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Buying and Selling Prioritized Regulatory Review: The Market for Priority Review Vouchers as Quasi-Intellectual Property

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ABSTRACT

Drug development is an expensive endeavor, and for decades, drug companies favored investing in drugs to treat diseases with commercially attractive markets rather than rare and neglected diseases. The U.S. Food and Drug Administration oversees numerous programs intended to incentivize the development of therapies for rare and neglected diseases, for example, by granting expedited review of applications and regulatory exclusivity periods. One such incentive program is the priority review voucher program. A priority review voucher may be awarded upon the approval of a treatment for a rare pediatric disease, a neglected tropical disease, or a bioterrorism threat. The priority review voucher entitles its owner to priority review of a subsequent application and is unique in that it does not attach to a particular product or sponsor, unlike expedited review and regulatory exclusivity. A priority review voucher is salable and transferable, much like ordinary property, and thus may be regarded and valued as quasi-intellectual property. This paper provides an analysis of the priority review vouchers that have been issued, transferred, and redeemed to date, as well as trends in the market for priority review vouchers.

I. BACKGROUND: DRUG DEVELOPMENT FOR RARE AND NEGLECTED DISEASES

Drug development is an expensive and time-consuming endeavor.[1] Substantial preclinical research is required to identify promising therapies. Of the promising therapies that advance to Phase I clinical trials, only one in 10 is approved by the U.S. Food and Drug Administration (FDA).[2] For particularly complex diseases, the success rate is even lower. For example, in the last two decades, the pharmaceutical industry has invested in 1,120 unique drugs to treat Alzheimer's disease, only four of which have been approved and marketed—a success rate of 0.4%.[3]

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[1] Dirk Calcoen et al., *What Does It Take To Produce A Breakthrough Drug*?, 14 NATURE REV. DRUG DISCOVERY 161 (2015).

[2] *Id.*

[3] *Id.*

According to the Pharmaceutical Research and Manufacturers of America (PhRMA), tens of thousands of molecules are studied in drug discovery and preclinical studies, each of which can span approximately three to six years.[4] A handful of those molecules advance to clinical trials, and it takes approximately six to seven years to complete Phase I, II, and III clinical trials. A drug company then submits a New Drug Application (NDA) or a Biologics License Application (BLA) for FDA review, which takes up to two years to complete. Once FDA has approved the drug, the company can begin large-scale manufacturing and marketing. The cost of developing a new drug is estimated to be $2.6 billion U.S. dollars (USD), according to the Tufts Center for the Study of Drug Development.[5]

At such staggering costs, companies generally assess disease prevalence, market size, and commercial potential to determine which drug programs to pursue. For example, does a company invest $2.6 billion USD in research and development to treat a widespread condition like cardiovascular disease (which affects 84 million people in the United States[6]), a rare disease like cystic fibrosis (which affects 30,000 people in the United States[7]), or a neglected tropical disease like dengue (which affects 100 million people in low-income regions of Africa, Asia, and South America[8])? For decades, companies favored investing in therapies with large market sizes in the developed world (and which were thus more likely to recoup research and development costs) to the exclusion of rare or neglected diseases. To incentivize investment in rare and neglected diseases, numerous government programs have been introduced in the United States.

II. EXPEDITED REVIEW PROGRAMS

FDA has several programs to facilitate the expedited review of certain NDAs and BLAs, including Priority Review, Fast Track, Breakthrough Therapy, and Accelerated Approval. Although expedited review programs are not restricted to rare and neglected diseases (for example, a common but deadly cancer with no available therapies may be eligible for expedited review), many rare and neglected disease therapies qualify for and benefit from expedited review.

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4 *Id.*

5 Rick Mullin, *Cost to Develop New Pharmaceutical Drug Now Exceeds $2.5B*, SCI. AM. (Nov. 24, 2014), https://www.scientificamerican.com/article/cost-to-develop-new-pharmaceutical-drug-now-exceeds-2-5b/ [https://perma.cc/9HS2-242Y].; *see also* Matthew Herper, *The Cost of Developing Drugs is Insane. That Paper That Says Otherwise is Insanely Bad,* FORBES, (Oct. 16, 2017, 10:58 AM), https://www.forbes.com/sites/matthewherper/2017/10/16/the-cost-of-developing-drugs-is-insane-a-paper-that-argued-otherwise-was-insanely-bad/#7a21578d2d45 [https://perma.cc/BM8Q-V6F5].

6 JOHNS HOPKINS MED., Health Library, Cardiovascular Diseases, *Cardiovascular Disease Statistics*, https://www.hopkinsmedicine.org/healthlibrary/conditions/cardiovascular_diseases/cardiovascular_disease_statistics_85,P00243 [https://perma.cc/XB5D-FVPW] (last visited May 10, 2018).

7 CYSTIC FIBROSIS FOUND., What is CF?, *About Cystic Fibrosis*, https://www.cff.org/What-is-CF/About-Cystic-Fibrosis [https://perma.cc/9C5Z-6DY9] (last visited May 10, 2018).

8 CTRS. FOR DISEASE CONTROL & PREVENTION, CDC A-Z Index, Dengue Fever, *Epidemiology*, https://www.cdc.gov/dengue/epidemiology/index.html [https://perma.cc/7TYK-2V3V] (last updated June 9, 2014).

A. Priority Review

Under the Prescription Drug User Fee Act (PDUFA) of 1992, FDA created a two-tiered system of review for drugs, standard review and priority review. For standard review, FDA's goal is to take action on an application within 10 months, but in practice FDA review can take up to 18 months.[9] A drug company may request priority review designation if its therapy treats a serious condition and would provide significantly improved safety or effectiveness, treats a qualified infectious disease, or if the application is a supplement that proposes a labeling change further to a pediatric study.[10] The request must be submitted with the original NDA or BLA or efficacy supplement. FDA responds to the request for priority review designation within 60 days of submission. Priority review designation "is intended to direct overall attention and resources to the evaluation of such applications" and shortens FDA action time to 6 months.[11]

B. Fast Track[12]

Fast Track is intended to fulfill unmet medical need by providing therapy where none exists or that is better than available treatment for serious diseases such as acquired immune deficiency syndrome (AIDS), Alzheimer's disease, and cancer.[13] A sponsor company may request Fast Track designation if its therapy is intended to treat a serious condition and data (clinical or nonclinical) demonstrate the potential to address an unmet need, or it is intended to treat a qualified infectious disease.[14] The request should preferably be submitted no later than the pre-NDA or pre-BLA meeting. FDA responds to the request for Fast Track designation within 60 days of submission.[15] Fast Track designation entitles the sponsor to more frequent meetings with FDA, more written communication from FDA, and rolling review of the sponsor's NDA or BLA instead of waiting until the application is complete.[16]

C. Breakthrough Therapy[17]

Breakthrough Therapy facilitates the review of a therapy that treats a serious disease and has "preliminary clinical evidence indicat[ing] that the drug may demonstrate substantial improvement over existing therapies."[18] A sponsor company may request Breakthrough Therapy designation if its therapy treats a serious condition and preliminary clinical evidence shows that the therapy may provide substantial

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9 David B. Ridley et al., *Developing Drugs for Developing Countries*, 25 HEALTH AFF. 313 (2006), https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.25.2.313 [https://perma.cc/S53V-WLWR].

10 FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS – DRUGS AND BIOLOGICS (May 2014), https://www.fda.gov/downloads/Drugs/Guidances/UCM358301.pdf [https://perma.cc/KV9M-A5ET].

11 *Id.* at 24.

12 *See* Federal Food, Drug, and Cosmetic Act § 506(b), 21 U.S.C. § 356(b) (2016).

13 *Id.*

14 *Id.*

15 *Id.*

16 *Id.*

17 *See* 21 U.S.C. § 356(a).

18 § 356(a)(1).

improvement on a clinically significant endpoint over available therapies.[19] The request should preferably be submitted no later than the end-of-Phase II meeting. FDA responds to the request for Fast Track designation within 60 days of submission.[20] Breakthrough Therapy designation entitles the sponsor to all of the Fast Track program features described above as well as intensive FDA guidance on efficient drug development starting as early as Phase I trials and FDA organizational commitment involving senior managers.

D. Accelerated Approval[21]

Accelerated Approval allows earlier approval of therapies to treat serious conditions by using a surrogate endpoint (e.g., a laboratory measurement or a radiographic image) that is not itself a measurable clinical benefit. A sponsor company may request Accelerated Approval designation if its therapy treats a serious condition, provides a meaningful advantage over available therapies, and shows a surrogate endpoint that is reasonably likely to predict clinical benefit (e.g., tumor shrinkage) or a clinical endpoint that is measured earlier than irreversible morbidity or mortality.[22] Accelerated Approval entitles the sponsor to approval based on a surrogate or intermediate clinical endpoint. There is no set timeline for when FDA responds to a request for Accelerated Approval, but the sponsor should preferably discuss the possibility of Accelerated Approval with FDA throughout development and trials.[23]

III. REGULATORY EXCLUSIVITY PROGRAMS

FDA regulates numerous exclusivities for pharmaceutical products, including orphan drug exclusivity, new chemical entity exclusivity, new clinical investigation exclusivity, pediatric exclusivity, first generic exclusivity, and biologics license application exclusivity. FDA regulatory exclusivity is intended "to promote a balance between new drug innovation and generic drug competition."[24] The length of regulatory exclusivity depends on the type of exclusivity and is separate from patent term exclusivity.

Regulatory exclusivity includes marketing exclusivity, which prevents others from receiving FDA permission to market its product, and data exclusivity, which prevents others from using an innovator company's clinical data, e.g., as the basis for the approval of a generic drug. Although a generic or biosimilar manufacturer is permitted to generate its own safety and efficacy data, this pathway is usually too lengthy and expensive to be attractive.[25]

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19 FOOD & DRUG ADMIN., *supra* note 10.

20 *Id.*

21 *See* 21 U.S.C. § 356(c).

22 *Id*.

23 *Id.*

24 *Patents and Exclusivity,* FDA/CDER SBIA CHRONICLES (Food & Drug Admin.) May 19, 2016, https://www.fda.gov/downloads/drugs/developmentapprovalprocess/smallbusinessassistance/ucm447307.pdf [https://perma.cc/KJ6M-GBYQ].

25 Robin Feldman, *Regulatory Property: The New IP*, 40 COLUM. J.L. & ARTS 53 (2016).

In 1983, Congress passed the Orphan Drug Act to provide special orphan status to products for the treatment of rare diseases.[26] The Orphan Drug Designation Program confers orphan status to therapies that treat rare diseases affecting fewer than 200,000 people in the United States, or diseases that affect more than 200,000 persons but are not expected to recover the costs of research and development.[27] Since 1983, over 600 therapies for rare diseases have been developed and marketed.[28] By contrast, from 1973 to 1983, only 10 therapies for rare diseases were developed and marketed.[29] Orphan designation entitles a sponsor company to seven years of regulatory exclusivity, tax credits, and an exemption from prescription drug user fee provisions.[30] During these seven years, FDA is prohibited from approving any applications for the same drug for the same orphan disease. Recently, the 2017 Tax Cuts and Jobs Act reduced the Orphan Drug Tax Credit by 50%,[31] with the National Organization for Rare Disorders contending that the change would "directly result in 33% fewer orphan drugs coming to market."[32]

A sponsor may apply for new chemical entity exclusivity if its drug contains a new chemical that is not a component of any other drug approved by the FDA. The duration of new chemical entity exclusivity is typically four or five years (depending on certain patent considerations under the Hatch-Waxman Act), during which time a generic drug manufacturer may not submit an application that relies upon the innovator company's safety and efficacy clinical data.

New clinical investigation exclusivity may be granted if the sponsor performs additional or follow-on clinical studies that are not bioavailability or bioequivalency studies. New clinical investigation exclusivity is three years, during which time FDA is prohibited from approving an application that relies on the sponsor's studies.

Pediatric exclusivity provides an additional six months of regulatory exclusivity if a sponsor has conducted and submitted pediatric studies. FDA may grant 180 days of exclusivity to the first sponsor to submit an abbreviated new drug application (ANDA).

Although the term "drug" is often broadly used across the pharmaceutical industry (and herein) to refer to both small molecule drugs and large molecule biologics,[33] a discussion of regulatory exclusivity requires precise terminology. Most therapies on the market today are so-called "small molecule" drugs with known chemical structures

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[26] *See* 21 U.S.C. §§ 360aa-ee.

[27] FOOD & DRUG ADMIN., For Industry, *Developing Products for Rare Diseases & Conditions,* https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/default.htm [https://perma.cc/NX5L-CJQW] (last updated May 23, 2018).

[28] *Id.*

[29] *Id.*

[30] Gayatri Rao, *The Rise in Orphan Drug Designations: Meeting the Growing Demand*, FDA VOICE (July 18, 2016), https://blogs.fda.gov/fdavoice/index.php/2016/07/the-rise-in-orphan-drug-designations-meeting-the-growing-demand/ [https://perma.cc/7KZK-4GV4].

[31] 26 U.S.C. § 45C, *amended by* Tax Cuts and Jobs Act § 13401 (2017).

[32] Zachary Tracer & Caroline Chen, *Drugmakers' Rare Disease R&D Incentives Cut in GOP Tax Bill,* BLOOMBERG, (Nov. 2, 2017, 3:01 PM), https://www.bloomberg.com/news/articles/2017-11-02/drugmakers-rare-disease-r-d-incentives-are-cut-in-gop-tax-bill [https://perma.cc/7W2U-XV9R].

[33] BAYER, Innovation + Partnering, Technologies and Trends, *Small and Large Molecules,*http://pharma.bayer.com/en/innovation-partnering/technologies-and-trends/small-and-large-molecules [https://perma.cc/96V9-MGD5] (last visited May 10, 2018).

that can be synthesized.[34] A biologic is a so-called "large molecule" that is generally derived from a living organism. In contrast to small molecule drugs, biologics are "complex mixtures that are not easily identified or characterized."[35] Biologics are entitled to 12 years of exclusivity, unlike the four or five years for small molecule drugs. Biologics are not entitled to any exclusivity for new clinical investigations, unlike the three-year exclusivity available for small molecule drugs. Like small molecule drugs, biologics are also entitled to six months of additive pediatric exclusivity.

The 1984 Drug Price Competition and Patent Restoration Act (also known as the Hatch-Waxman Act) allows the extension of patent term for a product that is undergoing regulatory approval. Patent term extension is intended to restore the portion of the patent's exclusivity term that is lost while the patent owner is awaiting FDA regulatory approval. The patent term may be extended by up to five years, and the total patent term inclusive of the extension may be up to 14 years after FDA approval.[36] According to FDA, patent term extension is available to drugs and biologics.[37] However, there is some statutory ambiguity regarding what constitutes an "active ingredient" with respect to a biologic, e.g., a primary amino acid sequence, a secondary or tertiary structure of a protein, or a measure of activity of the molecule.[38]

IV. PRIORITY REVIEW VOUCHER PROGRAM

The designations above generally attach to a sponsor's product. For example, if Drug X qualifies for Fast Track, then it is Drug X that receives expedited review. If Drug Y qualifies for orphan status, then it is Drug Y that receives seven years of regulatory exclusivity. These designations are not transferrable to another product, e.g., a cardiovascular drug. By contrast, an FDA priority review voucher may be earned, bought, and sold.

In 2007, Congress created a priority review voucher program under the Food and Drug Administration Amendments Act (FDAAA) to encourage the research and development of therapies for neglected tropical diseases. In 2012, Congress extended the priority review voucher program to include rare pediatric diseases under the Food and Drug Administration Safety and Innovation Act (FDASIA). In 2016, Congress added a provision to the 21st Century Cures Act to include medical countermeasure priority review vouchers for bioterrorism defense.[39] Such diseases often do not attract

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[34] *Id*.

[35] FOOD & DRUG ADMIN., Office of Medical Products and Tobacco, About the Center for Biologics Evaluation and Research, *What Are "Biologics" Questions and Answers*, https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cber/ucm133077.htm [https://perma.cc/B6ZS-LAFL] (last updated Feb. 6, 2018).

[36] 35 U.S.C. § 156 (2015).

[37] FOOD & DRUG ADMIN., Development & Approval Process (Drugs), CDER Small Business and Industry Assistance, *Small Business Assistance: Frequently Asked Questions on The Patent Term Restoration Program*, https://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069959.htm [https://perma.cc/2544-BQWQ] (last visited Nov. 21, 2017).

[38] Terry Mahn & Gina Nellesen, *Uncertainty in Patent Term Extension for Biologics*, Law360, May 17, 2017, available at https://www.law360.com/articles/921770/uncertainty-in-patent-term-extension-for-biologics [https://perma.cc/VCM4-3ASZ].

[39] *See*, Drug, and Cosmetic Act § 565, 21 U.S.C. § 360bbb-4 (2013) (added by the 21st Century Cures Act § 3056).

commercial interest due to the large cost of development and the small market of patients. According to advocates for the priority review program, "[v]ouchers are incentives for industry to shift resources to drugs for rare diseases. It's a carrot created by Congress."[40] A priority review voucher may be granted to a sponsor on approval of an NDA or a BLA, and the voucher then entitles the holder to priority review of a single subsequent application. The voucher may be redeemed for any application, including ones directed to a non-rare or non-neglected disease. Under 21 U.S.C. § 360, priority review vouchers are salable and transferable.

At the outset of the program, a neglected tropical disease voucher could only be transferred once and required 365-day notification prior to use. The notification period was particularly onerous and a "major weakness" of the neglected tropical disease voucher because drug companies typically submit an NDA or BLA soon after obtaining clinical data.[41] Thus, the neglected tropical disease voucher was less valuable than the rare pediatric disease voucher, which had a 90-day notification requirement and unlimited transfers. The limitations of the neglected tropical disease voucher program were lifted in 2014.[42] Now, all priority review vouchers, regardless of the program of origin, may be transferred an unlimited number of times and have a 90-day notification requirement. FDA levies a fee to redeem a priority voucher, which is about $2.8 million USD for 2018.

Priority review is intended to shorten FDA review time from 10 months to six months.[43] In practice, because the standard review time often exceeds 10 months, the priority voucher can reduce a sponsor's time-to-market by nearly a year.[44] However, the priority voucher does not guarantee that a product will reach the market sooner, and a voucher may be used on an application that does not ultimately receive approval.[45] Nevertheless, since the program was introduced in 2007, "sales of the vouchers . . . are booming."[46]

A. Industry Critique

Uncertainty regarding the priority review voucher program has been a major concern for pharmaceutical companies.[47] To bring a potential drug product to market, a company may spend over a decade in research and development. This means that the company must make a decision to pursue a rare or neglected disease long before it knows whether or not it will receive a priority review voucher. Further, redeeming a priority review voucher does not guarantee a six-month approval (or an approval at

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[40] Deborah Levenson, *Advocates Call for Long-term Extension of the FDA's Rare Pediatric Disease Priority Review Program,* 173 AM. J. MED. GENETICS 7, 7(Dec. 19, 2016).

[41] Kevin Khachatryan, *Incentivizing Drug Development: Novel Reforms in Pharmaceutical Innovation,* 18 COLUM. SCI. & TECH. L. REV. 139 (2016).

[42] *Id*.

[43] *FDA Priority Review Vouchers: Tracker,* PRACTICAL LAW LIFE SCIENCES, last visited June 18, 2018, at W-001-0774.

[44] Ridley et al., *supra* note 9.

[45] Kurt R. Karst, *Priority Review Vouchers – Not Much Bang for the Buck*, FDA LAW BLOG (July 11, 2011), http://www.fdalawblog.net/2011/07/priority-review-vouchers-not-much-bang-for-the-buck.

[46] PRACTICAL LAW LIFE SCIENCES, *supra* note 43.

[47] David B. Ridley, *Priorities for the Review Voucher*, 96 AM. J. TROPICAL MED. HYGIENE 14 (2017).

all).[48] Even if FDA approved the therapy on an accelerated timeline, it is difficult to predict how much value the acceleration would create for the company.

Until the enactment of the 21st Century Cures Act in December 2016, there was also significant legislative risk for the priority review voucher program. The original priority review voucher legislation was drafted with a sunset provision, so Congress could decline to renew the program. In October 2016, the Advancing Hope Act extended FDA's rare pediatric disease priority review voucher program by just three months, through December 31, 2016.[49] The National Organization for Rare Disorders (NORD) and the pediatric cancer organization Kids v. Cancer immediately began lobbying to extend the program.[50] NORD stated that "[c]ompanies may not invest in drugs [for rare pediatric diseases] if they don't know [whether the] vouchers will be there or not. A [10-year extension of the voucher program through its inclusion in the 21st Century Cures Act] gives regulatory certainty for companies." NORD argued that if the requirements and goals of the program may change over time, "[i]nvestors cannot be certain that a drug will win a voucher because they do not know how eligibility might evolve."[51] According to NORD, with "piecemeal extension, we will never know if the program works and if it's incentivizing companies to develop new therapies."[52] The 21st Century Cures Act extended the priority review program through 2020.

B. FDA Critique

To redeem a priority review voucher, a user must pay an additional FDA user fee of $2.8 million USD. However, because the issuance and redemption of priority review vouchers have been sporadic, "FDA cannot easily hire new staff each time a voucher is redeemed" [53] and must expedite the review of an application without additional resources. According to advocates for the priority review program, a "one-time user fee does not cover the cost of new long-term staff to assist with priority reviews."[54] An FDA spokesman stated that "the additional workload from the program strains the agency's resources."[55] For the program to be sustainable in the future, FDA would need a "steady stream of vouchers to be confident that it can commit to hiring staff."[56]

FDA officials have also expressed concerns that although they support incentives for companies to develop therapies for rare and neglected diseases, "some new drug applications submitted with vouchers do not treat serious conditions or provide significant safety or effectiveness over existing products."[57] They have further advised

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[48] Kyle Wamstad, *Priority Review Vouchers – A Piece of the Incentive Puzzle*, 14 VA. J.L. & TECH. 127 (2009).

[49] Levenson, *supra* note 40.

[50] *Id.*

[51] Ridley, *supra* note 47, at 14.

[52] Levenson, *supra* note 40.

[53] Ridley, *supra* note 47, at 14.

[54] Levenson, *supra* note 40.

[55] *Id*.

[56] Ridley, *supra* note 47.

[57] Levenson, *supra* note 40.

that this ability to "purchase a priority review at the expense of other important FDA work undermin[es] the FDA's public health mission and diminish[es] staff morale."[58] Further, although the priority review voucher program encourages drug development, it does not ensure access to the developed drugs.[59] The statute does not require that the approved drug be marketed, nor does it limit the cost of the drug on the market.[60]

V. PRIORITY REVIEW VOUCHERS AS QUASI-INTELLECTUAL PROPERTY

Intellectual property is a category of intangible property that traditionally includes patents, copyrights, and trademarks. Much like patent exclusivity pertains to the right to exclude others from making, using, or selling an invention,[61] regulatory exclusivity pertains to the right to exclude others from entering the market.[62] Some experts have proposed a category of "regulatory property" to describe FDA-conferred regulatory exclusivities.[63] Regulatory property has been defined as "a property right that governs information generated to satisfy a regulatory standard and appropriate to include in a submission to a regulatory agency."[64]

Although regulatory exclusivity does not have "an explicit right of transfer . . . [it] is a tradeable economic benefit, to some extent. One could always sell the company, transferring the economic value of the right along with it. The benefit might not transfer to another drug, but the overall economic value of the benefit from one drug transfers to the entire operation, as with any corporate asset."[65] Like regulatory exclusivity, priority review vouchers do not require congressional funding, "making them politically feasible incentives."[66] The priority review voucher program also has the benefit of "avoid[ing] the political divisiveness of pharmaceutical patent extensions."[67]

Unlike regulatory exclusivity, however, a priority review voucher may be fully alienated from a product and a sponsor and salable as an independent unit, not merely as an economic boost in a company's overall value. A priority review voucher is freely transferrable, much like an ordinary property right. In this way, a priority review voucher is more similar to quasi-intellectual property (like a license)[68] than regulatory property whose value attaches to a product and/or company. This paper analyzes the

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58 *Id*.

59 Ridley, *supra* note 47, at 15.

60 *See* Khachatryan, *supra* note 41.

61 35 U.S.C. § 271.

62 Feldman, *supra* note 25.

63 *Id*.

64 Jacob S. Sherkow, *Cancer's IP*, 96 N.C.L. Rev. 297 (2018).

65 Feldman, *supra* note 25.

66 *Id*.

67 Wamstad, *supra* note 48.

68 Technology and IP Law Glossary, *Quasi-Intellectual Property* (June 14, 2013), http://www.ipglossary.com/glossary/quasi-intellectual-property-quasi-ip-quasi-rights [https://perma.cc/W6KB-KSR6].

market for priority review vouchers and the trend in valuation over time. This paper also provides a summary of the priority review vouchers issued to date, whether and how vouchers have been transferred, and the outcomes when vouchers have been redeemed.

VI. FIRST WAVE OF ISSUED PRIORITY REVIEW VOUCHERS

FDA issued the first priority review voucher in 2009 to Novartis Pharmaceuticals for the approval of Coartem (artemether and lumefantrine).[69] FDA approved Coartem for the treatment of malaria, a neglected tropical disease. At the time, there was "significant debate about the value of a [priority review voucher]," and transactions by Novartis were being "closely watched."[70] In 2011, Novartis redeemed the voucher on a BLA for Ilaris (canakimumb) to treat gouty arthritis. FDA ultimately declined to approve the application, leading commentators to remark that priority review vouchers were "not much bang for the buck."[71]

The second priority voucher was issued in 2012 when Janssen Pharmaceutical received approval for Sirturo (bedaquiline).[72] FDA approved Sirturo for the treatment of tuberculosis, a neglected tropical disease. It was the first tuberculosis treatment to be approved in decades. Like Novartis, Janssen redeemed the voucher itself on a BLA for Tremfya (guselkumab) to treat psoriasis.[73] FDA approved the application on an accelerated timeline, thereby renewing hope in the priority review voucher program.[74]

Because neither the first nor the second issued priority review vouchers were transferred, the market value of a priority review voucher remained unknown for several more years.[75] Notably, at the time that those vouchers were issued, neglected tropical disease priority review vouchers had some onerous limitations. For example, a 365-day notice requirement prior to use and a one-time transfer limit made them less valuable than pediatric rare disease priority review vouchers that only required 90-day notification and had unlimited transfers.

The first priority voucher that FDA issued for a rare pediatric disease (and the third priority voucher ever issued) was awarded to BioMarin Pharmaceutical in 2014 for the approval of Vimizim (elosulfase alfa). FDA approved Vimizim for the treatment of mucopolysaccharidosis type IVA (Morquio A syndrome). That same year, BioMarin

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69 U.S. FOOD & DRUG ASS'N Approval Letter (Coartem) (Apr. 7, 2009).

70 Kurt R. Karst, *FDA Approves COARTEM with Priority Review Voucher; Voucher Market is Untested and Unclear*, FDA LAW BLOG (Apr. 8, 2009), http://www.fdalawblog.net/ 2009/04/fda-approves-coartem-with-priority-review-voucher-voucher-market-is-untested-and-unclear [https://perma.cc/229F-GF4E].

71 Karst, *supra* note 45.

72 U.S. FOOD & DRUG ASS'N, Approval Letter (Sirturo) (Dec. 28, 2012).

73 Janssen Press Release, *Janssen Announces U.S. FDA Approval of Tremfya (guselkumab) for the Treatment of Moderate to Severe Plaque Psoriasis* (July 13, 2017), https://www.jnj.com/media-center/press-releases/janssen-announces-us-fda-approval-of-tremfya-guselkumab-for-the-treatment-of-moderate-to-severe-plaque-psoriasis [https://perma.cc/J242-47GP]

74 Alexander Gaffney, Michael Mezher & Zachary Brennan, *Regulatory Explainer: Everything You Need to Know About FDA's Priority Review Vouchers,* REG. FOCUS (Dec. 19, 2017), https://www.raps.org/regulatory-focus/news-articles/2017/12/regulatory-explainer-everything-you-need-to-know-about-fdas-priority-review-vouchers [https://perma.cc/9HWP-7KVN].

75 Karst*, supra* note 70.

became the first company to publicly sell a priority review voucher as discussed in detail below.

As of May 2018, 19 priority review vouchers have been issued. (See Table 1.) All of the vouchers have been for rare pediatric diseases or neglected tropical diseases. As of May 2018, FDA has issued no countermeasure priority review vouchers.

Table 1: Priority Review Vouchers Issued To Date[76]

Year	Product	Company	Indication	Source
2009	Coartem (artemether/ lumefantrine)	Novartis	Malaria	https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2009/022268s000ltr.pdf
2012	Sirturo (bedaquiline)	Janssen (JNJ)	Tuberculosis	https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2012/204384Orig1s000ltr.pdf
2014	Vimizim (elosulfase alfa)	BioMarin	Morquio A syndrome	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/125460Orig1s000Approv.pdf
2014	Impavido (miltefosine)	Knight	Leishmaniasis	https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2014/204684Orig1s000ltr.pdf
2015	Unituxin (dinutuximab)	United Therapeutics	High-risk neuroblastoma	https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/125516Orig1s000ltr.pdf
2015	Cholbam (cholic acid)	Asklepion	Rare bile acid synthesis disorders	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/205750Orig1s000Approv.pdf
2015	Xuriden (uridine triacetate)	Wellstat	Hereditary orotic aciduria	https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/208169Orig1s000ltr.pdf

[76] Last updated May 2018.

Year	Product	Company	Indication	Source
2015	Strensiq (asfotase alfa)	Alexion	Hypophosphatasia	https://pink.pharmaintelligence.informa.com/PS057234/Priority-Review-Voucher-Not-For-Sale-Alexion-Says-Afterem-Strensiqem-Approval
2015	Kanuma (sebelipase alfa)	Alexion	Lysosomal acid lipase (LAL) deficiency	https://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/125561Orig1s000Approv.pdf
2016	Vaxchora	PaxVax	Cholera	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm506305.htm
2016	Exondys 51 (eteplirsen)	Sarepta	Duchenne muscular dystrophy	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm521263.htm
2016	Spinraza (nusinersen)	Biogen	Spinal muscular atrophy (SMA)	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm534611.htm
2017	Emflaza (deflazacort)	Marathon	Duchenne muscular dystrophy	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm540945.htm
2017	Brineura (cerliponase alfa)	BioMarin	Batten disease	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm555613.htm
2017	Benznidazole	Chemo Research	Chagas	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm573942.htm
2017	Tisagenlecleucel	Novartis	B-cell acute lymphoblastic leukemia	https://www.fda.gov/downloads/BiologicsBloodVaccines/CellularGeneTherapyProducts/ApprovedProducts/UCM574106.pdftisagenlecleucel

Year	Product	Company	Indication	Source
2017	Mepsevii	Ultragenyx	Mucopolysaccharidosis VII	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585308.htm
2017	Luxturna (voretigene neparvovec-rzyl)	Spark	Biallelic RPE65 mutation-associated retinal dystrophy	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm589467.htm
2018	Crysvita (burosumab-twza)	Ultragenyx	X-linked hypophosphatemia	https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm604810.htm

VII. TRANSFERRED PRIORITY REVIEW VOUCHERS

Although the issuance of a priority review voucher is public, the sale of a voucher need not be public.[77] Of the 19 issued vouchers, two vouchers were used by their original recipients (Novartis and Janssen, as discussed above). Several vouchers have been transferred anonymously (in some cases, the transferor chose to remain anonymous; in other cases, the transferee chose to remain anonymous). Other companies have stated that their priority review vouchers are not for sale and will be used in-house.[78] The transfers of priority review vouchers that have been publicly disclosed are summarized in Table 2 and detailed below in chronological order.

A. Analysis of Priority Review Vouchers Transferred To Date

The first public sale of a priority review voucher was in 2014 by BioMarin Pharmaceutical. As explained above, BioMarin was the first company to receive a rare pediatric disease priority review voucher upon approval of Vimizim for the treatment of mucopolysaccharidosis type IVA (Morquio A syndrome). BioMarin sold its priority review voucher to Regeneron for $67.5 million USD.[79] Regeneron and Sanofi-Aventis announced a plan to use the voucher for their BLA submission for Praluent (alirocumab) to treat high cholesterol.[80] FDA approved the application on an

[77] Practical Law Life Sciences, *supra* note 43.

[78] Sue Sutter, *Priority Review Voucher Not for Sale, Alexion Says After Strensiq Approval*, PHARMA INTELLIGENCE (Nov. 2, 2015), https://pink.pharmaintelligence.informa.com/PS057234/ Priority-Review-Voucher-Not-For-Sale-Alexion-Says-Afterem-Strensiqem-Approval.

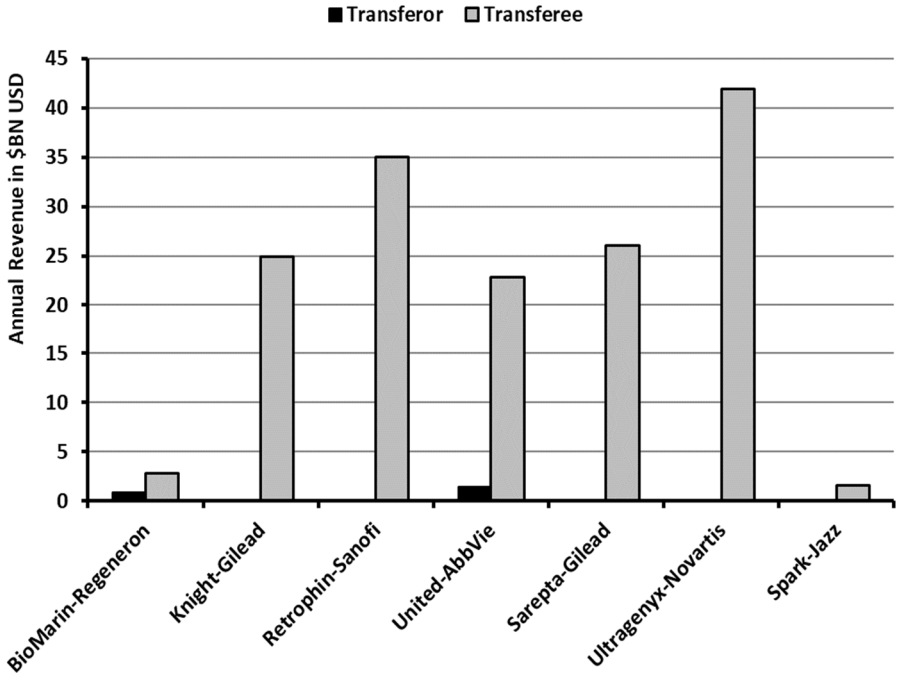
[79] Regeneron Press Release, *Regeneron and Sanofi Announce Plan to Use Priority Review Voucher for Alirocumab U.S. FDA Submission* (July 30, 2014), http://investor.regeneron.com/release detail. cfm?releaseid=863087 [https://perma.cc/W7PP-MBVT].

[80] *Id.*

accelerated timeline.[81] The time that "Sanofi 'saved' in getting the drug approved might make a $1 billion difference in revenue."[82] The priority review voucher was also credited with helping the sponsors "beat Amgen (another big drug developer) to the market in obtaining FDA approval."[83] At the time, seller BioMarin's annual revenues were $889 million USD, while buyer Regeneron's annual revenues were $2,819.6 million USD according to their respective annual reports and Securities and Exchange (SEC) filings. See Fig. 1.

Knight Therapeutics sold its priority review voucher to Gilead Sciences for $125 million USD later in 2014. Knight Therapeutics earned a neglected tropical disease priority review voucher for Impavido (miltefosine) to treat leishmaniosis, a parasitic

Fig. 1: Transferor vs. Transferee Annual Revenue



disease, and amoeba infections. Gilead used the voucher on an NDA submission for Odefsey, a human immunodeficiency virus (HIV) drug regimen comprising rilpivirine, emtricitabine, and tenofovir alafenamide.[84] FDA approved the NDA on an accelerated timeline.[85] At the time, seller Knight's annual revenue was $365,323 Canadian dollars ($328,790 USD using the 2014 exchange rate), while buyer Gilead's

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[81] Gaffney, Mezher & Brennan, *supra* note 74.

[82] Khachatryan, *supra* note 41.

[83] *Id.*

[84] Gilead Press Release, *Gilead Submits New Drug Application to U.S. Food and Drug Administration for Single Tablet Regimen for HIV Containing Rilpivirine, Emtricitabine and Tenofovir Alafenamide* (July 1, 2015), http://www.gilead.com/news/press-releases/2015/7/gilead-submits-new-drug-application-to-us-food-and-drug-administration-for-single-tablet-regimen-for-hiv-containing-rilpivirine-emtricitabine-and-tenofovir-alafenamide-rftaf [https://perma.cc/6M69-XQTJ].

[85] Gaffney, Mezher & Brennan, *supra* note 74.

annual revenues were $24.9 billion USD according to their respective annual reports and SEC filings. See Fig. 1.

Asklepion Pharmaceuticals received a rare pediatric disease priority review voucher for the approval of Cholbam for the treatment of rare bile synthesis disorders. Asklepion sold the voucher in 2015 to Retrophin for $27 million in cash, about 700,000 shares of Retrophin stock, and $37 million in future milestone payments.[86] In the same year, Retrophin sold the voucher to Sanofi-Aventis for $245 million USD. Sanofi-Aventis redeemed the voucher on Soliqua, an insulin glargine and lixisenatide combination therapy to treat type 2 diabetes.[87] The review timeline extended beyond six months after FDA requested additional information regarding the drug delivery device.[88] At the time, Asklepion was a privately held company, Retrophin was in development and reported no annual revenues, and Sanofi reported annual revenues of about $35 billion USD according to its SEC filings. See Fig. 1.

United Therapeutics sold its priority review voucher to AbbVie in 2015 for $350 million USD, the highest amount paid for a voucher to date. United Therapeutics earned a rare pediatric disease priority review voucher for Unituxin to treat neuroblastoma. AbbVie has not disclosed how it plans to use the voucher.[89] At the time, United Therapeutics reported annual revenues of $1.47 billion USD and AbbVie reported annual revenues of $22.8 billion USD in their respective annual reports and SEC filings. See Fig. 1.

Agreements have also been made prior to the issuance of a priority review voucher. WellStat Therapeutics earned a rare pediatric disease priority review voucher in 2015 upon the approval of Xuriden to treat hereditary orotic aciduria, which was immediately transferred to AstraZeneca under an existing agreement with undisclosed terms.[90] At the time, WellStat was a privately held company, and AstraZeneca was one of the top 10 pharmaceutical companies in the world by revenue ($24.7 billion USD).[91]

There has also been a trend in voucher transactions involving at least one undisclosed party. In 2016, Gilead's SEC filings reported the acquisition of a priority review voucher from an undisclosed source. In 2017, GlaxoSmithKline redeemed a priority review voucher obtained from an undisclosed source for $130 million USD on an application for Juluca, an HIV drug regimen comprised of Tivicay (dolutegravir)

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[86] Ben Fidler, *With Asklepion Deal, Retrophin Gets a New Drug – And a Voucher*, XCONOMY (Mar. 18, 2015), https://www.xconomy.com/new-york/2015/03/18/with-asklepion-deal-retrophin-gets-a-new-drug-and-a-voucher [https://perma.cc/45RE-JCGQ].

[87] Krystle Vermes, *FDA Delays Approval Decision for Sanofi's Insulin Glargine, Lixisenatide Pen for Diabetes,* PHARM. TIMES (Sept. 1, 2016), http://www.pharmacytimes.com/product-news/ fda-delays-approval-decision-for-sanofis-insulin-glargine-lixisenatide-pen-for-diabetes [https://perma.cc/2GKC-7VS4].

[88] *Id.*

[89] Gaffney, Mezher & Brennan, *supra* note 74.

[90] John Carroll, *AstraZeneca Nabs Priority Review Voucher as Wellstat Bags FDA OK,* FIERCEBIOTECH (Sept. 8, 2015), https://www.fiercebiotech.com/regulatory/astrazeneca-nabs-priority-review-voucher-as-wellstat-bags-fda-ok [https://perma.cc/N43A-RXXL].

[91] Leah Cannon, *Top 10 Pharma Companies 2015-2016*, LIFE SCI. NETWORK (Aug. 15, 2016), https://lifesciencenetwork11.connectedcommunity.org/blogs/leah-cannon/2016/08/15/top-10-pharma-companies-2015-2016 [https://perma.cc/6Y28-WB5J].

and Edurant (rilpivirine).[92] Its application received accelerated review. In 2017, BioMarin sold its second priority review voucher for $125 million USD to an undisclosed buyer.[93] BioMarin earned a rare pediatric disease priority review voucher for the approval of Brineura to treat tripeptidyl peptidase 1 deficiency.

In 2017, Sarepta Therapeutics sold its priority review voucher to Gilead for $125 million USD. Sarepta earned the rare pediatric disease priority review voucher upon the approval of Exondys 51 to treat Duchenne muscular dystrophy. Gilead redeemed the voucher on its NDA submission for Biktarvy, an HIV combination therapy (bictegravir, emtricitabine, and tenofovir alafenamide) and received approval in February 2018 on an accelerated review timeline.[94] In 2017, Sarepta reported annual revenues of about $150 million USD,[95] and Gilead reported annual revenues of $26 billion USD according to their respective annual reports and SEC filings. See Fig. 1.

In December 2017, Ultragenyx Pharmaceutical sold its priority review voucher to Novartis Pharmaceuticals for $130 million USD. Ultragenyx earned a rare pediatric disease priority review voucher for the approval of Mepsevii to treat mucopolysaccharidosis type VII.[96] Novartis has not disclosed how it plans to use the voucher.[97] In 2017, Ultragenyx reported annual revenues of $2.6 million USD, and Novartis reported annual revenues of $41.9 billion USD in their respective annual reports and SEC filings. See Fig. 1.

In 2018, Spark Therapeutics sold its priority review voucher to Jazz Pharmaceuticals for $110 million USD. Spark earned a rare pediatric disease priority review voucher for the approval of Luxturna to treat biallelic RPE65 mutation-associated retinal dystrophy.[98] Jazz has not disclosed how it plans to use the voucher. In 2017, Spark reported annual revenues of $12 million USD, and Jazz reported annual revenues of $1.6 billion USD in their respective annual reports and SEC filings. See Fig. 1.

The publicly disclosed priority review voucher transactions to date are summarized in Table 2.

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[92] *GSK and ViiV Healthcare Use $130 Million Priority Review Voucher to Expedite HIV Therapy,* FDA NEWS (June 9, 2017), https://www.fdanews.com/articles/182089-gsk-and-viiv-healthcare-use-130-million-priority-review-voucher-to-expedite-hiv-therapy [https://perma.cc/W2SR-TL3D].

[93] *BioMarin Sells Second Priority Review Voucher for $125 Million,* PR NEWSWIRE (Nov. 27, 2017), https://www.prnewswire.com/news-releases/biomarin-sells-second-priority-review-voucher-for-125-million-300561105.html [https://perma.cc/F2H9-7NX5].

[94] U.S. FOOD & DRUG ASS'N, Approval Letter (Biktarvy) (Feb. 7, 2018).

[95] Margaret Patrick, *Analyst Ratings for Sarepta Therapeutics and Peers in 2017*, MARKET REALIST (Nov. 1, 2017), https://marketrealist.com/2017/11/analysts-recommendations-sarepta-therapeutics-peers-2017 [https://perma.cc/7SD2-XVMZ].

[96] U.S. FOOD & DRUG ASS'N, *FDA Approves Treatment for Rare Genetic Enzyme Disorder* (Nov. 15, 2017), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585308.htm [https://perma.cc/XYF6-54P7].

[97] Ned Pagliarulo, *Novartis Buys Regulatory Fast Pass for $130M*, BIOPHARMA DIVE (Dec. 18, 2017), https://www.biopharmadive.com/news/novartis-ultragenyx-priority-review-voucher-sale-130-million/513303 [https://perma.cc/N59R-6CVW].

[98] U.S. FOOD & DRUG ASS'N, *FDA approves novel gene therapy to treat patients with a rare form of inherited vision loss* (Dec. 19, 2017), https://www.fda.gov/NewsEvents/ Newsroom/PressAnnouncements/ ucm589467.htm [https://perma.cc/NZ9B-73WK].

Table 2: Priority Review Vouchers Publicly Transferred To Date[99]

Transfer Year	Transferor	Voucher Drug	Transferee	Cost (MM USD)	Redemption Drug
2014	BioMarin Pharmaceutical	Vimizim	Regeneron	$67.5	Praluent (accelerated)
2014	Knight Therapeutics	Impavido	Gilead Sciences	$125.0	Odefsey (accelerated)
2015	Asklepion Pharmaceuticals	Cholbam	Retrophin	$36-73	Soliqua (delayed beyond 6 months)
	Retrophin	Cholbam	Sanofi-Aventis	$245.0	
2015	United Therapeutics	Unituxin	AbbVie	$350.0	Undisclosed
2015	WellStat Therapeutics	Xuriden	AstraZeneca	Undisclosed terms in agreement prior to issuance of voucher	Undisclosed
2016	Undisclosed	Undisclosed	Gilead Sciences	Undisclosed	Undisclosed
2017	Undisclosed	Undisclosed	GlaxoSmith Kline	$130.0	Juluca (accelerated)
2017	BioMarin Pharmaceutical	Brineura	Undisclosed	$125.0	Undisclosed
2017	Sarepta Therapeutics	Exondys 51	Gilead Sciences	$125.0	Biktarvy (accelerated)
2017	Ultragenyx Pharmaceutical	Mepsevii	Novartis Pharmaceuticals	$130.0	Undisclosed

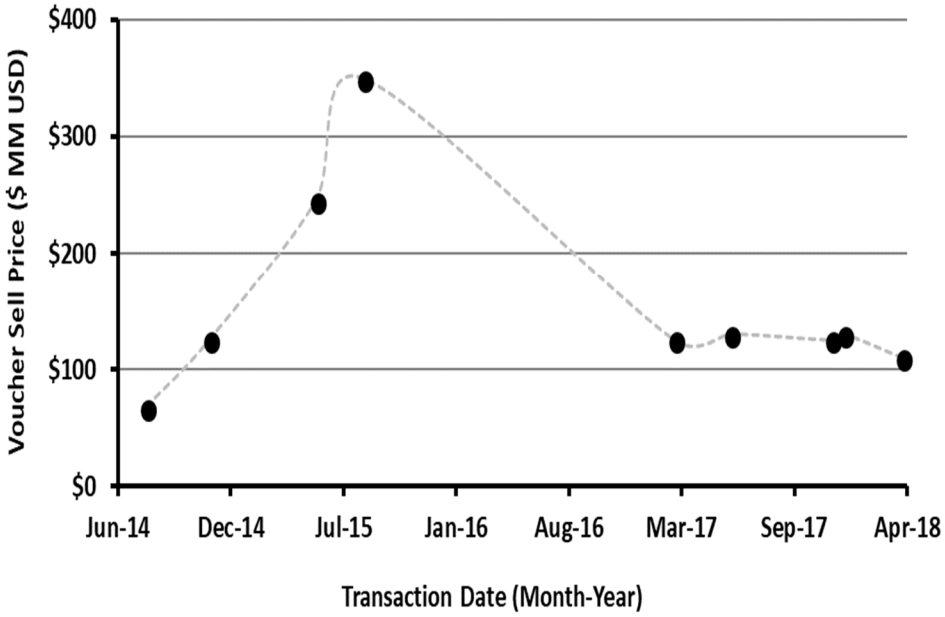
[99] Last updated May 2018.

Transfer Year	Transferor	Voucher Drug	Transferee	Cost (MM USD)	Redemption Drug
2018	Spark	Luxturna	Jazz Pharmaceuticals	$110.0	Undisclosed

B. Trends in Priority Review Voucher Transactions Over Time

The purchase price for a priority review voucher rose from $67.5 million USD in 2014 to a peak of $350 million USD in 2015 and plateaued at $110-130 million USD in 2018. See Table 2. The trend in priority review sale prices is shown in Fig. 2. Priority review voucher sales generally involve all-cash deals rather than milestone payments and royalties. Redeemed priority review vouchers have generally been used on treatments for non-rare conditions: gouty arthritis, plaque psoriasis, high cholesterol, type 2 diabetes, and HIV. See Table 3.

Fig. 2: Priority Review Voucher Sale Prices Over Time

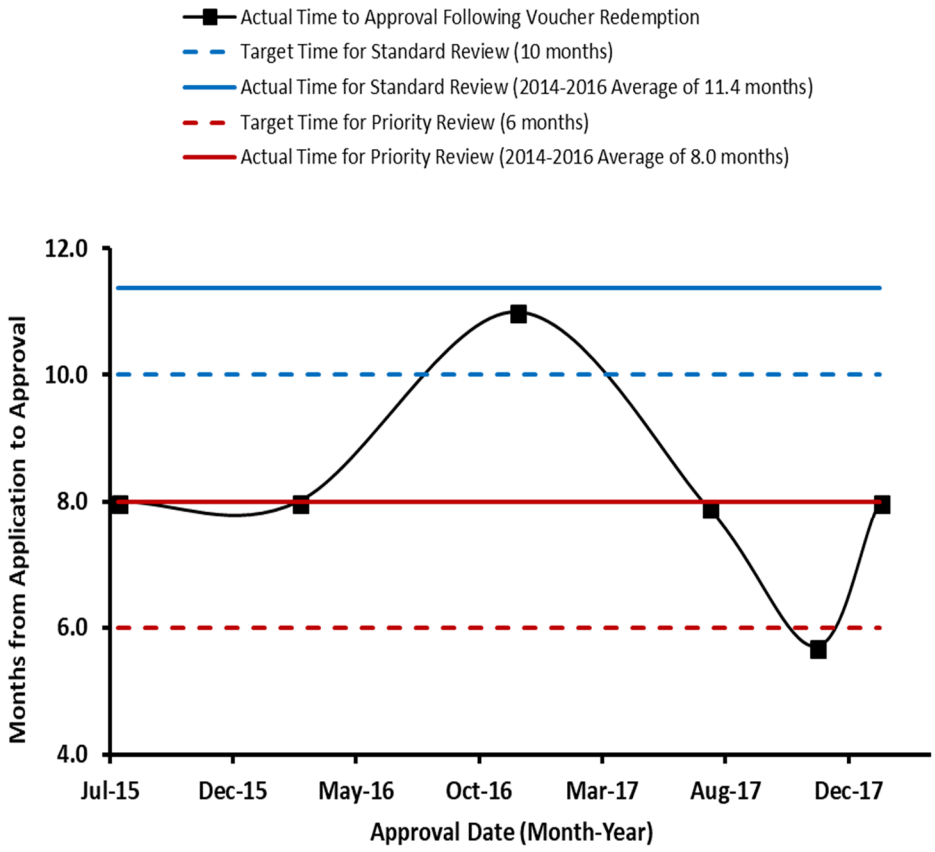


In priority review voucher transactions, the buyer tends to be bigger than the seller, as measured by annual revenue. See Fig. 1. In several cases, the seller did not have any substantive annual revenue, i.e., was still in development stages. The first priority review voucher transfer involved a buyer and a seller with annual revenues that were comparable, i.e., within an order of magnitude. Subsequently, the disparity between the size of the buyer and the seller has grown, and the annual revenues of the buyer tend to be many orders of magnitude higher than the annual revenues of the seller.

Redemption of a priority review voucher generally does accelerate the review of an NDA or BLA submission as compared to standard review. For comparison, the median FDA approval time for standard review was 12.0 months in 2014, 12.0 months in 2015,

and 10.1 months in 2016[100] (the target is 10 months). The median FDA approval time for priority review was 8.0 months in 2014, 8.0 months in 2015, and 8.0 months in 2016[101] (the target is 6 months). The first redemption of a priority review voucher by Novartis, which did not result in expedited approval, appears to be a rare exception. As shown in **Fig. 3**, the review time for an application for which a voucher has been redeemed is faster than the average time for standard review (shown in blue) and comparable to the average time for priority review (shown in red). See also **Table 3**.

Fig. 3: Time to Approval Following Redemption of Priority Review Voucher



[100]U.S. FOOD & DRUG ASS'N, *NDA and BLA Approval Times* (Feb. 9, 2017), https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/NDAandBLAApprovalReports/ucm373415.htm [https://perma.cc/N698-N87A].

[101]*Id.*

Table 3: Redeemed Priority Review Vouchers

Redemption Company (Source Company)	Redemption Drug or Biologic	Indication	Outcome	NDA or BLA Date	Approval Date	Months to Approval
Novartis (in-house)	Ilaris (canakinumab)	Gouty arthritis	Unsuccessful[102]			
Regeneron and Sanofi (purchased from BioMarin)	Praluent (alirocumab)	High cholesterol	Accelerated [103]	11/24/2014	7/24/2015	**8.0**
Gilead (purchased from Knight)	Odefsey (rilpivirine, emtricitabine, and tenofovir alafenamide)	HIV	Accelerated [104]	7/1/2015	3/1/2016	**8.0**
Sanofi (purchased from Asklepion-Retrophin)	Soliqua (insulin glargine and lixisenatide)	Type 2 diabetes	FDA requested additional information regarding drug delivery device[105]	12/21/2015	11/21/2016	**11.0**
Janssen (in-house)	Tremfya (guselkumab)	Plaque psoriasis	Accelerated [106]	11/16/2016	7/13/2017	**7.9**
ViiV Healthcare and GSK (purchased from undisclosed source)	Juluca (dolutegravir and rilpivirine)	HIV	Accelerated [107]	6/1/2017	11/21/2017	**5.7**

[102]Ben Adams, *FDA Rejects Novartis' Ilaris for Gouty Arthritis*, PHARMAFILE (June 22, 2011), http://www.pharmafile.com/news/160467/fda-rejects-novartis-ilaris-canakinumab-gouty-arthritis [https://perma.cc/Y4KF-ZS3Z].

[103]U.S. FOOD & DRUG ASS'N, Approval Letter (Praluent) (July 24, 2015).

[104]U.S. FOOD & DRUG ASS'N, Approval Letter (Odefsey) (Mar. 1, 2016).

[105]U.S. FOOD & DRUG ASS'N, Approval Letter (Soliqua) (Nov. 21, 2016).

[106]U.S. FOOD & DRUG ASS'N, Approval Letter (Tremfya) (July 13, 2017).

[107]U.S. FOOD & DRUG ASS'N, Approval Letter (Juluca) (Nov. 21, 2017).

Redemption Company (Source Company)	Redemption Drug or Biologic	Indication	Outcome	NDA or BLA Date	Approval Date	Months to Approval
Gilead (purchased from Sarepta)	Biktarvy (bictegravir, emtricitabine, and tenofovir alafenamide)	HIV	Accelerated [108]	6/10/2017	2/7/2018	**8.0**

Finally, whereas press releases were commonly issued regarding the purchase or the redemption of a priority review voucher in 2014 and 2015, there has been an increasing trend toward secrecy regarding voucher transactions. By 2017, it was increasingly common for a buyer, a seller, or both to remain undisclosed. In many cases, the acquisition or the redemption of a priority review voucher was only discovered after a careful review of a company's SEC filings or upon FDA approval.

VIII. CONCLUSIONS

While incentives such as patents are intended to be rewards that "'pull' research rather than 'push' research,"[109] the priority review voucher program is intended as a legislative push toward rare pediatric diseases, neglected tropical diseases, and bioterrorism defenses. Because medicines take many years to develop, the first companies to be awarded priority review vouchers received them unexpectedly "because the program did not exist when the drugs being considered were in the product pipeline."[110]

Some of the original expectations for the priority review voucher program have not borne out. Despite initial speculation that a voucher could be worth up to $1 billion,[111] the market value of a priority review voucher has dropped from a peak of $350 million USD in 2015 to a plateau of $110-130 million USD through 2018. See Fig. 2.

Contrary to fears that a priority review voucher would not be "much bang for the buck"[112] after the failure of the first voucher redemption, most applications that have used a priority review voucher were successfully accelerated. See Table 3. Although priority review vouchers have not achieved the target of six-month review, those applications have been reviewed as quickly as a priority review application not using a voucher and significantly more quickly than a standard review application. See Fig. 3.

As predicted, voucher transfers have typically involved large companies buying vouchers from smaller companies.[113] However, large companies have also shepherded

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[108] U.S. FOOD & DRUG ASS'N, Approval Letter (Biktarvy) (Feb. 7, 2018).

[109] Wamstad, *supra* note 48.

[110] *Id.*

[111] Donna Young, *Priority Review Vouchers: The Next 'Golden Ticket'?,* 19 BIOWORLD TODAY 49 (Mar. 12, 2008), http://www.bioworld.com/content/priority-review-vouchers-next-golden-ticket.

[112] Karst, *supra* note 45.

[113] *Id.*

drugs for rare or neglected diseases through to FDA approval and earned priority review vouchers themselves. The difference is that large companies generally do not sell those vouchers (at least publicly).

Importantly, the question of whether the priority review voucher program has been successful in producing therapies for rare and neglected diseases will require several years to answer. Although the priority review voucher program commenced in 2007, its original sunset provision was a looming specter that dampened the intended incentive to invest in rare and neglected diseases. It was not until December 2016 that the 21st Century Cures Act meaningfully extended the priority review voucher program, providing much-needed certainty to stakeholders (like investors making development decisions and FDA making hiring decisions), and thus the second decade of the priority review voucher program will likely provide a better reflection of its full potential.