Big pharma moves from 'blockbusters' to 'niche busters'

Since its passage in 1983, the US Orphan Drug Act has led to the approval of more than 350 drugs for around 200 rare diseases, mostly thanks to small biotech startups looking for a unique niche in the marketplace. Yet with the demise of big pharma's traditional business model, some of the world's largest drug makers are aggressively entering the rare disease sector.

"There's a trend toward the death of the blockbuster, so people are moving toward the niche buster," says Christopher Milne, associate director of the Tufts Center for the Study of Drug Development in Boston.

The latest company to enter the orphan market is New York–based Pfizer, which in June announced the creation of a new research unit devoted to developing and commercializing new biologics to treat rare diseases. The move follows GlaxoSmithKline's February announcement that the London-based firm was forming a similar stand-alone unit. Other companies, including the Swiss drug maker Novartis and Indiana's Eli Lilly, have made similar investments.

"It's the industry saying, 'where is there an unmet need, and how can I address it?'" says Edward Mascioli, who is heading up Pfizer's new unit, based in Cambridge, Massachusetts.

According to Milne's calculations, the share of orphan product approvals in the US by large biopharma grew from 35% ten years ago to 56% in 2006–2008, the last years that records were kept (*Tufts CSDD Impact Rep*. **12**, 1–4, 2010). Milne also found that only four orphan drugs were among the top 200 bestselling medications in the US a decade ago; by 2006–2008, the number had quadrupled to 16 orphan products, with annual sales ranging from $200 million to nearly $2 billion each.

With drying drug pipelines and increasing generic competition, the orphan drug sector offers several attractions for pharma. It provides tax credits on clinical trial expenses, grant funding from the US Food and Drug Administration (FDA), seven years of marketing exclusivity after an orphan drug is approved and a waiver of user fees. "The economics are much more attractive for rare diseases than they were in the past," says Usama Malik, Pfizer's head of business innovation. What's more, orphan drugs are often given high price tags to help recoup costs within the small market, which further boosts pharma's bottom line.

> "Society is turning away from us and saying, 'this is a raw deal'."

Beyond profitability, pharma's shift toward rare diseases also helps in the court of public opinion, notes Bernard Munos, a former advisor on corporate strategy for Eli Lilly (who retired last month). With few new drug entities emerging from the industry's pipeline, and more than 6,000 diseases affecting an estimated 25 million Americans still without a therapeutic option, "society is turning away from us and saying, 'this is a raw deal; this is not the covenant that we agreed to,'" Munos says. "Ultimately, the acid test of success for the industry is our impact on public health."

To complement the private sector, federal agencies are also searching for new ways to bolster research into orphan products. In March, for example, the FDA created the Rare Disease Review Group (which held its first public hearings this summer), and the regulatory agency has teamed up with the National Institutes of Health to run a rare disease investigator training course, scheduled for October. At the two agencies' request, the Institute of Medicine is also conducting a review of national policy for rare disease research and product regulation; recommendations are due next month.

Elie Dolgin

Advocates to bring rare disease philanthropy under one umbrella

NORTH BETHESDA, MARYLAND—Rare diseases, defined in the US as those occurring in fewer than 200,000 people in the country, collectively affect around 10% of individuals worldwide. Yet the majority of the public can hardly name a single rare disease. As a result, most orphan disorders fall under the radar and remain poorly funded.

Patient advocacy groups are one of the primary backers of research into rare diseases. But the hundreds of disease-specific foundations and organizations out there rarely work together to raise funds, and the rare disease landscape has remained fractured and siloed. To remedy the situation, the R.A.R.E. Project, an initiative launched in 2008 to raise awareness and accelerate the development of therapies for rare diseases, is rolling out a new platform to serve as a one-stop shop for innovative research into all 6,000-plus rare diseases.

"We're trying to bring new people in to care about rare disease," says Nicole Boice, founder and president of the Children's Rare Disease Network, part of the R.A.R.E. Project. "The idea in fact is that we will stimulate foundations to think differently about funding and research," adds R.A.R.E. Project CEO Jonathan Jacoby.

Modeled after services such as Kiva and Save the Children, where donors can precisely match their contributions to the specific project of their choice, R.A.R.E. is launching a website, called the Global Genes Fund, intended as a clearinghouse for rare disease philanthropy, where people can select projects to fund. Jacoby hopes that by bringing hundreds of research projects under one umbrella, individuals, foundations and corporations will be more likely to donate to multiple causes.

Last month, R.A.R.E. secured $50,000 for a beta version of the site, which the organization plans to make public later this year, Boice and Jacoby announced here at the Genetic Alliance annual conference on 16 July.

For projects listed on the page—which will be vetted through some as yet undefined criteria—supporters will be able to read an affected child's personal story, the details of the study and why the research is important, among other details.

"The challenge with rare diseases is that they're rare, and there aren't that many families that can raise money," says Geraldine Bliss, research chair of the Phelan-McDermid Syndrome Foundation. "A concept like [the Global Genes Fund] is really great because it allows you to reach beyond your immediate circle of support."

"The rare disease community is large enough and deserving enough to have an effort like this and to succeed at it," Boice says. "It's time, it's really time."

Elie Dolgin