Orphan disease specialists find home with Big Pharma

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Tumbling over the patent cliff, many big pharma companies are being forced to find new strategies for sustaining sales growth, wherever possible minimising the risk of generic competition. One of the sectors often cited as an opportunity for this is orphan drugs, where companies are provided incentives to develop drugs for these rare disorders, which might otherwise be less commercially viable. The biggest and most pertinent benefit clearly being the guaranteed seven-year exclusivity period. Unsurprisingly then, Big Pharma (companies with branded prescription pharmaceutical sales in excess of $10bn) has bought into orphan drugs in a major way, most notably Sanofi with its acquisition of Genzyme.

Indeed, Big Pharma now has the lion’s share of the orphan drugs market, as 77% of approved orphan drug sales in 2011 are derived from Big Pharma players. The implications of this are two-fold: in recent years, Big Pharma has been shifting away from the primary care blockbuster model while placing greater focus on specialty sectors and personalized medicines targeting smaller patient populations with high value drugs. Consequently, many established companies have turned to deal-making activity with specialist players in an effort to secure promising pipeline candidates.

M&As have played an integral strategy for Big Pharma’s expansion into the orphan drug sector, traditionally a field dominated by small biotech companies. M&A has provided a rapid entry route into this niche sector, enabling companies to secure valuable drug candidates, manufacturing capabilities and highly specialized sales forces. In fact several companies have already undertaken this strategy. Again, this is perhaps best exemplified by Sanofi’s acquisition of Genzyme, a global leader in lysosomal storage disorder (LSD) enzyme replacement therapies. Through this deal (completed in April 2011), Sanofi is now positioned as a prominent player in the orphan drug sector, with a solid position in Gaucher’s disease (Cerezyme, imiglucerase alpha), Fabry’s disease (Fabrazyme, agalsidase beta), and Pompe disease (Myozyme, alglucosidase alpha). Genzyme represents a key acquisition for Sanofi, significantly accelerating its broader diversification strategy whilst also providing a platform for long term revenues.
Similarly Roche’s acquisition of Genentech allowed the combined company to become the leading player in the lucrative oncology market. Roche can be credited as the first Big Pharma company to target the emerging monoclonal antibody market: in 1990, Roche acquired a 56% stake in the US biotech for $2.1bn, and subsequently purchased the remaining 44% shares in March 2009 for $47bn. As a result, Roche secured MabThera/Rituxan (rituximab), with orphan drug approvals in non-Hodgkin’s B-cell lymphoma (NHL), chronic lymphocytic leukemia (CLL), as well as for the treatment of patients with Wegener’s Granulomatosis and microscopic polyangiitis. Thanks to its indication expansion strategy, MabThera/Rituxan became the first monoclonal antibody to generate blockbuster sales and prove commercially successful in the oncology market. Subsequently, in February 2006 MabThera/Rituxan gained FDA approval in the larger non-orphan indication of rheumatoid arthritis, further expanding its patient population (of note, rheumatoid arthritis sales are not included in this analysis). Through Roche’s acquisition of Genentech, the Big Pharma player also secured Herceptin (trastuzumab), which gained its first FDA approval in September 1998 for HER2-positive metastatic breast cancer (non-orphan indication), and in October 2006 its indication was expanded for the treatment of HER2-positive metastatic stomach cancer (orphan indication).

Going forwards, however, several orphan drugs marketed by Big Pharma companies are to experience a slowdown in sales growth: with brands becoming more mature, these will face intensifying competitive pressures, largely from novel brands but also from biosimilars to a smaller extent (in the monoclonal antibody landscape in ex-US markets). Indeed Big Pharma players have not been shy in stating their interest in M&A activity, searching for the next wave of promising orphan drugs of the future. For example, in January 2012 Merck & Co. stated to be searching for acquisition targets (Grogan, 2012). In July 2012 Novartis announced its interest in bolt-on acquisitions, rather than a large purchase (Bennett, 2012). In October 2012 AstraZeneca followed suit, when it was rumored to be on the lookout for new deals to boost its mid-stage pipeline.

As illustrated in Figure 1, companies with a below-average net orphan drug sales difference (2011–17) are largely Big Pharma players such as Merck & Co., Novartis, and AstraZeneca. Datamonitor expects these players to eye
more deals in the orphan drug arena, and may even undertake intense bidding wars to secure lucrative assets. And with the US National Institutes of Health (NIH) listing nearly 7,000 rare diseases but only about 200 of these have approved therapies, there is still room for pharma to expand in this sector. Indeed looking outside the Big Pharma peer set, it is notable that collectively Datamonitor’s Mid Pharma (companies with branded prescription pharmaceutical sales totaling less than $10bn) and Emerging Pharma peer sets are forecast higher sales growth ($6.6bn) over 2011 to 2017 than Big Pharma’s orphan drugs portfolio ($4.4bn).

**Net orphan drug sales difference, by company ($m), 2011–17**

In light of these factors, and Big Pharma’s acquisitive tendencies – even if the era of mega-mergers is truly behind us – many of these Mid and Emerging Pharma companies represent plausible takeover targets for Big Pharma.
Indeed, eight companies particularly stand out as attractive candidates, purely from a sales growth perspective: Celgene, Allergan, Shire, Alexion, BioMarin, UCB, NPS Pharmaceuticals, and Vertex.

These eight companies would be within the reach of Big Pharma, although the most costly of the selection would be Celgene and Allergan, which currently have market caps of $32bn and $28bn, respectively. An interesting metric is to take each of the company’s 2011-17 sales growth from orphan drugs, and drive out a ratio (compared to its market cap figure). In doing so, the stand out target for acquisition would be NPS Pharmaceuticals, which has an orphan drug sales return quotient of almost 89% (the value of the company’s current market cap being generated by orphan drug sales by 2017).

In fact, when assessing the other quotients from the above group, two cluster of similar performing companies are evident: Vertex (7.9%), Celgene (7.8%), BioMarin (7.0%), Alexion (6.6%), Shire (4.7%), and on the lowest end: UCB (2.9%) and Allergan (1.6%).

Given that the average acquisition carries with it a control premium of 20–50% (the amount the buyer is willing to pay over the market cap at the time of acquisition), this would position the likes of Celgene and Shire as pricey acquisitions, for moderate returns. Whereas the likes of Vertex and Alexion would be less costly, for an expected higher orphan drug sales return.

With Sanofi having splashed the cash in 2011 for Genzyme and with Pfizer’s acquisition of FoldRx in 2010, coupled with the rumored takeover of BioMarin in June 2012, further deal-making activity is on the horizon, and needless to say, it will have an exciting premium.