IN brief

Baxter carves out biopharma division

Following the recent path of other diversified healthcare firms, Baxter is splitting its biopharmaceutical operations from its medical products division. The newly formed drug business will retain a portfolio consisting mostly of treatments for hemophilia and other bleeding disorders. The restructuring will also allow the Deerfield, Illinois–based company to focus on opportunities to innovate in hematology, oncology and biosimilars—areas where Baxter has recently begun to invest. Baxter's lead drug product is Advate, a full-length, recombinant factor VIII for treating hemophilia, which accounts for about 15% of its pharmaceutical business. It also sells an extended half-life (pegylated) version of the molecule, Bax 855, and other blood factors and biotherapeutics. But it has been branching out, too. In April, Baxter obtained a phase 1 gene therapy for hemophilia B by acquiring collaborator Chatham Therapeutics, of Chapel Hill, North Carolina, for $70 million upfront. In November 2013, Baxter paid $60 million upfront for rights to Seattle-based Cell Therapeutics' small-molecule pacritinib, now in late-stage trials for treating the bone marrow disorder myelofibrosis. Two months earlier, it inked a deal with Coherus Biosciences in Redwood City, California, to develop a biosimilar version of Enbrel (etanercept) in Europe, Canada, Brazil and other markets, a program now advancing to phase 3 trials. Baxter is also working with Cambridge, Massachusetts–based Momenta Pharmaceuticals to develop biosimilars (none have entered the clinic: two anti-inflammatory compounds are preclinical). Baxter also holds European rights to the Newtown, Pennsylvania, biotech Onconova's rigosertib, which recently failed a phase 3 trial in severe myelodysplastic syndromes and is also in late-stage trials in pancreatic cancer. The decision to carve out its biopharma division, announced in March and expected to be completed next year, took analysts by surprise, given management's previous assertions supporting a diversified medtech company model. That said, Baxter has made similar decisions in the past, having spun out cardiovascular device specialist Edwards Lifesciences in 2000, its Allegiance hospital supply business in 1996, and the at-home intravenous drug and nutrition services unit Caremark in 1992. The current spinoff, however, is the first aimed at bolstering the company's biopharmaceuticals development. The move mirrors those of fellow Illinois medtech company Abbott Laboratories, in Abbott Park, which spun out its pharmaceutical operations (as AbbVie) in 2013, and Dublin-based Covidien, which separated its pharmaceutical business Mallinckrodt, also last year. They are "comparable examples where shareholders benefitted from a separation with divisions that had divergent end-markets, customers, capital needs, risk profiles and interested investor bases," commented analyst Danielle Antalffy of Leerink Research in Boston. *Mark Ratner*

founder of Burgedel, Germany–based life science consultancy IMI, says, "It would be very different if this was a first-in-man study," adding that it is unlikely that Josh Hardy would have been exposed to an experimental drug where the potential toxicity was unknown. Brea-Krüger played an instrumental role in managing the fallout from Würzburg-based TeGenero's phase 1 crisis in 2006 (*Nat. Biotechnol.* **24**, 475–476, 2006).

But the incident demonstrates the difficulties these issues can present to CEOs attempting to shepherd products through to approval with limited resources. As Kenneth Widder, a partner at San Francisco–based Latterell Venture Partners, notes, the Hardy situation diluted the control the CEO should have over the use of his company's drug. Social media pressure brought about an acceptable outcome—the open-label pilot trial—but Moch was in a difficult position. He had to reverse a prior decision and could have jeopardized a critical clinical program if a serious adverse event or a drug-related fatality resulted.

Despite talk of creating a new system in which the burden of deciding who qualifies for compassionate use is managed by an independent third party, Widder believes the decision should rest with the company. "Having some independent party dictate how you prosecute the development of your drug, that puts the company at risk," he says. And it does so in a way that probably wouldn't take into account factors like cash availability, the company's ability to divert resources, previous data obtained with the agent in a similar setting and aspects of pediatric dosing.

Investors will likely consider these factors in evaluating companies focused on life-threatening diseases. A potential repeat of the Hardy situation changes the risk profile of these companies. But the real risk, says Widder, is that a drug may be co-opted, under compassionate use, in an indication different from the one pursued by the company.

Marc Blaustein, CEO of pediatric rare disease specialist Dart Therapeutics in Cambridge, Massachusetts, thinks the spat may help stimulate interest in catastrophic diseases by demonstrating that there is high demand from patients and families, and broad public support for making these drugs available. Herndon, too, does not expect that investors will stay away from these companies because of a concern about red flags arising from compassionate use. Instead, she questions how the Hardy controversy will affect the plans of companies and their backers going forward.

Without a change in government policy, companies would do well to build compassionate use into their clinical programs in phase 2, and start collecting data on those patients, regardless of age. Larger, well-capitalized companies typically have compassionate use programs in place early on, with a website, a video and individuals to contact. Smaller, cash-constrained companies often do not.

Tony Russo, CEO of life science PR firm Russo Partners in New York, urges companies to have compassionate use policies clearly stated on their websites, although he acknowledges that, for smaller companies, "the thought of adopting a crisis plan is often not on their radar screen." A partial solution, particularly in the era of social media, is to recruit more patients into randomized, placebo-controlled trials to preempt compassionate use requests. The maintenance of online patient communities by organizations like PatientsLikeMe or the Digital Patient Unit of Quintiles is one way of improving recruitment.

An important outcome from Chimerix's experience is that companies in a similar situation might seek to defuse a media blitz by working with FDA to quickly start up an open-label pilot trial. Blaustein sees the incident as illustrating that "when companies and FDA work together, there are creative mechanisms to accelerate availability of these drugs." The drawback to an expanded access open-label protocol, Widder notes, is that although such trials may advance knowledge of the drug's safety profile, "the outcomes from that kind of study aren't really highly respected."

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Another issue is whether a company, particularly a small company, has the capacity to deal with a bump in demand that can result from such requests. Capitulating to Hardy might have opened a floodgate of individual requests. Chimerix's former CEO Moch was reported to be in favor of a more equitable way of distributing the drug, providing it in a supervised setting to a modest number of qualifying patients. Moch was replaced in his role by former chief medical officer Michelle Berrey. The reasons for his resignation are unclear, but weathering the dark side of social media possibly took its toll.

Michael Goodman *New York*