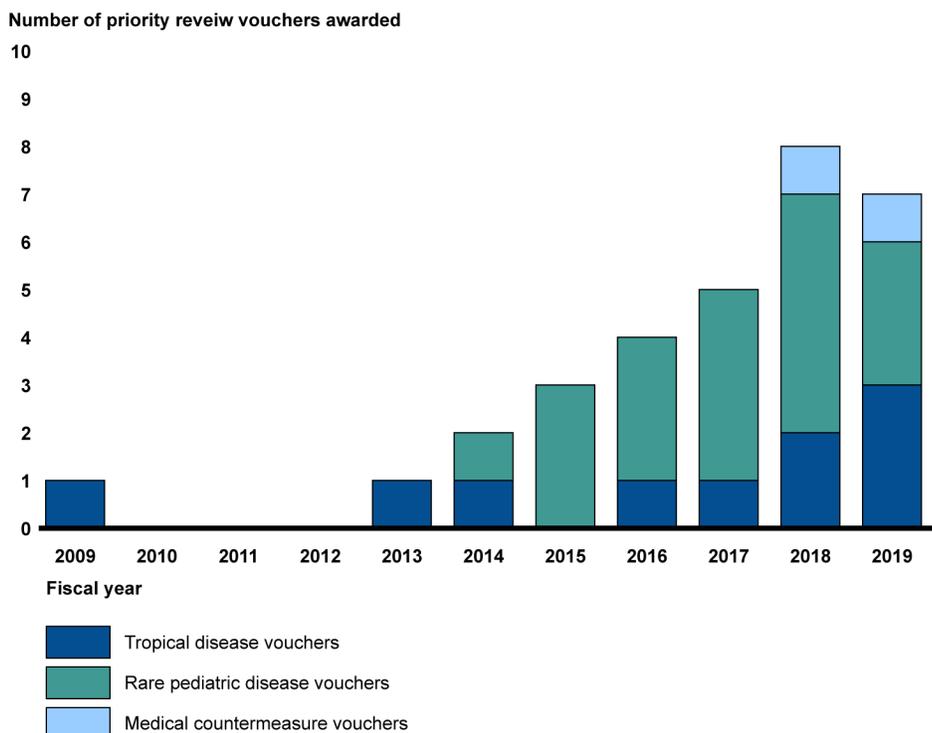
Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-251

Notes: Percentages do not add to 100 due to rounding. The tropical disease PRV program was first authorized in 2007, the rare pediatric disease PRV program was first authorized in 2012, and the medical countermeasure PRV program was first authorized in 2016.

²⁵A medical countermeasure PRV was awarded for a drug that prevents both smallpox and monkeypox, a disease similar to smallpox.

The first PRV was awarded in fiscal year 2009, 2 years after the start of the tropical disease PRV program, and none were awarded in fiscal years 2010 through 2012. The first rare pediatric disease PRV was awarded in fiscal year 2014—about 2 years after that PRV program was authorized—and, beginning in fiscal year 2015, the majority of PRVs awarded were for rare pediatric diseases. In fiscal year 2018, FDA awarded eight PRVs, including the first medical countermeasure PRV, the most awarded in a single fiscal year (see fig. 3).

Figure 3: Number of Priority Review Vouchers (PRV) Awarded by FDA, by Program Type, Fiscal Years 2009-2019



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-251

Note: The tropical disease PRV program was first authorized in 2007, the rare pediatric disease PRV program was first authorized in 2012, and the medical countermeasure PRV program was first authorized in 2016.

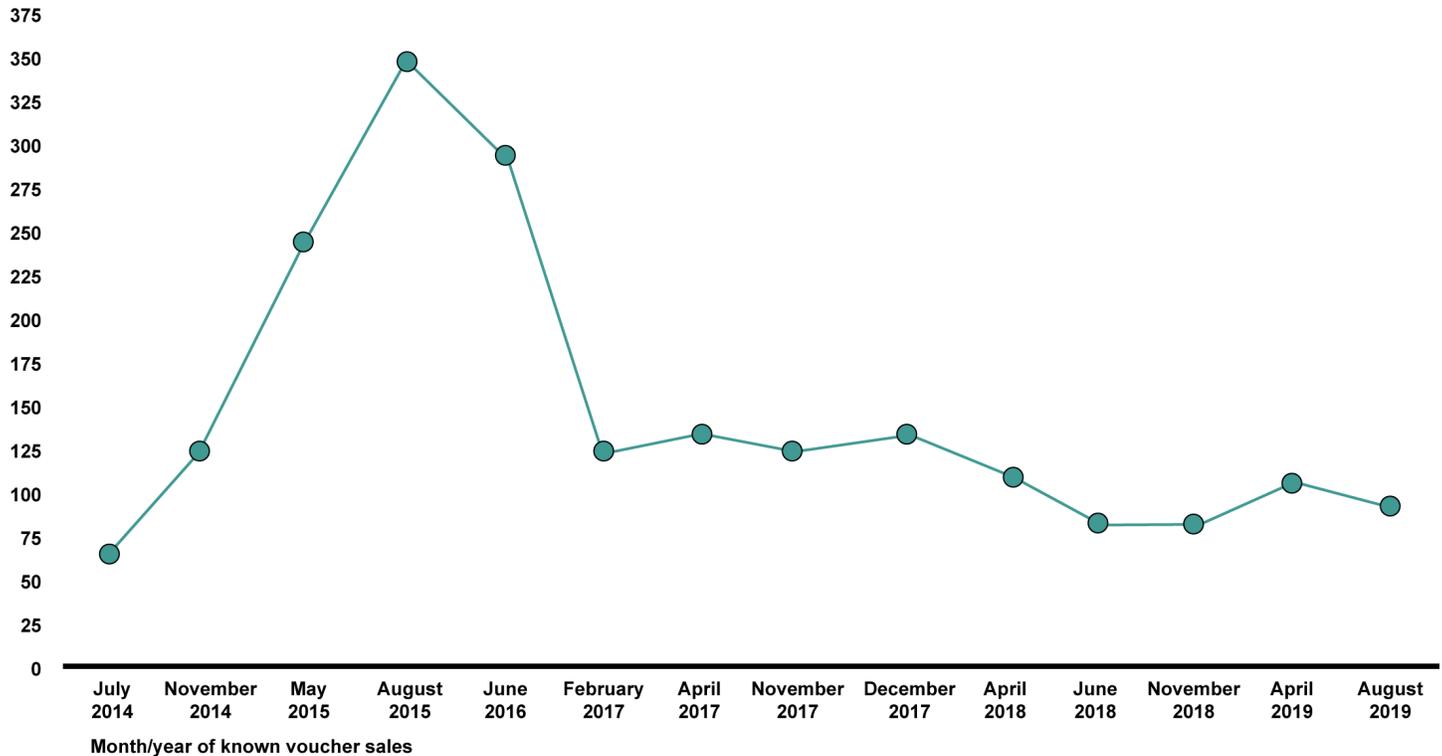
Of the 31 PRVs that FDA awarded to drug sponsors, available data indicate 17 PRVs were subsequently sold to another drug sponsor, providing revenue to the sponsor selling the PRV. For 14 of these 17 PRVs, we were able to determine a sales price, which ranged from \$67.5 million for a PRV sold in fiscal year 2014 to \$350 million for a PRV sold in

fiscal year 2015. However, the available sales prices of the PRVs sold since February 2017 have varied less than those sold previously, ranging from \$80 to \$130 million (see fig. 4). Because drug sponsors are only required to notify FDA of sales of rare pediatric disease PRVs at the time the sale occurs, additional transfers or sales of PRVs may have occurred.²⁶

²⁶FDA is notified of rare pediatric disease PRV sales or transfers when a PRV is transferred to another drug sponsor; however, the agency may only learn of tropical disease PRV and medical countermeasure PRV sales and transfers when a PRV is redeemed by another drug sponsor. As a result, FDA may not have information on PRV sales and transfers if PRVs have not yet been redeemed. Additionally, PRV sales prices are not reported to FDA. We obtained available PRV sales prices from company-issued press releases and other public statements and information filed with the Securities and Exchange Commission.

Figure 4: Available Sales Prices of Priority Review Vouchers (PRV), as of September 30, 2019

Sales prices of priority review vouchers (dollars in millions)



Source: GAO analysis of publicly available information on priority review voucher sales. | GAO-20-251

Note: This figure presents available sales price information for 14 PRVs. Two of these 14 PRVs were originally transferred to a different drug sponsor as part of the company's acquisition of drug-related assets and subsequently sold to another drug sponsor. The figure includes the reported sales price of the PRV when sold individually, not as part of the asset transfer. For three additional PRVs, the sales price or the seller was not publicly reported at the time of our analysis.

The drug sponsors, stakeholders, and researchers we interviewed noted that several factors could influence whether a drug sponsor keeps a PRV for future use, sells the PRV to another drug sponsor, or purchases a PRV to use on a drug that would not otherwise qualify for priority review. The PRV programs allow PRVs to be transferred multiple times, and according to stakeholders and drug sponsors we spoke with, the revenue gained from such sales may be a motivating factor for drug sponsors to sell them. For example, three stakeholders we interviewed said they believe drug sponsors consider the drugs in their development pipeline when deciding to keep, sell, or purchase a PRV, and one stated that drug sponsors need to determine if they would benefit more from using the PRV or the money they could make from selling it. One researcher

commented that price variation for PRVs can affect how a drug sponsor perceives the incentive and that low prices for PRVs may signify the need for additional incentives for drug development. However, two drug sponsors told us that they would continue to pursue PRVs as long as they were available and useful for a particular drug in their pipeline.

More than Half of the PRVs Awarded Have Been Redeemed for Drugs Treating a Variety of Conditions

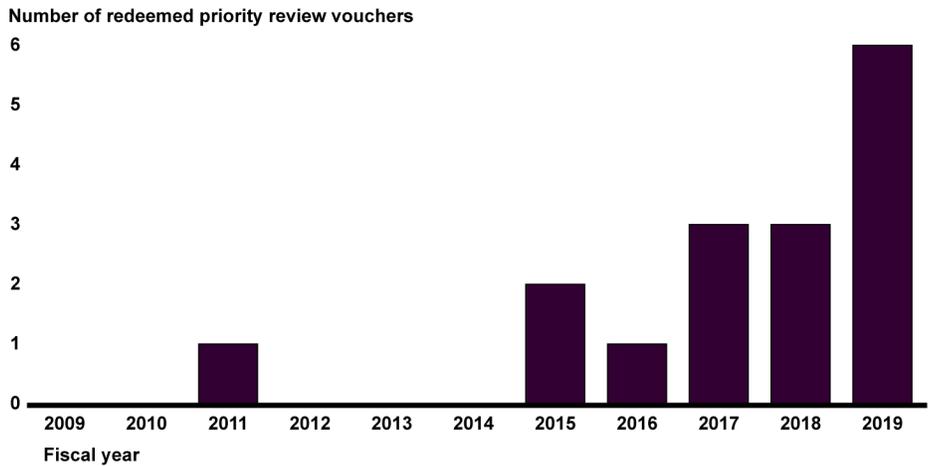
As of September 30, 2019, drug sponsors redeemed 16 of the 31 PRVs—that is, they submitted the PRV to obtain priority review for a drug application for a drug that would not otherwise qualify for a priority review.²⁷ The drugs for which the PRVs were redeemed treat or prevent a variety of conditions and diseases, including human immunodeficiency virus (HIV), type 2 diabetes, and different forms of arthritis. (See appendix II for a complete list of PRV redemptions.)

The first PRV was redeemed in fiscal year 2011, about 2 years after the first PRV was awarded, and the second PRV was redeemed in fiscal year 2015. Since 2017, drug sponsors have redeemed between three and six PRVs each year (see fig. 5).²⁸

²⁷For reporting purposes, PRVs are considered redeemed if FDA has completed review of the drug application for which they were redeemed or if the company has made public statements regarding its redemption. Additional PRV redemptions, if any, may not be reported in this report.

²⁸For an overview of key milestone dates of the PRV programs, see app. III.

Figure 5: Redeemed Priority Review Vouchers (PRV) by Fiscal Year, Fiscal Years 2009 through 2019



Source: GAO analysis of Food and Drug Administration (FDA) data and publicly available information. | GAO-20-251

Notes: The first PRV was awarded in fiscal year 2009; no PRVs were redeemed in fiscal years 2009, 2010, 2012, 2013, or 2014. In this figure, PRVs are considered redeemed if FDA has completed review of the drug application for which they were redeemed or if the company has made public statements regarding its redemption. Additional PRV redemptions, if any, may not be reported in this figure.

The 16 PRVs were redeemed by 10 different drug sponsors.²⁹ Twelve of the 16 redeemed PRVs were purchased and redeemed by a drug sponsor different from the original PRV awardee.³⁰ All 16 redeemed PRVs were redeemed within 4 years of FDA awarding them (see fig. 6).

²⁹Two drug sponsors redeemed two PRVs each, and two others redeemed three PRVs each; the remaining six drug sponsors each redeemed one PRV.

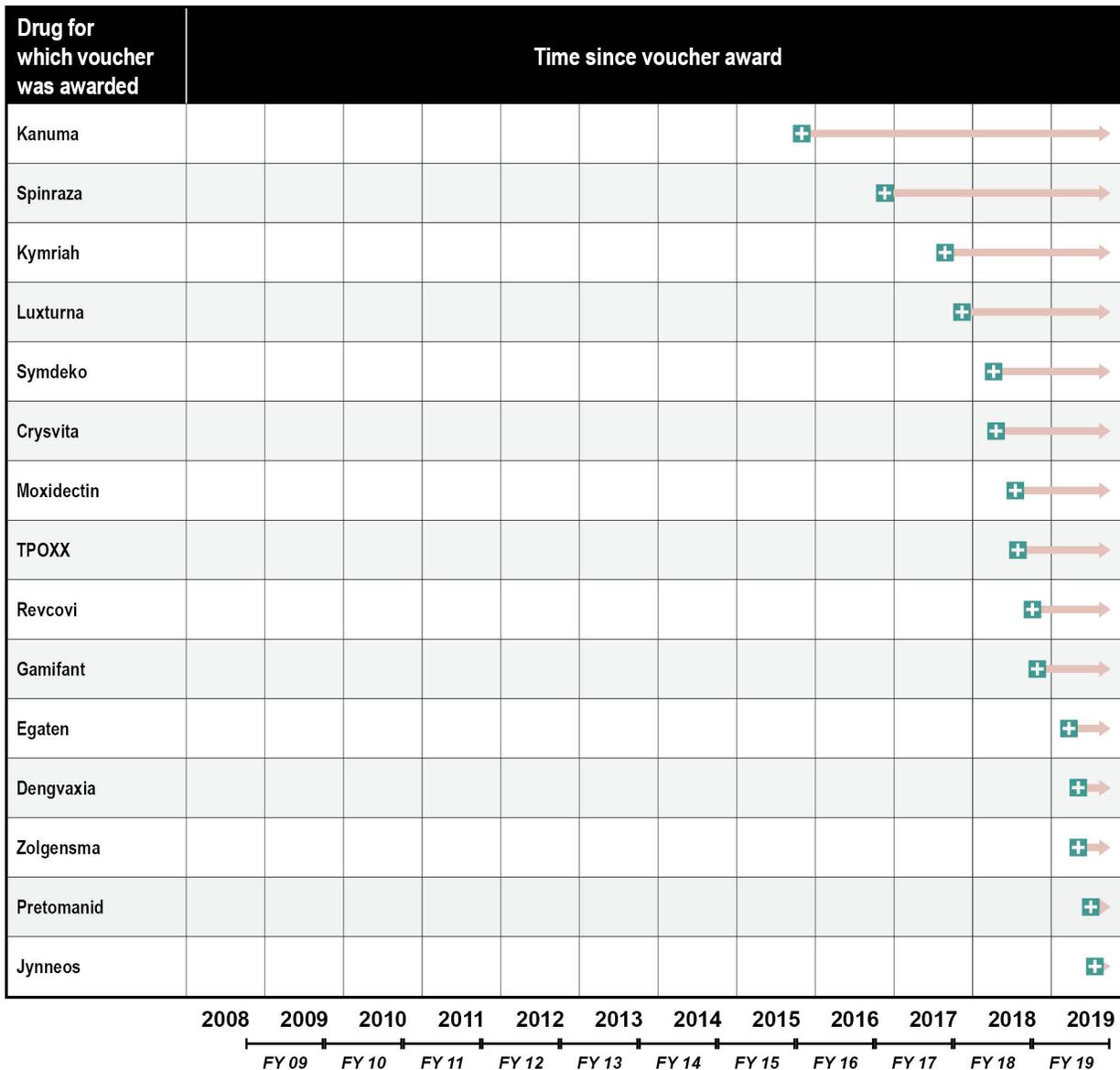
³⁰These 12 PRVs have been redeemed by eight different drug sponsors.

application for which they were redeemed or if the company has made public statements regarding its redemption. Additional PRV redemptions, if any, may not be reported in this figure.

Of the 15 PRVs that were not redeemed as of September 30, 2019, 12 were awarded in fiscal years 2018 or 2019, and one was awarded in early fiscal year 2016.³¹ (See fig. 7.)

³¹For reporting purposes, PRVs are considered redeemed if FDA has completed review of the drug application for which they were redeemed or if the company has made public statements regarding its redemption. As a result, some PRVs in this report may have been redeemed, but redemption information is not publicly available.

Figure 7: Timespans of Unredeemed Priority Review Vouchers (PRV), by Drug, as of September 30, 2019



+ Date PRV was awarded **→** Timespan after PRV award and not yet redeemed as of September 30, 2019

Source: GAO analysis of Food and Drug Administration (FDA) data and publicly available information. | GAO-20-251

Notes: The drug sponsor awarded the PRV can use the PRV on a future drug or sell it to be redeemed by another drug sponsor. For this figure, PRVs are considered redeemed if FDA has completed review of the drug application for which they were redeemed or if the company has made public statements regarding its redemption. As a result, some PRVs in this figure may have been redeemed, but redemption information is not publicly available.

Drug sponsors we contacted told us that decisions on when to redeem PRVs are largely strategic and take into consideration their drug development pipeline and market competition. For example, three of the drug sponsors told us they might choose to redeem a PRV to help a drug reach the market faster than a competitor's drug, and two drug sponsors told us they may hold a PRV to use to obtain priority review for a particular drug that is in development. Another drug sponsor told us it considers the likelihood of a drug receiving approval from FDA when deciding when to use a PRV (since the PRV only affects the time frames for FDA's review and does not guarantee approval), and if a drug in its pipeline could receive priority review from FDA on its own merit.

Almost half of the awarded PRVs had not been redeemed as of the end of fiscal year 2019, which may affect FDA's ability to forecast resources needed in the future. In 2016, we reported that FDA told us that the rare pediatric disease PRV program placed a substantial strain on its workload, explaining that performing a priority review on a drug that would otherwise merit a standard review requires the agency to conduct significant work in a compressed time frame.³² Between fiscal years 2011 and 2018, PRV redemptions have accounted for less than 1 percent of FDA's reviews in any given year, according to FDA.³³ While FDA receives 90 days' notice of a PRV redemption, the notice period may not be enough time to ensure the appropriate staff are available to review a drug application that the agency does not consider to be a public health priority, according to FDA. However, one researcher noted that this uncertainty exists for all drug applications, as FDA cannot know in a given year how many drug applications will be submitted in any particular therapeutic area or how many of these applications will qualify for priority review. Furthermore, two drug sponsors, one researcher, and one stakeholder we spoke with noted that FDA collects additional user fees for PRV redemptions specifically to support the priority review for a drug that would not normally qualify for one. Since fiscal year 2011, FDA has

³²GAO-16-319, 14.

³³These include reviews of all original new drug applications, biologics license applications, and efficacy supplements. PRV redemptions accounted for 1.4 percent of all priority reviews conducted in fiscal years 2011 through 2018, according to FDA. Data for fiscal year 2019 were not available at the time of our analysis.

collected almost \$44 million in PRV user fees for the 16 redeemed PRVs.³⁴

FDA does not track the resources it uses specifically for the PRV programs, so the agency cannot determine if the PRV user fees paid when PRVs are redeemed cover the associated costs. According to FDA, the agency cannot anticipate the therapeutic area for which a PRV will be redeemed, so PRV user fees may not ameliorate the effect of PRV redemptions on the review divisions or provide for rapid hiring of additional review staff with relevant experience and technical expertise. FDA officials told us that each new PRV program—and changes made to existing PRV programs—requires additional resources to implement. The agency reports that the services of over 11 offices within FDA are required to work on some aspect of the PRV programs, which may at times require FDA to shift resources from its public health priorities. According to FDA, the PRV programs also expend and divert agency resources to draft and revise PRV-related guidance; update webpages; research, draft, and publish notices and orders to add or decline to add diseases to the list of eligible tropical diseases; respond to inquiries from sponsors, potential sponsors, investors, attorneys, and other interested individuals; and respond to requests for a rare pediatric disease designation.

³⁴Since fiscal year 2011, the user fees, set annually by FDA, have ranged from \$2.33 million to \$5.28 million. To redeem a PRV, a drug sponsor pays the PRV user fee in addition to other user fees required for all drug applications.

The Few Studies That Examined PRV Programs Found Little or No Effect on Drug Development; Improvements and Alternatives Were Suggested

The Few Studies Examining PRV Programs Found Little or No Effect on Drug Development and Views of the Programs Are Mixed

Our literature review found three studies—one for each of the PRV programs—that examined and drew conclusions about how PRV programs affect drug development; of these, one study found evidence of an effect of a PRV program on drug development.³⁵ Specifically, it found that drugs to treat rare pediatric diseases, which could be eligible for a rare pediatric disease PRV, were more likely to advance from phase I to phase II clinical trials when compared to rare adult disease drugs.³⁶ The studies examining the other two PRV programs did not find an effect on drug development.

- **Rare pediatric disease PRV program.** A 2019 study found that the rare pediatric disease PRV program was not associated with an increase in the number or rate of new pediatric disease drugs that started or completed clinical trials. However, the study found that, after the creation of the rare pediatric disease PRV program, drugs the study authors determined could be eligible for a rare pediatric

³⁵One additional 2016 study we found concluded that the PRV programs appear to be on track to stimulate drug development, but more time was needed before a conclusion could be made on whether the programs have achieved their goals because of the long drug development cycle. See C. Bialas, E. Higbee-Dempsey, C. Y. Chen, C. Ward, O.A. Marcos-Contreras, D. Mulreany, A.B. Reitz, and D.M. Gross, “Analyzing the FDA Priority Review Voucher Program’s Stimulation of Research and Public Health Impact,” *Technology Transfer and Entrepreneurship*, vol. 3, no 2 (2016).

³⁶Clinical trials are designed to evaluate and test new interventions, such as medications. Clinical trials are generally conducted in three phases, with a fourth phase for some drugs occurring after approval, and each phase has a different purpose. See 21 C.F.R. §§ 312.21 and 312.85 (2019).

disease PRV were more likely to advance from phase I to phase II clinical trials compared to rare adult disease drugs, which are not eligible for a PRV under this program. Additionally, the study found the time it took for drugs to progress to the next stage of development was shorter among drugs eligible for a rare pediatric disease PRV compared to drugs for rare adult diseases, across all three phases of clinical development.³⁷

- **Tropical diseases PRV program.** A 2017 study found that this PRV program was not associated with an increase in tropical disease drugs starting clinical testing. The study found the proportion of tropical disease drugs among all drugs in development decreased slightly after the PRV program was created. Study authors suggested the relatively small number of approved tropical disease products in the last decade indicates the PRV program did not serve as a stimulus for completing late-stage drug development.³⁸
- **Medical countermeasure PRV program.** A 2018 study reported that 25 of 26 medical countermeasures undergoing clinical trials received direct or indirect public support, such as funding from the Department of Defense. Authors stated that, given the extent to which development of medical countermeasures already occurs via direct or indirect federal funding, alternatives other than the PRV program could better stimulate development of medical countermeasures.³⁹

While the few studies of the PRV program found little to no effect on drug development, the seven drug sponsors we contacted told us the PRV programs were an incentive—that is, a factor in their decisionmaking—for drug development. In contrast, the seven researchers and seven

³⁷T. Hwang, F. Bourgeois, J.M. Franklin, and A.S. Kesselheim, “Impact Of The Priority Review Voucher Program On Drug Development For Rare Pediatric Diseases,” *Health Affairs*, vol. 38, no 2 (2019).

³⁸N. Jain, T. Hwang, J.M. Franklin, and A.S. Kesselheim, “Association of the Priority Review Voucher with Neglected Tropical Disease Drug and Vaccine Development,” *JAMA*, vol. 318, no. 4 (2017). The study found that the tropical disease PRV program was not associated with an increase in innovative, early-stage development for neglected tropical disease drugs starting clinical testing. While this study examined new drugs for neglected tropical diseases entering phase I clinical trials before and after the creation of the tropical disease PRV program, it did not examine whether PRVs encouraged companies with drugs already in development into phase II and phase III clinical trials.

³⁹M.S. Sinha, N. Jain, T. Hwang, and A.S. Kesselheim, “Expansion of the Priority Review Voucher Program under the 21st Century Cures Act: Implications for Innovation and Public Health,” *American Journal of Law and Medicine*, vol. 44 (2018).

stakeholders we contacted reported mixed views of the PRV programs as an incentive for drug development.

- **Drug sponsors.** All seven drug sponsors told us the PRV programs were a factor in drug development decisions—six sponsors said it was one of a number of factors, and one sponsor said it was pivotal in its development of a drug. For example, three drug sponsors told us PRVs were important to help fund drug development and one of these drug sponsors told us the PRV program supported its decision to move a drug already under development to market. Four drug sponsors told us PRV programs may be a more significant incentive for small drug sponsors, with one small, nonprofit drug sponsor noting that it entirely relied on the profits from the sale of its PRV to ensure its drug would become available to those who need it. Additional factors drug sponsors reported considering included whether the sponsor has a drug in their development pipeline that could particularly benefit from a PRV, and whether its drug development program has public financial support, such as direct federal funding.
- **Researchers.** The seven researchers reported mixed views of the PRV programs as an incentive for drug development, and their perceptions of the three programs varied. For example, when asked to describe the incentive for drug development provided by the tropical disease PRV program, two researchers described it as “not significant,” and two researchers described it as “somewhat significant.” However, one of these researchers told us the tropical disease PRV program encouraged drug development, particularly for diseases such as tuberculosis and malaria for which a drug is potentially more commercially viable. Regarding the rare pediatric disease PRV program, three researchers told us they have heard anecdotally that the program is an incentive to develop or continue development of rare pediatric disease drugs. In contrast, one researcher told us many drug sponsors have received a rare pediatric disease PRV for drugs they would have produced anyway, and another told us he did not believe the rare pediatric disease PRV provided an adequate incentive for adding new drugs into a drug sponsor’s pipeline. Finally, four researchers told us it was too early to evaluate the medical countermeasure PRV program as an incentive.
- **Stakeholders.** The seven stakeholders also reported mixed views on the PRV programs as an incentive for drug development. For example, one stakeholder told us that drug sponsors have entered particular drug development areas because of the PRV programs, and the PRV program has been pivotal to the financial planning of small drug sponsors working in the medical countermeasures and rare

pediatric disease spaces. In contrast, two other stakeholders told us the PRV programs are an incentive to obtain FDA approval for a drug that has already been developed and marketed outside of the United States but are not an incentive for developing new drugs.⁴⁰ One of these stakeholders and an additional stakeholder also noted that PRVs are often a source of additional revenue to drug sponsors that would have developed their PRV drug anyway and did not need the PRV to finance drug development.

The number of PRVs awarded by FDA could influence the effectiveness of the PRV programs as incentives, according to several drug sponsors, researchers, and stakeholders we contacted. Specifically, some indicated that the potential revenue from the sale of a PRV could decline if more PRVs are awarded, and there is an increased supply of PRVs available for sale. Specific comments included the following:

- One drug sponsor told us that, while the number of PRVs on the market was a concern, they have remained valuable. Another drug sponsor told us it was not concerned with the relative value of PRVs, because it did not plan to sell its remaining PRVs and would purchase more in the future if PRVs would benefit drugs in its pipeline.
- One researcher told us lower prices for PRVs merited concern, because the PRV alone might not be sufficient to motivate drug development. The researcher indicated that a drug would also need either sufficient sales or additional government incentives.
- Two stakeholders told us the sales prices of PRVs (and potential revenue from selling them) might be more of a concern for small drug sponsors than large drug sponsors, as these stakeholders told us small drug sponsors are more likely to sell their PRV instead of using it for another drug in their portfolio.

Drug sponsors, researchers, and stakeholders we contacted also reported mixed views on whether the rare pediatric disease and medical countermeasure PRV programs—set to expire by 2022 and 2023,

⁴⁰To qualify for the tropical disease PRV program, applications must contain reports of one or more new clinical investigations (other than bioavailability studies) that are essential to the approval of the application and conducted or sponsored by the sponsor, and an attestation from the sponsor that such reports were not submitted as part of an application for marketing approval or licensure by a regulatory authority in India, Brazil, Thailand, or any country that is a member of the Pharmaceutical Inspection Convention or the Pharmaceutical Inspection Cooperation Scheme prior to September 27, 2007. This may preclude certain drugs that were developed and marketed outside of the United States prior to 2007 from tropical disease PRV program eligibility.

respectively—should be reauthorized. While FDA officials reported that, as of April 2019, the agency does not have a position on the reauthorization of these two PRV programs, drug sponsors generally indicated support for their reauthorizations, with some noting that PRV program expirations may negatively affect overall drug development and the willingness of drug sponsors to work in these areas. The researchers we contacted offered mixed opinions on reauthorization. For example, one recommended reauthorizing both PRV programs, but indicated that his opinion could change if a better incentive was developed. In contrast, another researcher supported the expiration of these two programs, noting that their expiration could ultimately raise the potential revenue from the sale of an available PRV and could also make the tropical disease PRV program, which does not require reauthorization, more popular to encourage drug development. Most stakeholders we contacted did not offer a clear opinion on reauthorization; those that did generally supported reauthorization.

Drug Sponsors, Researchers, and Stakeholders Suggested Improvements and Alternatives to the PRV Programs

Drug sponsors, researchers, and stakeholders we contacted suggested several improvements to the PRV programs, including those described below.

- **Require innovation for PRV-eligible drugs.** Two researchers and two stakeholders noted that the PRV programs, particularly the tropical disease PRV program, have been criticized for not providing incentives for innovation and suggested PRV awards be limited to drugs new to the global market.⁴¹ Currently, drug sponsors can receive a PRV for a drug that has already been developed and marketed outside of the United States, but which qualifies for a PRV because the drug has not been approved for marketing in the United States.⁴² One researcher suggested the federal government should not provide an incentive, like a PRV, for drugs already in existence outside of the United States, for which most research and development was already completed. However, one drug sponsor told us that requiring a tropical disease drug to be approved first in the United States to qualify for a PRV would delay entry of the drug into

⁴¹We did not determine the extent to which awarded PRVs were for drugs that were not new to the global market.

⁴²A drug may be disqualified if its active ingredient has been previously approved by FDA in another drug application. FDA does not evaluate whether the active ingredient is in use outside of the United States.

the international markets that need it the most. Additionally, two stakeholders told us that drugs that have already been developed may have significant benefits to patients when combined or used to treat other diseases.

- **Require drug sponsors to guarantee access to PRV-eligible drugs.** One researcher and two stakeholders suggested drug sponsors submit an access plan to help ensure the drug reaches the populations in need of the treatment, and one drug sponsor suggested they supply at cost the drugs for which the PRV was awarded. One of these stakeholders noted that a weakness of the PRV program is that drug sponsors awarded a PRV have no obligation to make the approved drug available at an affordable price. It suggested that requiring an access plan may result in drugs for which a PRV was awarded being more available and accessible to the populations that need them. However, three stakeholders noted that FDA may not have the resources or authority to enforce such access commitments.
- **Limit PRVs to drug sponsors with financial need.** One drug sponsor and one researcher suggested awarding a PRV only to drug sponsors that financially require it to develop their drug, such as a nonprofit organization that must leverage potential revenue from the PRV to help offset drug development costs.
- **Make administrative changes.** One drug sponsor told us FDA's process for determining the list of tropical diseases eligible for a PRV was not transparent and wanted clarification on FDA's timeline for editing this list.⁴³ Another drug sponsor told us it wanted clarification on whether a drug would merit priority review on its own, so the sponsor could determine whether to redeem a PRV for that drug.⁴⁴

In addition to suggesting improvements to the PRV programs, drug sponsors, researchers, and stakeholders we contacted, as well as our

⁴³FDA maintains a public docket in which interested parties can submit suggestions for the list of tropical diseases that qualify for a PRV. According to FDA's website, FDA reviews this public docket on an ongoing basis and intends to publish its decisions in the Federal Register four times per year.

⁴⁴This drug sponsor also suggested allowing user fees for rare pediatric disease PRV redemptions to be paid upon the sponsor's submission of the PRV drug to FDA for review—as they are for the tropical disease and medical countermeasure programs—rather than when the drug sponsor notifies FDA of its intent to use the PRV. It suggested this change would prevent drug sponsors from losing their PRV user fees if they do not submit the drug application after notifying FDA it had intended to use the PRV. According to FDA, this change would require a statutory amendment.

literature review, identified potential alternatives to the PRV programs that provide incentives for drug development (see table 2).

Table 2: Potential Alternative Incentives for Drug Development According to Selected Drug Sponsors, Researchers, Stakeholders, and Literature

	Incentive	Description
Push incentives Incentives that reduce research and development costs to drug sponsors	Tax credits on research and development	Credits allowing pharmaceutical companies to deduct a percentage of qualifying research and development costs from the company's tax liability
	Direct federal funding or grant	Subsidies offered to organizations for the research and development of novel drugs
	Product development partnerships or public-private partnership	A collaborative agreement to share development risk and reward between a public or quasi-public organization and one or more private developers
Pull incentives Incentives that increase the market reward perceived by drug sponsors as they embark on a research and development program	Market exclusivity ^a	Certain delays and prohibitions on approval of competitor drugs available upon approval of a drug
	Advanced market commitment	An agreement to fully or partially finance the purchase of a specified amount of a medical product at a pre-arranged price, prior to its development
	Prize for successful research	A monetary reward that encourages the development of drugs in a particular area
	Patent extension	An extension of a property right granted by the United States Patent and Trademark Office anytime during the development of a drug

Source: GAO analysis of interviews conducted and literature reviewed. | GAO-20-251

Notes: This table presents information on potential alternative incentives to the priority review voucher programs to encourage development of drugs for tropical diseases, rare pediatric diseases, and medical countermeasures. These alternatives were identified by drug sponsors, researchers, and stakeholders we contacted, as well as in studies we reviewed.

^aTwo drug sponsors, a researcher, and two stakeholders referred to transferrable exclusivity, in which market exclusivity rights can be transferred to another drug in the sponsor's portfolio.

Agency Comments

We provided a draft of this report to HHS for review and comment. HHS provided technical comments, which we incorporated as appropriate.

We are sending copies of this report to the appropriate congressional committees, the Secretary of Health and Human Services, and other interested parties. In addition, the report is available at no charge on GAO's website at <http://www.gao.gov/>.

If you or your staff have any questions about this report, please contact me at (202) 512-7114 or dickenj@gao.gov. Contact points for our Office of Congressional Relations and Office of Public Affairs can be found on the last page of this report. Other major contributors to this report are listed in appendix IV.



John E. Dicken
Director, Health Care

Appendix I: Priority Review Vouchers (PRV) Awarded by the Food and Drug Administration

Table 3: Characteristics and Transfer Status of Awarded Priority Review Vouchers (PRV) as of September 30, 2019

Date PRV was awarded	Drug name Drug sponsor	Indication	Transfer status	Sale date	PRV purchaser ^a	Sales price (dollars in millions)
Tropical disease PRVs						
April 2009	Coartem Novartis Pharmaceuticals Corporation	Treatment of acute, uncomplicated malaria infections	X	—	—	—
December 2012	Sirturo Janssen Pharmaceutical Companies	Treatment of pulmonary multi-drug resistant tuberculosis	X	—	—	—
March 2014	Impavido Paladin Therapeutics, Inc. ^b	Treatment of various leishmaniasis strains	✓	November 2014	Gilead Sciences, Inc.	125
June 2016	Vaxchora Pax Vax Bermuda Ltd.	Indicated for use as a cholera vaccine for travelers	✓	June 2016	Gilead Sciences, Inc. ^c	290
August 2017	Benznidazole Chemo Research S.L.	Treatment of Chagas disease	✓	Unknown	Novo Nordisk Inc.	Unknown
June 2018	Moxidectin Medicines Development for Global Health	Treatment of onchocerciasis, also known as river blindness	✓	May 2019	Novo Nordisk Inc.	Unknown
July 2018	Krintafel GlaxoSmithKline	To prevent relapse of Plasmodium vivax malaria	X	—	—	—
February 2019	Egaten Novartis Pharmaceuticals Corporation	Treatment of fascioliasis	X	—	—	—
May 2019	Dengvaxia Sanofi	Prevention of dengue disease	X	—	—	—
August 2019	Pretomanid The Global Alliance for TB Drug Development (TB Alliance)	Treatment of multidrug resistant pulmonary tuberculosis	X	—	—	—
Rare pediatric disease PRVs						
February 2014	Vimizim BioMarin Pharmaceutical Inc.	Treatment of mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome)	✓	July 2014 ^d	Sanofi	67.5

**Appendix I: Priority Review Vouchers (PRV)
Awarded by the Food and Drug Administration**

Date PRV was awarded	Drug name Drug sponsor	Indication	Transfer status	Sale date	PRV purchaser^a	Sales price (dollars in millions)
March 2015	Unituxin United Therapeutics Corporation	Treatment of children with high risk neuroblastoma	✓	August 2015	AbbVie Inc.	350
March 2015	Cholbam Asklepiion Pharmaceuticals, LLC	Treatment of (1) bile acid synthesis disorders due to single enzyme defects, and (2) peroxisomal disorders	✓	May 2015	Sanofi ^e	245
September 2015	Xuriden Wellstat Therapeutics Corporation	Treatment of hereditary orotic aciduria	✓	September 2015	Teva Pharmaceutical USA, Inc. ^f	Unknown
October 2015	Strensiq Alexion Pharmaceuticals Inc.	Treatment of hypophosphatasia (HPP)	X	—	—	—
December 2015	Kanuma Alexion Pharmaceuticals Inc.	Treatment of Lysosomal Acid Lipase (LAL) deficiency	X	—	—	—
September 2016	Exondys 51 Sarepta Therapeutics, Inc.	Treatment of Duchenne muscular dystrophy (DMD) in patients with a DMD gene mutation	✓	February 2017 ^g	Gilead Sciences, Inc.	125
December 2016	Spinraza Biogen, Inc.	Treatment of spinal muscular atrophy	X	—	—	—
February 2017	Emflaza Marathon Pharmaceuticals, LLC	Treatment of Duchenne muscular dystrophy (DMD)	✓	Between February and June 2017	ViiV Healthcare Company ^h	130
April 2017	Brineura BioMarin Pharmaceutical Inc.	Treatment of tripeptidyl peptidase 1 (TPP1) deficiency (Batten disease)	✓	November 2017	Novartis Pharmaceuticals Corporation ⁱ	125
August 2017	Kymriah Novartis Pharmaceuticals Corporation	Treatment of B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse	X	—	—	—
November 2017	Mepsevii Ultragenyx Pharmaceutical Inc.	Treatment of mucopolysaccharidosis type VII (MPS VII, Sly syndrome)	✓	December 2017	Novartis Pharmaceuticals Corporation	130
December 2017	Luxturna Spark Therapeutics, Inc.	Treatment of biallelic RPE65 mutation-associated retinal dystrophy	✓	April 2018	Jazz Pharmaceuticals plc	110

**Appendix I: Priority Review Vouchers (PRV)
Awarded by the Food and Drug Administration**

Date PRV was awarded	Drug name Drug sponsor	Indication	Transfer status	Sale date	PRV purchaser ^a	Sales price (dollars in millions)
February 2018 ^j	Symdeko Vertex Pharmaceuticals Inc.	Treatment of cystic fibrosis with certain mutations	X	—	—	—
April 2018	Crysvita Ultragenyx Pharmaceutical Inc.	Treatment of X-linked hypophosphatemia (XLH)	✓	June 2018 ^k	Gilead Sciences, Inc.	80.6
June 2018	Epidiolex GW Research, Ltd.	Treatment of seizures associated with Lennox Gastaut-Syndrome and Dravet syndrome	✓	April 2019	Biohaven Pharmaceuticals, Inc. ^l	105
October 2018	Revcovi Leadiant Biosciences, Inc.	Treatment of adenosine deaminase-severe combined immunodeficiency (ADA-SCID)	X	—	—	—
November 2018	Gamifant Novimmune S.A.	Treatment of primary hemophagocytic lymphohistiocytosis (HLH)	✓	July 2019	AstraZeneca ^m	95
May 2019	Zolgensma Avexis, Inc.	Treatment of pediatric patients with spinal muscular atrophy (SMA)	X	—	—	—
Medical countermeasure PRV						
July 2018	TPOXX SIGA Technologies, Inc.	Treatment of smallpox disease	✓	November 2018	Eli Lilly and Company	80
September 2019	Jynneos Bavarian Nordic A/S	Prevention of smallpox and monkeypox	X	—	—	—

Legend: ✓ = transferred from original drug sponsor; X = no public announcement of transfer; — = not applicable.

Source: GAO analysis of Food and Drug Administration (FDA) information and publicly available accounts of PRV sales information. | GAO-20-251

Notes: This table presents known award and transfer information for PRVs as of Sept. 30, 2019. FDA is notified of rare pediatric disease PRV sales when a PRV is transferred to another drug sponsor; however, the agency may only learn of tropical disease PRV and medical countermeasure PRV sales or transfers when a PRV is redeemed by another drug sponsor. As a result, FDA may not have information on these PRV sales or transfers if the PRVs have not yet been redeemed. Additionally, PRV sales prices are not reported to FDA. A complete list of indications is not included for the drugs in the table; please refer to drug labeling for complete information.

^aPRV purchaser indicates the PRV owner as of Sept. 30, 2019.

^bPaladin Therapeutics, Inc. submitted a new drug application for Impavido in April 2013. In February 2014, Endo Health Solutions, Inc. acquired Paladin Therapeutics, Inc. From this transaction, Knight Therapeutics, Inc., a subsidiary of Paladin Therapeutics, formed as a new independent company. Knight Therapeutics, Inc. subsequently received rights to Impavido and the awarded PRV.

^cPaxVax Bermuda Ltd. announced that it sold its PRV in 2016 to an undisclosed purchaser. In a Securities and Exchange Commission filing, the company disclosed that it sold its PRV for \$290 million in 2016. Gilead Sciences, Inc. indicates in Securities and Exchange Commission filings that it purchased a PRV in the second quarter of 2016, meaning sometime between April 1 and June 30, 2016.

**Appendix I: Priority Review Vouchers (PRV)
Awarded by the Food and Drug Administration**

^dIn a press release, BioMarin Pharmaceutical Inc. announced that it had sold a PRV for \$67.5 million.

^eIn January 2015, Retrophin, Inc. entered into an agreement with Asklepios Pharmaceuticals, LLC to acquire the rights and ownership of assets related to cholic acid, the active ingredient in Cholbam, upon FDA approval. The drug was approved as Cholbam in March 2015. In May 2015, Retrophin, Inc. announced that it had sold the PRV to Sanofi for \$245 million.

^fWellstat Therapeutics Corporation announced that it had sold the PRV to AstraZeneca, but it did not disclose the sales price. In a Securities and Exchange Commission filing, Teva announced that it had redeemed a PRV for fremanezumab, approved as Ajoovy. Teva reported purchasing the PRV for \$150 million but did not identify the seller. It is unknown if the PRV was transferred additional times before it was redeemed by Teva.

^gSarepta Therapeutics, Inc. disclosed in a press release that it sold a PRV for \$125 million.

^hViiV Healthcare Company announced in a press release that it used a PRV it purchased for \$130 million when it redeemed a PRV for the drug Juluca.

ⁱBioMarin Pharmaceutical Inc. announced in a press release that it sold the PRV for \$125 million.

^jFDA initially declined to award a rare pediatric disease PRV when Symdeko was approved but later determined that the PRV should have been granted. FDA considers February 2018 the date the PRV was awarded, as it was the date the PRV was earned by the sponsor.

^kUltragenyx sold the PRV awarded for Crystiva for \$80.6 million in June 2018, according to a Securities and Exchange Commission filing.

^lGW Research, Ltd. announced in a March 2019 press release that it sold its PRV for \$105 million. On the same day, Biohaven Pharmaceuticals, Inc. announced it purchased a PRV for \$105 million.

^mIn July 2019, Sobi announced that it gained access to the PRV from Novimmune SA as part of an acquisition of Gamifant-related assets. In August 2019, Sobi announced that it had sold the PRV to AstraZenca for \$95 million.

Appendix II: Redeemed Priority Review Vouchers (PRV)

Table 4: Characteristics of Redeemed Priority Review Vouchers (PRV) as of September 30, 2019

Redemption date	Redeeming drug sponsor	Drug and indication	Date original PRV was awarded	Drug sponsor originally awarded PRV
Tropical diseases PRVs				
February 2011	Novartis Pharmaceuticals Corporation	Ilaris Treatment of gouty arthritis	April 2009	Novartis Pharmaceuticals Corporation
July 2015	Gilead Sciences, Inc.	Odefsey Treatment of HIV-1 infection	March 2014	Paladin Therapeutics, Inc.
November 2016	Janssen Pharmaceutical Companies	Tremfya Treatment of adult patients with moderate-to-severe plaque psoriasis	December 2012	Janssen Pharmaceutical Companies
June 2017	Gilead Sciences, Inc.	Biktarvy Treatment of HIV-1 infection	June 2016	Pax Vax Bermuda Ltd.
October 2018	ViiV Healthcare Company ^a	Dovato Treatment of HIV-1 infection	July 2018	GlaxoSmithKline
March 2019	Novo Nordisk Inc.	Rybelsus An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	August 2017	Chemo Research, S.L.
Rare pediatric disease PRVs				
November 2014	Sanofi	Praluent A lipid altering agent	February 2014	BioMarin Pharmaceutical Inc.
December 2015	Sanofi	Soliqua Long-acting human insulin analog	March 2015	Asklepion Pharmaceuticals, LLC
June 2017	ViiV Healthcare Company	Juluca Treatment of HIV-1 infection	February 2017	Marathon Pharmaceuticals, LLC
October 2017	Teva Pharmaceuticals USA, Inc.	Ajovy Preventive treatment of migraine in adults	September 2015	Wellstat Therapeutics Corporation
March 2018	Novartis Pharmaceuticals Corporation	Mayzent Treatment of relapsing forms of multiple sclerosis (MS)	April 2017	BioMarin Pharmaceutical Inc.
June 2018	Alexion Pharmaceuticals Inc.	Ultomiris Treatment for adults with paroxysmal nocturnal hemoglobinuria	October 2015	Alexion Pharmaceuticals Inc.
December 2018	AbbVie Inc.	Rinvoq Treatment of adults with moderately to severely active rheumatoid arthritis	March 2015	United Therapeutics Corporation

Appendix II: Redeemed Priority Review Vouchers (PRV)

Redemption date	Redeeming drug sponsor	Drug and indication	Date original PRV was awarded	Drug sponsor originally awarded PRV
April 2019	Gilead Sciences, Inc.	Descovy To reduce the risk of sexually acquired HIV-1 infection among individuals who are HIV-negative and at risk for HIV	September 2016	Sarepta Therapeutics, Inc.
February 2019	Novartis Pharmaceuticals Corporation	Beovu For the treatment of wet age-related macular degeneration (AMD)	November 2017	Ultragenyx Pharmaceutical Inc.
April to June 2019	Biohaven Pharmaceuticals, Inc.	rimegepant Zydis orally dissolving tablets (ODT) For acute and preventive treatment of migraine	June 2018	GW Research, Ltd.

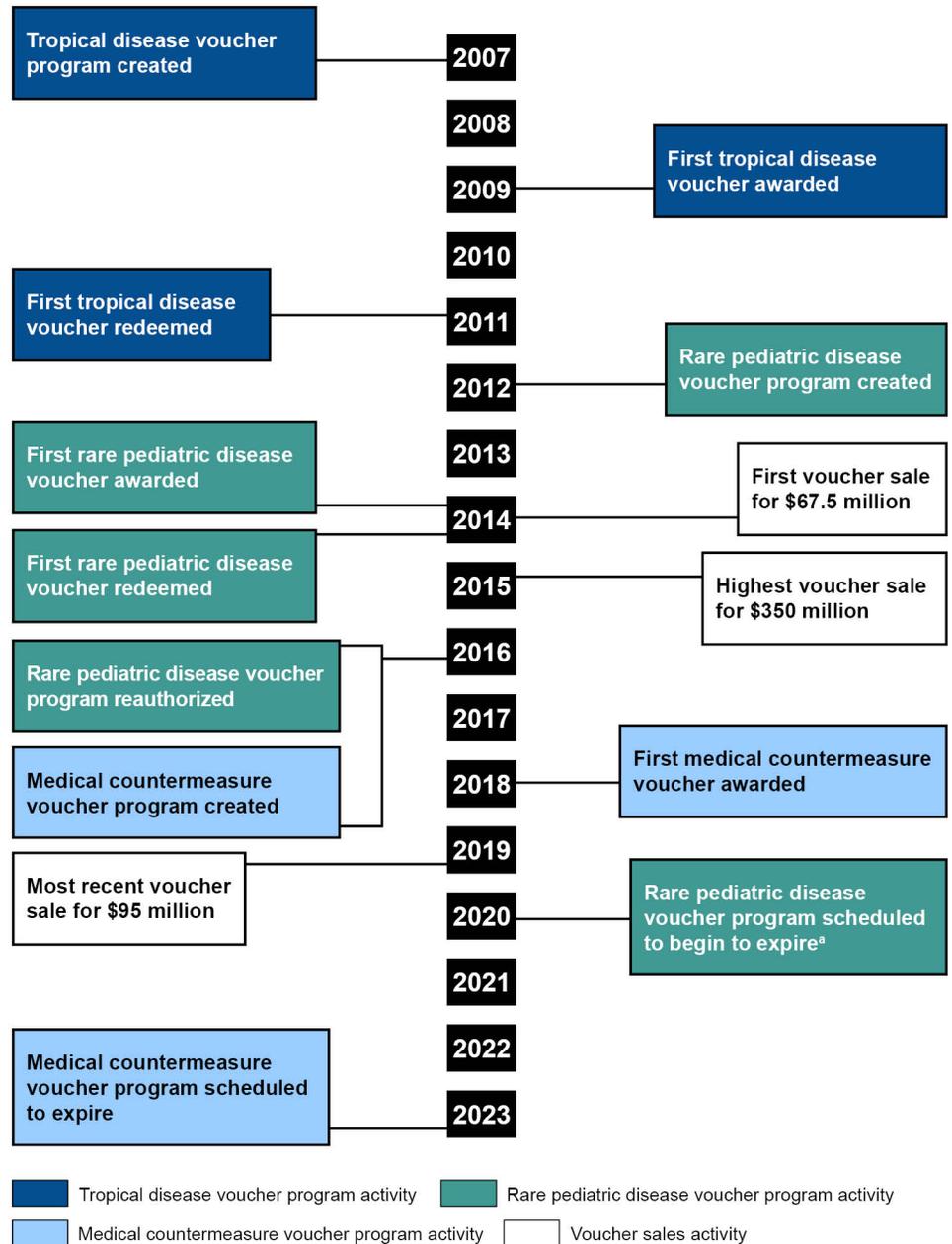
Source: GAO analysis of Food and Drug Administration (FDA) data and publicly available information. | GAO-20-251

Note: For this table, PRVs are considered redeemed if FDA has completed review of the drug application for which they were redeemed or if the company has made public statements regarding its redemption. Additional PRV redemptions, if any, may not be reported in this table. A complete list of indications is not included for the drugs in the table; please refer to drug labeling for complete information.

^aViiV Healthcare is majority owned by GlaxoSmithKline.

Appendix III: Key Milestones of the Priority Review Voucher Programs

Figure 8: Key Milestones of the Priority Review Voucher Programs



Source: GAO analysis of priority review voucher related legislation, Food and Drug Administration (FDA) data on awarded and redeemed priority review vouchers, and publicly available information on priority review voucher sales. | GAO-20-251

*FDA may not award any rare pediatric disease priority review vouchers after September 30, 2020, unless the drug has received a rare pediatric disease designation by that date, and FDA has approved the drug application by September 30, 2022.

Appendix IV: GAO Contact and Staff Acknowledgments

GAO Contact

John E. Dicken at (202) 512-7114 or dickenj@gao.gov

Staff Acknowledgments

In addition to the contact named above, Kim Yamane (Assistant Director), Erin C. Henderson (Analyst-in-Charge), Kaitlin Farquharson, Laurie Pachter, Vikki Porter, Helen Sauer, Meghan Shrewsbury, and Merrile Sing made key contributions to this report. Also contributing were Leia Dickerson, Hayden Huang, and Yesook Merrill.

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