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Few Clouds On High-Priced, Ultra-Orphan Drug Horizon

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WITH BIOMARIN'S *BRINEURA* HITTING THE MARKET with a $702,000 annual price tag, recent experience for other high-priced rare disease drugs supports the theory that payers will accept high costs for ultra-rare pediatric disease therapies.

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Pricing has never really been an issue for rare disease drugs, given the low exposure payers have to the therapies and the significant benefits usually offered. But with ultra-orphan price tags ticking higher and higher and drug pricing a simmering political controversy in the US, it is worth checking on the experience of recent launches as **BioMarin Pharmaceutical Inc.** introduces its Batten disease therapy *Brineura* (cerliponase alfa) at just over $700,000.

Two antisense oligonucleotide therapies approved last year for different neurodegenerative conditions, **Biogen/Ionis Pharmaceuticals Inc.**'s *Spinraza* (nusinersen) for spinal muscular atrophy (SMA) and **Sarepta Therapeutics Inc.**'s *Exondys 51* (eteplirsen) for Duchenne muscular dystrophy (DMD), offer relevant case studies for the sort of reception BioMarin could face for Brineura.

Both drugs, like Brineura, were the first approval for rare, life-threatening diseases that affect children – a fact that could mean a lot to payers as companies seeks favorable reimbursement. But the Biogen/Ionis and Sarepta drugs both came to market with extremely high prices in the midst of a volatile debate over rising prescription drug prices; Spinraza costs $750,000 for the first year and $375,000 each year after that, and Exondys comes in at $300,000 annually.

And, in February, **Marathon Pharmaceuticals LLC** was set to debut its DMD therapy *Emflaza* (deflazacort) at a cost of $89,000, but abandoned the launch days later amid controversy over the price. **PTC Therapeutics Inc.** purchased the rights to Emflaza, which has been available generically overseas for decades, and has signaled it will revisit pricing. *(Also see "PTC Gambles On Success With Emflaza; Says Price Revision Is Needed" - Scrip, 16 Mar, 2017.)*

That has left lingering concerns about whether high prices would put up any roadblocks to access for Spinraza and Exondys, which would likely also affect Brineura. The companies' first-quarter sales and earnings reports, however, show that the expensive therapeutics are performing well right out of the gate.

Spinraza's Startling Success Story

Biogen reported Spinraza is off to a strong start – a performance that was unexpected given that the company was signaling a gradual uptake while reimbursement was put into place. *(Also see "Biogen Forecasts Gradual Launch For Life-Transforming Drug Spinraza" - Scrip, 26 Jan, 2017.)*

"We are still in the early days of the launch and have much more to achieve. We will not be satisfied until all of the patients and families that seek this treatment are able to receive therapy," CEO Michel Vounatsos told the firm's April 24 earnings call. "This will take some time and tremendous effort from many, such as the dedicated medical teams that treat SMA, the passionate families, the remarkable advocates that rally for these patients, and our team of committed Biogen professionals, all of whom have been working seemingly non-stop to secure access and building up point of care."

Vounatsos hinted at a couple of factors that have proven to be critical in successful rare disease launches – working with patient advocacy groups and offering a

suite of support services, including running interference with insurers. BioMarin has its own "RareConnections" support program and will work on disease awareness.

Biogen's CEO estimated that 75% of commercially insured lives in the US have a health plan with an established policy on Spinraza, and half of those have broad access. So far, the drug has been approved for individual use by 100 commercial plans, he said. As for Medicaid, 65 plans have covered use with 20 having a formal policy and half of the covered lives having broad access, he added.

There had been concerns that use would initially be limited to patients with Type 1 SMA, the form that is most severe and affects infants, though the approval covers all types in adults and children. Most Spinraza patients have been Type 1, but there has been approval for Type 2 and 3, Vounatsos said. Even in plans without a policy or with a restricted Type 1 policy, "often patients are still able to get approval through an appeal process or medical necessity request," the CEO added. Biogen also has new data from the CHERISH trial it thinks will help expand use and access.

"In the US, it continues to be our goal that no patient will forego treatment because of financial limitation or an insurance denial. To date, roughly 25% of units dispensed have been provided through the free drug program," Vounatsos said.

Outside of the US, Biogen has 353 Type 1 patients enrolled in an expanded access program "across 20 countries, of which 306 of those patients are in Europe." Spinraza was recommended for approval in the EU on April 21, though regulators called for long-term data to show sustained effect. *(Also see "Biogen's Spinraza Needs Long-Term Confirmatory Data, Says EMA" - Scrip, 25 Apr, 2017.)*

"With respect to Europe, we effectively have been putting pre-launch efforts in place on a country-by-country basis, prioritizing, obviously, those countries that we expect to get reimbursements earlier as opposed to later," CFO Paul Clancy added, including Germany, the Nordic countries and the UK. "And I think it's going to be a very similar dynamic with respect to trying to accommodate and get through infusion capacity."

The price tag hasn't been the only obstacle for Spinraza – the infrastructure for administering the drug is also a challenge. So management was clear that obstacles remain. "Insurance coverage has been and remains a bottleneck," Vounatsos declared. But "motivated families, patients, parents, advocacy groups, a professional team at Biogen, dedicated providers, the leadership of the hospital," have all been factors helping to progress the launch.

"It's a battle every day, and we are not yet where we want to be," the CEO stated.

Sarepta Winning Over Payers

Sarepta reported in its April 27 call that the Exondys launch was going well. The drug was approved after a controversial review by FDA in September 2016, securing labeling with no restrictions for age or ambulatory status, despite concerns about the efficacy data supporting the filing.

Payers initially balked at the annual price of $300,000, with some denying coverage, but the company says they have been coming around.

Sarepta reported $16.3m in first-quarter sales of Exondys 51, up from $5.5m from its short time on the market in the fourth quarter. Pleased with the launch, the company raised its full year revenue guidance from $80m to exceeding $95m.

Alexander Cumbo, senior vice president of global commercial development, said that the company continues to have productive discussions with payers and has made significant progress securing reimbursement for patients.

The mix of commercial to Medicaid carrier coverage among current patients taking the drug is about 60%/40%. Medicaid coverage continues to grow – most states take six months to review a new drug and a lot of plans put a policy in place this quarter, Cumbo said. One of the biggest ones to come on board is California, with the help of key opinion leaders (KOLs).

"California put out a policy that's very favorable. It's broad access. And they reached out to a lot of the KOLs to help design this policy. A lot of the KOLs throughout the country understand what California did and they're pushing their states to do the same. And a lot of the state plans are actually looking toward California, of how they came up with this policy. So I think it's a very positive trend to come. Obviously, we have a lot of work to do. We do have a lot more visibility heading into Q2 than we did in Q1," Cumbo said.

Much like getting patient advocacy groups involved, something Sarepta benefited from throughout the regulatory process, leveraging KOLs and mobilizing the practitioner community can be a significant factor in gaining coverage. Roger Longman, CEO of reimbursement consultancy Real Endpoints, suggested physician requests might help improve market access for PCSK9 inhibitors – cholesterol-lowering drugs that have been criticized for costing roughly $14,000 per year for a much wider population. *(Also see "Will Physician Demand For Repatha Put Pressure On Payer Restrictions?" - , 19 Mar, 2017.)*

Despite concern about payers limiting use to only the most severe patients, the experience with Exondys and Spinraza is not bearing that out. Much like Biogen reported that Spinraza is being cleared for use in patients with different levels of SMA, Cumbo noted that "both ambulatory and non-ambulatory [DMD] patients are obtaining access" to Exondys.

Cumbo also said that Sarepta has not observed issues with reauthorizations for access to the drug, which are a standard part of the reimbursement process.

Awareness matters: Sarepta reported genetic testing has been increasing and will help make for a successful launch. Biogen execs noted that a key element for Spinraza will be newborn screening for SMA.

Thinking globally, where market access can be even more difficult, Sarepta is working on distribution agreements and a managed access program in territories outside the US and expects those agreements to be finalized in the coming months.

CEO Edward Kaye announced during the call that he is resigning as president and CEO when his current employment term ends this year in order to "focus on the next series of key initiatives for Sarepta." These include approval of Exondys in Europe and development of next-generation therapies for DMD, such as gene therapy – a category of treatment that's also likely to ring pricing alarms.

Kaye said that he will be helping recruit a candidate for the position of president and CEO, and will then serve as an active board member and special regulatory and scientific advisor.

Of course BioMarin, a pioneer of enzyme replacement therapies, is no stranger to rare diseases or high cost therapies. The company helped establish the orphan drug business model, giving presentations over the years about the financial benefits of low development costs relative to pricing for rare disease drugs. *(Also see "Orphan Drug Economics: What's The Right Price For Rare Disease Drugs?" - Pink Sheet, 15 Nov, 2013.)* But even though there's experience and evidence behind Brineura, it's not just the payer climate that sponsors must be wary of – the political climate is still poised for change.

President Donald Trump has repeatedly called out the biopharma industry for high drug prices, notably accusing pharma companies in January of "getting away with murder," and the populist president is expected to return to the issue at some point during his term. *(Also see "Trump Throws Pharma A Curve Ball On The Third Day Of J.P. Morgan" - Scrip, 12 Jan, 2017.)*

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