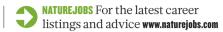
CAREERS

TURNING POINT Molecular biologist tells how he's held on to his grant for 30 years **p.283**

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PHARMACEUTICAL SECTOR

Delicate transition

With lay-offs rife in the drug industry, life scientists and chemists are seeking fresh career paths.

BY CHARLOTTE SCHUBERT

ocals were irate when the drug giant Pfizer closed its 70-hectare research and development (R&D) facility in Ann Arbor, Michigan, in 2007. T-shirts sporting the word 'Pfired' appeared on the streets; the governor called the lay-offs a "punch to the gut"; and

the state of Michigan pledged US\$1 million to help the 2,100 displaced workers find new jobs.

The pharmaceutical industry has faced major upheaval in recent years, with a disappointing drug pipeline, major revenue losses as patents expire on blockbuster drugs, and a spate of mergers and acquisitions. From 2006 through to the first quarter of 2012, some 263,000

positions have been eliminated from major pharmaceutical and large biotechnology companies, says Kenneth Getz, a senior research fellow at the Tufts Center for the Study of Drug Development in Boston, Massachusetts. R&D operations have accounted for 7–10% of the lay-offs since 2008, which have been only partially offset by new hiring, endangering what was once a stable source of jobs for life scientists and chemists.

But despite such convulsions, there are positive signs in the job market. In the Ann Arbor region, dozens of contract-research organizations (CROs), many founded by former Pfizer employees, offer outsourced services ranging from medicinal chemistry to toxicology testing. The abandoned Pfizer facility has been reborn: the University of Michigan bought it and now uses some of it as research facilities and rents out another part to Lycera, a biotechnology spin-off from the university that partners with pharmaceutical company Merck and employs some former Pfizer scientists.

"What we are seeing in front of our eyes is the slow-motion implosion of the big pharma companies as we know them, and the rebirth of the industry with different models and in different forms," says Bernard Munos, founder of the InnoThink Center for Research in Biomedical Innovation in Indianapolis, Indiana.

Researchers looking for work in this environment need to adapt their skills to an industry in flux, says Munos, and consider how to use their experience to secure a new type of job. They should also be aware that laid-off researchers may have to take jobs at lower salaries at CROs or biotechnology start-ups, or in other industries. In short, to weather the cuts — which show no signs of abating — pharma employees and new graduates "are going to have to hustle", says Munos.

R&D BREAKDOWN

In the face of declining pharmaceutical revenues, a variety of strategies has emerged to increase productivity and decrease costs. Companies such as GlaxoSmithKline, headquartered in London, have broken up research departments into smaller, more nimble units, and many firms are outsourcing R&D that would once have been done in-house. Meanwhile, research areas have been cut back. For example, Novartis, based in Basel, Switzerland, has reduced development of drugs that affect the central nervous system, considered a high-risk, expensive field (see *Nature* **480**, 161–162; 2011).

Firms, including Novartis, are shifting

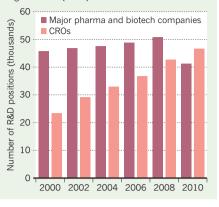
operations to areas such as Boston, where they can mine academia and biotech companies for early-stage discoveries, and China, an emerging market with a growing scientific workforce. Outsourcing may account for much of the net workforce reductions over the past several years, which occurred even as total investment in R&D by major pharmaceutical and biotechnology companies increased. An estimated 41,275 workers were employed in pharmaceutical- and biotechnology-industry R&D worldwide in 2010, down from 50,750 in 2008, according to the Tufts Center (see 'Outsourcing on the rise').

The closures affect all workers, from laboratory heads to technicians. But some jobs seem to be more vulnerable than others. When Pfizer, which is based in New York City, laid off employees in Ann Arbor, it offered jobs to hundreds of them at other locations. Most were scientists with transferable skills, such as computational biologists, or worked in hot areas such as oncology, says John LaMattina, who oversaw the lay-offs as head of global R&D at Pfizer and is now a senior partner at Puretech Ventures, a life-sciences venture-capital company in Boston. Specialists in waning fields are often most vulnerable, he says.

Bench scientists who work in the earliest stages of drug research may also be at high risk, as many pharmaceutical companies turn to academia and biotechnology companies for leads. "Major R&D organizations within big pharma have just been slashing without a lot of regard

OUTSOURCING ON THE RISE

As pharma downsizes, contract-research organizations (CROs) have added workers.



in drug discovery," says John Archer, founder of Catalyst Advisors in New York City, which recruits executives for pharmaceutical and biotechnology companies. People who work in clinical research and regulatory affairs seem to be better buffered from lay-offs, he says.

STAYING AHEAD

It is difficult to trace where the jobs are going, but a lot of people do manage to find work. In the United Kingdom, for instance, about 2,000 chemists at pharmaceutical companies were laid off last year, estimates Charlotte Ashley-Roberts, a careers adviser at the Royal Society of Chemistry, based in Cambridge, UK.

More than 85% found jobs within three months, and 60% in chemistry. "You are starting to see a whole different cadre of opportunities," says John Arrowsmith, a life-sciences adviser at Thomson Reuters in London.

Many former pharmaceutical researchers are heading to CROs (see 'Prepare and contrast'), which have been growing steadily in the United States, Europe, India and China in recent years (see Nature 466, 280-281; 2010). In 2010, 46,550 people were employed in R&D at CROs worldwide, up from 42,687 in 2008, estimates the Tufts Center.

People with skills beyond bench work are moving into consultancy, as experts in areas such as regulatory affairs, clinical-trial management and biostatistics (see 'Use your skills'). But there are no hard numbers on who is taking this route — or on how many consultants are effectively underemployed.

Yet other workers are retooling their skills for related industries that remain strong, including development of medical food (such as 'gut-healthy' yogurt), medical-device engineering and biomanufacturing, says Clifford Minz, founder of BioInsights, a career consultancy in Princeton, New Jersey. Patent specialists and medical writers are also in demand, he adds.

THE GREAT LEAP SIDEWAYS

Alex Flood is a former pharma researcher who has successfully made the transition to one growing niche sector: non-profit work. He "cut his teeth" at Wyeth and weathered that company's 2009 buy-out by Pfizer, but for many years he had aspired to a job in public health. Since 2010, he has been employed at PATH, a global-health non-profit organization in Seattle, Washington, where he works on vaccine stabilization — by, for example, devising ways to keep vaccines fresh over time. To find new work, "you have to be flexible", says Flood, who adapted his pharma training to his new job.

Peter Corr, co-founder of Celtic Therapeutics, a private-equity drug-development firm in New York City, hires senior and junior pharmaceutical professionals with a wide range of experience, from outsourcing to finance. He was head of science and technology at Pfizer until 2006, and says that it helps if candidates have an understanding of the whole drug-development pipeline. "Spend some time in your off hours in other parts of the company," he advises potential applicants. For example, bench scientists should expand their skill sets by learning about regulatory affairs or business development. Being open to relocation also helps, says Archer, given the geographic shifts in the industry.

The best candidates show passion for what they do and have taken on challenges, says Corr. "You see people who are moving to gain new experiences," he says. "These people are constantly stretching themselves." ■

Charlotte Schubert is a freelance journalist based in Seattle, Washington.

INTO CONTRACT RESEARCH

Prepare and contrast

Contract-research organizations (CROs) are increasingly taking on tasks previously done within the pharmaceutical industry, from clinical-trial management to medicinal chemistry. Many former employees of big pharmaceutical companies are moving to CROs — and liking it. "I thought the environment was going to be significantly different," says Jim Kremidas, who made the leap in 2008. But the change "was not as traumatic as I thought it was going to be".

Kremidas had spent more than 20 years in various jobs at Eli Lilly in Indianapolis, Indiana, culminating in a role as head of patient recruitment. But as the company downsized in preparation for patent expirations, he accepted a severance package. Knowing what lay ahead, Kremidas had time to prepare.

Before his retirement, Kremidas began developing his contact network. He also took on speaking engagements through the Drug Information Association, an international industry trade group based in Horsham,

Pennsylvania. The exposure helped to build his reputation as a leader in patient recruitment, he says, and in 2008 he was offered a job doing just that at Quintiles, a CRO based in Durham, North Carolina. This February, Kremidas became head of market development for digital patient recruitment at the firm, using the Internet and online patient databases to gather volunteers.

Kremidas advises pharmaceutical employees who are worried about lay-offs to broaden their experiences to prepare themselves for a variety of future challenges. "I knew I had a skill set that was needed in industry, and Quintiles seemed like a logical place for me to land," he says.

Pharma and CRO work have similarities, but Kremidas says that CROs require employees to be more flexible and nimble: "You have a lot of different customers who have a lot of different ways of doing things." Some customers micromanage, whereas others let the CRO researchers make their own decisions. "They respect your opinions and it's more collaborative," he says. C.S.

CONSULTANCY

Use your skills

In many ways, Beat Widler was ideally placed to start a consultancy. He had spent decades in regulatory affairs and clinical research at Roche, the pharmaceutical firm based in Basel, Switzerland. Most recently, he was global head of clinical quality, ensuring that clinical trials protected human subjects and maintained data integrity. Now, he is a consultant in the same area.

Working out of his home in Zug, Switzerland, Widler takes advantage of a network of contacts in the pharmaceutical industry, contractresearch organizations and regulatory agencies. Even so, setting up a company was risky. "If we are able to break even this year we can be extremely proud of ourselves," he says.

Widler had been thinking for years about starting a company. When Roche offered him an early-retirement package in 2011, he took the plunge, setting up Widler & Schiemann with former Roche colleague Peter Schiemann this year.

Widler says that the shifts in the industry are making it easier for former pharma employees to set up shop, as big companies and small biotechs turn to an outsourcing model with low overhead costs. And cost pressures are leading companies to rely on experts to help them trim the fat from their clinical trials, while keeping standards high.

Widler's network includes connections at professional organizations such as the European Forum for Good Clinical Practice in Brussels and the Drug Information Association, based in Horsham, Pennsylvania, where he has served on committees and given talks. That experience, he says, helped him to build his reputation and meet clients.

Without the infrastructure of a large organization, Widler has had to adapt. For example, he spent hours creating the template for a form for auditing a client. "You do everything from scratch. It's pretty intense, but it's pretty fun," he says.

He has no regrets and remains optimistic, but is mindful of how long his personal funds can last while he builds up his business. "Be very realistic about finances," he says. "It is critical to do your homework." C.S.

TURNING POINT Jim Hoch

In April, Jim Hoch, a molecular biologist at the Scripps Research Institute in San Diego, California, celebrated the ninth renewal of the grant supporting his study of bacterial signalling proteins. Here, he reflects on how his efforts to unravel sporulation led to a threedecade US National Institutes of Health (NIH) grant — one of the longest-running at Scripps.

How did your research get started?

I came to Scripps after an NIH-funded postdoc at the Molecular Genetics Centre in Gif-sur-Yvette, France, where I learned about mapping genetics in bacteria. Once here, I applied the technique to begin to sort out the mechanisms that trigger sporulation, the process by which bacteria or fungi suspend their growth to form tough, seed-like spores. Since we started, my team and I have learned about the genes and proteins involved, but we are still piecing together how it works. The signalling mechanisms are a mess to unravel.

Was your first grant, to study the bacterium *Bacillus subtilis*, a turning point in your career? I owe my career to this grant from the US National Institute of General Medical Science. I've been told that you should have several grants, but I had just one that I bundled everything into. If I had lost that grant at any renewal, I would have been dead. The renewal process is fairly traumatic, but it has motivated me to work hard each grant cycle. Because Scripps started hosting graduate students only recently, I have employed technicians, various undergraduates and some postdocs. And we managed to do pretty amazing things.

How have modern technologies influenced your research?

The evolution of technology has driven the experiments. I started with genetics, but molecular cloning and DNA sequencing changed everything — letting us find out about the proteins encoded by the genes. Using biochemistry, we could work out their functions. From there we used crystallography and nuclear magnetic resonance to establish the structure of the proteins. Most recently, we have been working with statistical physicists to determine how these proteins interact. Every year is a complete learning process — a quantum leap from one technology to the next. It has been a hell of a journey.

How have NIH requirements changed?

Proposals used to be more than 20 pages long, and the study sections that review grants lasted for three days. Now, proposals are 12 pages,



study sections last one day and half of the applications, the less-impressive ones, are not even discussed. There is a lesson here. Applications of 12 pages need to be clear and concise to make them understandable outside the field. Most importantly, they need to be exciting to read. A proposal needs to have clearly articulated goals that transmit your excitement.

Have you ever thought that your grant wouldn't get renewed?

It has become more difficult over the years; there is more competition. I was worried in the latest round. I broke my leg and was recovering for a year. Normally, I have five or six publications a year, so that every four years, when it is time for renewal, I have 20–25 papers showing my progress. I didn't have that this time, but I squeaked by with a few good papers in good journals.

Your career has been mostly in basic research. Have there been any interesting applications?

There have been some spin-offs. When I first came to Scripps, I was working on genes involved in the hyperproduction of proteolytic enzymes. One of my postdocs ended up as an executive at the biotechnology company Genentech, based in South San Francisco, California. He recognized that proteases could be important in the production of detergent. The proteases in most US soaps come from different species of *Bacillus*, and from some hyperproduction genes that we discovered. A company was spun off: Genencor, which is now owned by Dupont. It has produced more than US\$1 billion's worth of enzymes. ■

INTERVIEW BY VIRGINIA GEWIN