Priority Review Voucher (PRV) Market Update

Mid-Year 2024 Outlook

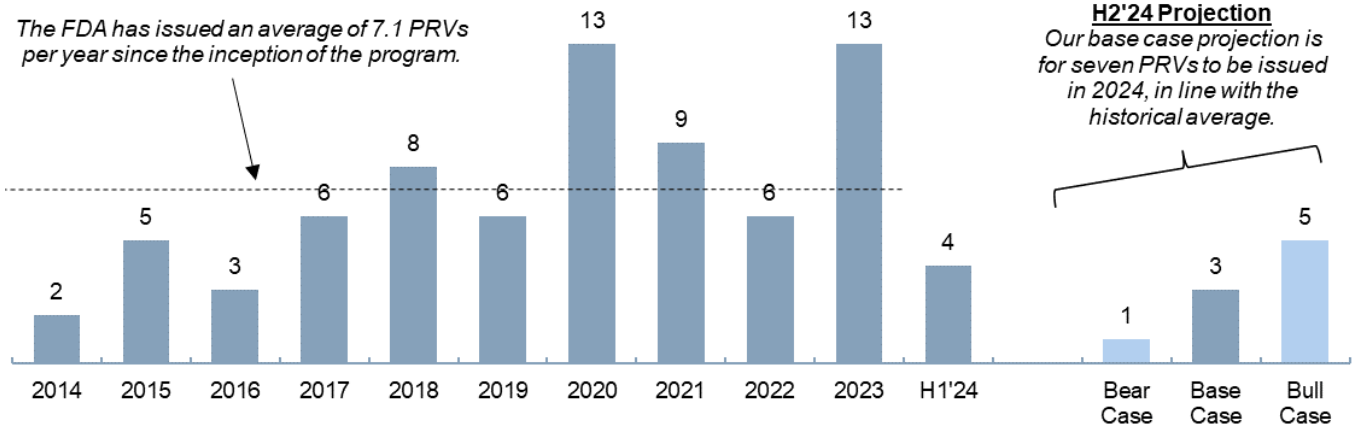
Looking ahead, **we see a healthy marketplace for priority review vouchers (PRVs)**. On top of the four PRVs already issued this year, we anticipate three new PRVs to potentially be awarded in the second half of 2024 – which would put 2024 in line with the prior ten-year average of seven PRVs annually. All seven vouchers expected in 2024 would be issued through the rare pediatric disease (RPD) PRV program, which we believe will be extended before it expires in September. Also, importantly, the price environment for PRVs has been relatively stable with the last four PRVs pricing in a relatively narrow range of $103M to $108M. We believe there could be near-term upside to pricing in the second half of the year due to a relative scarcity of PRVs in 2024 (vs 2023). This adds visibility to the potential cash proceeds of PRV sales and facilitates cash planning for smaller biopharma firms. Finally, each of the last two PRVs awarded were sold relatively quickly – in 37 days or less.

Demand for PRVs has been resilient across multiple therapeutic areas for both pipeline products and follow-on indications. In our view, large pharma companies will continue to be the primary acquirors of PRVs as they look for ways to accelerate the launch of new blockbusters in order to replace potentially lost revenue from upcoming patent cliffs. Also, we see strong demand for PRVs in emerging competitive therapeutic areas like RSV vaccines – though updated CDC guidelines may slow down future redemptions here. Finally, in the large cap biotech space, we are seeing a large proportion of PRV redemptions alongside supplemental filings where launch trajectories are more predictable.

A Healthy Volume of PRV Issuances Through Year End

In our bull-case scenario, **we see the potential for up to nine PRVs to be awarded in 2024**. Our tally comprises **four PRVs already awarded** in the first half of 2024, three potential PRVs tied to upcoming PDUFA dates, and two PRVs that were delayed following FDA Complete Response Letters (CRLs). This is down from the 13 issued in 2023 (and the 13 issued in 2020), but we still think this is a healthy number that is generally in line with historical levels. **Zevra Therapeutics (NAS: ZVRA)**, **Applied Therapeutics (NAS: APLT)**, and **Neurocrine Biosciences (NAS: NBIX)** are on track to receive PRVs by September, November, and December, respectively, if the FDA reviews their novel rare disease medicines favorably. Both **Rocket Pharmaceuticals** (**NAS: RCKT**) and **Abeona Therapeutics** (**NAS: ABEO**) were hopeful of receiving PRVs in the first half of 2024, but they were both given CRLs requesting additional CMC information. Refer to **Figure 1**.

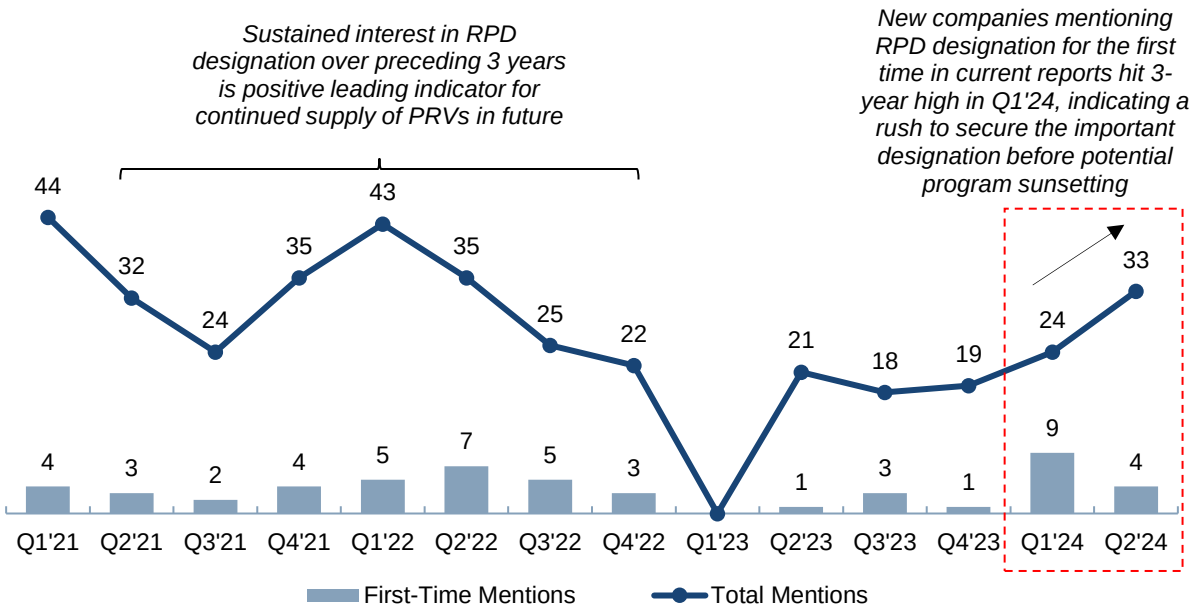
Figure 1: Our Bull Case Scenario Suggests Up to Nine (9) New PRVs Issued in 2024



Source: Bourne Partners Research

Beyond 2024, **we are optimistic that the rare pediatric disease (RPD) PRV program will be renewed** ahead of its expiration on **September 30** – based on discussions with various industry stakeholders. We think most industry experts recognize that the RPD program is critically important to the broader PRV ecosystem because it accounts for ~70% of the PRVs issued to date (54 of 77) – as well as all seven of the most recently issued PRVs. In June, the *Creating Hope Reauthorization Act* was introduced in the Senate to extend the RPD PRV program for another six years through September 2030. This would be a longer reauthorization than the two prior extensions in 2016 and 2020 (each of four years). As it stands, only companies that received a RPD designation prior to the September expiration would be eligible to receive a PRV if they gain a qualifying approval over the subsequent two-year period. The FDA would not award any PRVs after September 2026, regardless of when the designation was granted. Clinical-stage companies with qualifying rare disease product candidates are racing to take advantage of this financial incentive. Nine companies filed Current Reports mentioning rare pediatric disease designation for the first time in 1Q24 (a 3-year high) and the total number of reports mentioning this designation has also climbed over the past three quarters, indicating increasing interest in the program among publicly traded biotechs. Refer to **Figure 2**.

Figure 2: Mentions of *Rare Pediatric Disease Designation* in Current Reports (Total and First-Time Reports)



Source: SEC 8-K Filings

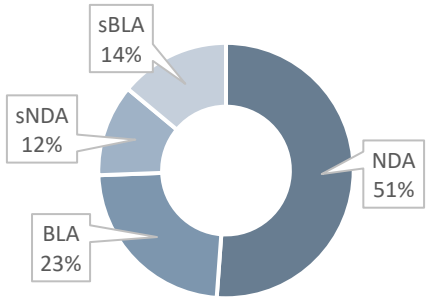
As an aside, **we are watching for a potential renewal of the Medical Countermeasure (MCM) PRV program**. This program has been inactive after quietly expiring in October 2023. Only nine PRVs have been awarded through the MCM PRV program to date, many of which were associated with COVID-19. The latest was awarded to **Pfizer (NYSE: PFE)** for its COVID-19 therapy Paxlovid, after its emergency use authorization was converted to a full approval in May 2023. Of note, a piece of legislation was introduced in September 2023 to extend the MCM PRV program – i.e., the *Material Threat Medical Countermeasure Priority Review Voucher Reauthorization Act*. However, this legislation has not moved forward, to our knowledge. Renewed or not, we see the MCM PRV program as much less of a productive program (vs the RPD and Tropical Disease PRV programs).

Redemptions Coming from Both Big Pharma and Large Cap Biotech

We anticipate Big Pharma will continue to be the primary user of PRVs, particularly given the need to replace lost revenue from upcoming patent expirations. In our view, Big Pharma buyers have been targeting both pipeline products and follow-on indications with $1B+ of potential incremental peak sales. For instance, **Novartis (NYSE: NVS)** gained approval of its PNH treatment Fabhalta in December 2023 after redemption of a PRV, and they intend to redeem another PRV alongside a supplemental filing for its breast cancer drug Kisqali. Also, we think **Merck (NYSE: MRK)** had possibly been contemplating a PRV redemption for BTK inhibitor *evobrutinib* prior to the failure of its late-stage Phase III programs.

Of note, **PRVs have been particularly relevant for Big Pharma in the highly competitive Respiratory Syncytial Virus (RSV) vaccine market**, although recent recommendations by the Centers for Disease Control and Prevention (CDC) may lessen the use of PRV in the RSV space going forward. In May 2023, the FDA approved **GSK's (NYSE: GSK)** Arexvy as the first RSV vaccine and it racked up an impressive $1.5B of sales in its first two quarters on the market. Shortly thereafter, in August 2023, **Pfizer** won approval for its vaccine Abrysvo. Then, playing catch-up with **GSK** and **Pfizer**, **Moderna (NAS: MRNA)** redeemed a PRV to accelerate mResvia, which then gained FDA approval in May 2024. Finally, to strengthen its position in the market, GSK redeemed a PRV alongside a supplemental filing to expand its label to patients over 50 years old, gaining approval in June 2024. The heavy use of PRVs for RSV vaccines parallels the use of PRVs in previous periods of elevated competition – i.e., **Viiv Healthcare** versus **Gilead (NAS: GILD)** in the HIV space (from 2015 and 2019), and **Novo Nordisk (NYSE: NVO)** and **Lilly (NYSE: LLY)** in the GLP-1 space (recently).

Figure 3: Breakdown of PRV Redemptions by Filing Category



Source: Bourne Partners Research; Company Announcements

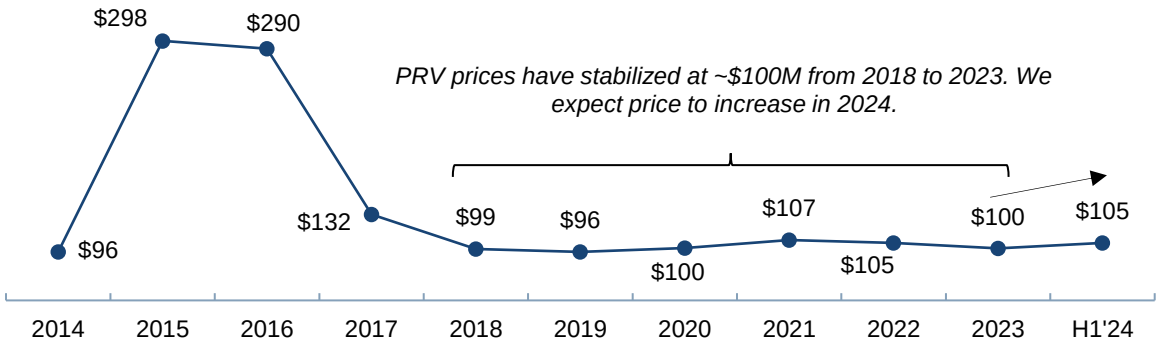
Separately, **large cap biotech companies are increasingly leaning into the program, with a large mix of redemptions for supplemental filings.** In our view, this indicates a preference to redeem PRVs for assets with more predictable launch trajectories in follow-on indications (where the $100M+ expense for the PRV is more justifiable). For instance, **argenx (NAS: ARGX)** redeemed a PRV with a supplemental filing for its key product Vyvgart Hytrulo for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP); the label expansion was approved by the FDA in June 2024. Argenx also used a PRV to expedite the initial approval of Vyvgart Hytrulo in 2023. **Vertex Pharmaceuticals (NAS: VRTX)** and **Alnylam (NAS: ALNY)** each announced plans to redeem PRVs for *vanzacaftor/tezacaftor/deutivacaftor* (for cystic fibrosis), and Amvuttra (a supplemental filing for transthyretin amyloid cardiomyopathy), respectively. Refer to **Figure 3**.

Recent Transactions Suggest Stable and Increasing Pricing

We continue to be encouraged by the relative price stability and maturity of the PRV marketplace. The average publicly disclosed PRV price has modestly increased to $105M across the four transfers in 2024 (ranging from $103M to $108M) – up from the $100M average price in 2023. Also, each of the last two awarded PRVs were sold within 35 days. This gives smaller biopharma companies developing PRV-eligible drugs visibility to potential cash proceeds from PRV sales (facilitating cash management planning). In fact, we analyzed a cohort of publicly traded biotech companies that earned and sold PRVs, and we saw minimal share price volatility prior to and after the announcement of PRV sales. Recall, in the early years of the PRV market, prices fluctuated wildly, as showcased by the

difference between **BioMarin's (NAS: BMRN)** sale for $67.5M in 2014 and **United Therapeutics' (NAS: UTHR)** sale for $350M just over a year later in 2015. Refer to **Figures 4 and 5**.

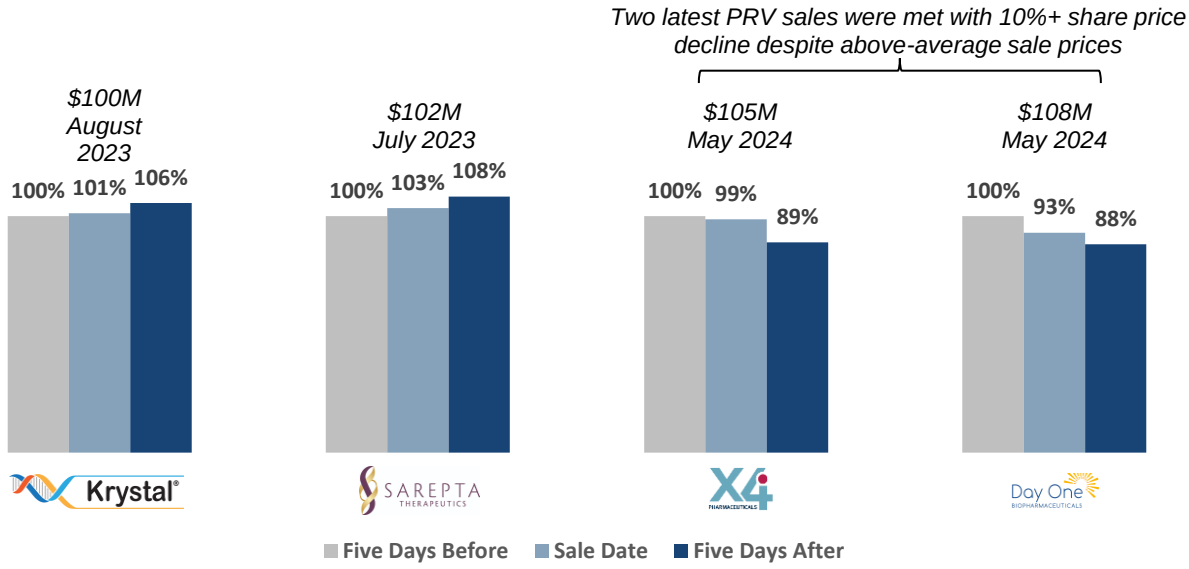
Figure 4: Modestly Increasing Pricing for PRVs with the Potential for Additional Pricing Upside Going Forward



Note: Includes certain proprietary data points that were not disclosed publicly
Source: Bourne Partners Research; Company Announcements

Of note, looking ahead, **we see the potential for upside in PRV pricing in the second half of 2024 and 2025** due to the relative scarcity of PRVs expected in 2024 (vs 2023) -- i.e., seven potentially issued in 2024 (vs 13 issued in 2023) -- in the face of strong demand from big pharma and large cap biotech sponsors.

Figure 5: Share Price Impact on Select PRV Sellers (Closing Price Five Days Before and After PRV Sale Announcement)



Source: S&P Capital IQ

Supporting Detail

Table 1: Companies That Have Received PRVs This Year

Company Receiving PRV	Date PRV Issued	Product	Indication	Pertinent Program
Orchard Therapeutics Kyowa Kirin	3/18/2024	Lenmeldy (*atidarsagene autotemcel*)	Metachromatic leukodystrophy (MLD)	RPD
Italfarmaco Private	3/21/2024	Duvyzat (*givinostat*)	Duchenne muscular dystrophy (DMD)	RPD
Day One Biopharmaceuticals (NAS: DAWN)	4/23/2024	Ojemda (*tovorafenib*)	Pediatric Low-Grade Glioma (pLGG)	RPD
X4 Pharmaceuticals (NAS: XFOR)	4/29/2024	Xolremdi (*mavorixafor*)	WHIM Syndrome	RPD

Source: Bourne Partners Research; Company Announcements

Table 2: Notable Planned / Completed Redemptions of PRVs, Where Sponsors Seek or Have Sought to Expedite FDA Review

Company Redeeming PRV	Product	Indication	FDA Review Status
Novartis (NYSE: NVS)	Fabhalta (*iptacopan*)	paroxysmal nocturnal hemoglobinuria (PNH)	NDA approved 12/5/2023
Moderna (NAS: MRNA)	mResvia (*respiratory syncytial virus vaccine*)	RSV vaccine	BLA approved 5/31/2024
argenx (NAS: ARGX)	Vyvgart Hytrulo (*efgartigimod alfa and hyaluronidase-qvfc*)	chronic inflammatory demyelinating polyneuropathy (CIDP)	sBLA approved 6/25/2024
GSK (NYSE: GSK)	Arexvy (*respiratory syncytial virus vaccine, adjuvanted*)	RSV vaccine	sBLA approved 6/7/2024
Novartis (NYSE: NVS)	Kisqali (*ribociclib*)	early breast cancer	sNDA filed in Q1 2024
Vertex Pharmaceuticals (NAS: VRTX)	*vanzacaftor/tezacaftor /deutivacaftor*	cystic fibrosis	NDA filed in Q1 2024
Alnylam Pharmaceuticals (NAS: ALNY)	Amvuttra (*vutrisiran*)	transthyretin amyloid cardiomyopathy (ATTR-CM)	sNDA submission planned for late 2024

Source: Bourne Partners Research; Company Announcements

Table 3: Recent Publicly Disclosed PRV Transactions

Seller	Date	Price ($ in millions)	Time Between PRV Award and Sale Announcement (days)
Krystal Biotech (NAS: KRYS)	8/21/2023	100.0	81
Sarepta Therapeutics (NAS: SRPT)	7/5/2023	102.0	13
bluebird bio (NAS: BLUE)	10/30/2023	103.0	N/A[1]
Valneva (NAS: VALN)	2/5/2024	103.0	87
Orchard Therapeutics Kyowa Kirin	3/18/2024	N/A[2]	N/A
X4 Pharmaceuticals (NAS: XFOR)	5/9/2024	105.0	10
Day One Biopharmaceuticals (NAS: DAWN)	5/30/2024	108.0	37

Notes: (1) bluebird bio announced an agreement to sell its PRV to Novartis for $103M, however the deal has not yet closed since the FDA has not awarded the PRV as was anticipated; (2) Orchard Therapeutics (acquired by Kyowa Kirin in January 2024) transferred its PRV to GSK upon receipt, pursuant to a prior licensing agreement
Source: Bourne Partners Research; Company Announcements

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