

Search and development

In an effort to rein in costs and galvanize its discovery effort, Merck is following the industry vogue for externalizing early-stage R&D. Is it going to cast its net far and wide enough?

In recent weeks, the magnitude of reorganization in Merck's R&D operations has come into full focus. As well as cutting in-house research by a whopping \$1.25 billion in the coming year, the New Jersey-based pharma plans to establish four new 'innovation hubs' in Boston, San Francisco, London and Shanghai. These centers will serve as regional bases for a network of scouts aiming (among other things) to seek out local faculty working on promising new biology that can form the basis for innovative drug-discovery programs. The hubs will be in direct competition with the innovation centers of several other pharma companies already established in the same locations. The question is whether Merck, or any other pharma company for that matter, will find enough good ideas—especially if many companies are looking under the lampposts of the same academic institutions? In the coming years, the success of the search and development strategy is likely to depend on reaching the widest possible pool of researchers across the globe.

Merck's restructuring of operations involves 8,500 layoffs, a refocusing of the pipeline on fewer therapeutic areas and the sale of several internal compounds, including experimental therapies against glaucoma, psychiatric disorders and male infertility. The rationale for these cuts is the same across the industry and runs something like this: investors face dwindling earnings as a result of blockbuster products going off patent, ineffective in-house research programs and spiraling R&D costs. The management's response is to reduce headcount; maximize outreach to the academic community; outsource 'non-essential' research, clinical and manufacturing functions; and rationalize discovery programs to move products quickly into proof-of-concept human testing and kill duds quickly.

Merck's overhaul appears to tick many of the above boxes. But compared with strategies of some other companies, the emphasis on external academic collaboration is perhaps more surprising, given the company's tradition of in-house research excellence. Companies like Pfizer have made great fanfare about academic collaborations (e.g., its Centers for Therapeutic Innovation in San Francisco, New York, Boston and elsewhere), but it is not so widely appreciated that Merck has been quietly engaging in hundreds of research collaborations with academic institutions every year. Indeed, Merck's scouting system has long been a staunch supporter of SciCafés, academic partnering events hosted by *Nature Biotechnology* and *Nature Medicine* (*Nat. Biotechnol.* 27, 869, 2009).

So why does Merck need to adopt an innovation hub model when Pfizer, Johnson & Johnson, GlaxoSmithKline and Bayer already have similar initiatives in the same places? The answer is that it cannot afford not to. Academic collaborations are the earliest facet of many types of deals in preclinical research that Merck scouts must pursue, but the latter must also work with the investment and management teams that support early-stage ventures, and these teams are primarily located in Boston and San Francisco. It makes sense for a company to establish a base of operations in an area where it can access both academics and startups.

At the same time, it is clear that there are great numbers of promising translational researchers outside of these clusters. Data gathered from *SciBX*, a joint venture from *BioCentury* and Nature Publishing Group that systematically identifies papers of translational interest, illustrate the problem. Boston area-based institutions produce about twice as many translational papers as those on the West Coast. But New York is not far behind Boston. And researchers at institutions in Texas or in southern California also produce as many papers as those in northern California (including San Francisco, Berkeley and Stanford). Similarly, although the UK translational research outstrips European output, Germany, France and Switzerland are not far behind. And in Asia, although China dominates, Singapore, Taiwan and South Korea all have substantial output. So a key challenge for any search and development strategy is to provide enough scouts to identify and reach all these researchers, particularly when many papers supporting new target mechanisms appear not in 'luxury' journals like *Nature*, *Science* and *Cell* but in journals with lower impact factors.

As companies increasingly look for collaboration opportunities at earlier and earlier stages, the skill sets of existing scouts may also become obsolete. Scouts that spent most of their time in previous decades negotiating deals with startups or bigger companies might not be equipped with the requisite scientific knowledge to connect with academics. For this reason, and to ensure that collaborations remain on track, it will be very important that there is close (even direct) and frequent involvement of internal R&D staff working on pipeline projects with external academics.

What's more, greater emphasis needs to be placed on junior faculty rather than senior academic key opinion leaders. Compared with assistant and associate professors, key opinion leaders are easier to identify and have star power. But in traditional clusters, these individuals can end up completely oversubscribed by industry and investors alike.

A final issue with so many companies going after (and sharing) the same, limited pool of academic investigators is confidentiality. In recent years, companies have become less secretive about their preclinical research; indeed, GlaxoSmithKline's new Immuno-Oncology Consortium exemplifies the newfound openness—the pharma company is partnering with six cancer centers so that affiliated academics can view and evaluate the company's nonpublic early-pipeline programs.

Thus, an effective search and development strategy will depend not only on an adequately resourced scout network but also on continued support for in-house R&D expertise; strong internal discovery groups are essential for effective external academic collaborations—a fact perhaps lost on some cost-cutting executives. Given the rudimentary state of most of our biological knowledge and the poor predictability of early-stage projects, casting the net as wide as possible will be a key ingredient for success. As George Merck famously noted half a century ago, "That's serendipity, and our business is full of it." 