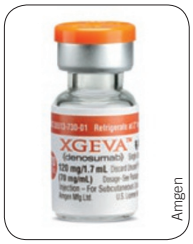
IN brief

Amgen's bone-metastasis win



Amgen

Xgeva for mets

The US Food and Drug Administration approved Amgen's monoclonal antibody (mAb) Xgeva (denosumab), which targets the receptor activator of NF-κB ligand (RANKL) to reduce skeletal-related events in individuals with bone metastasis from solid tumors. The agency's go-ahead, announced in November, was based on three pivotal phase 3 trials comparing the human anti-RANKL mAb with the standard of care bisphosphonate Zometa (zoledronic acid) from Novartis of Basel. Results from the three Xgeva trials—one in people with castration-resistant prostate cancer, one in breast cancer and one in individuals with solid tumors or multiple myeloma—show Xgeva's superiority in breast and prostate cancer trials and noninferiority to Zometa in solid tumors and multiple myeloma. Xgeva also reduced pain and improved quality of life compared with Zometa. "Xgeva could eat into the existing market share of the bisphosphonates," says Ranjith Gopinathan, industry analyst in life sciences at Frost & Sullivan. "Xgeva is expected to generate sales of about $2.4 billion in 2015," Gopinathan adds. The Thousand Oaks, California–based company's mAb was already approved back in June 2010 as Prolia to treat osteoporosis in postmenopausal women (*Nat. Biotechnol.* **28**, 640, 2010). The dose given to cancer patients is 12 times higher than to patients with bone loss indications, but so far the antibody has not shown the worrying side-effects associated with bisphosphonates, which include renal toxicity, atypical fractures of the thigh and osteonecrosis of the jaw. As questions mount over bisphosphonate use, clinicians may well favor treatment with the biologic. Robert Coleman, professor of medical oncology at Sheffield University, UK, believes Xgeva could potentially replace bisphosphonates as standard of care because of its efficacy, ease of administration (Xgeva is injected subcutaneously and Zometa is an intravenous infusion) and less severe side effects. "The only limitation could be the cost—many of the bisphosphonates are just about to come off patent, so doctors would need to balance cost and efficacy," says Coleman. Amgen is currently developing denosumab for rheumatoid arthritis, and rare giant cell tumors of the bone, which are very dependent on RANKL. *Suzanne Elvidge*

of the interests of the academic investigators and the industrial partners," says David Mack of the venture firm Alta Partners, in San Francisco, either because the academics were driven by other basic research questions or because of a lack of appreciation for the cost, risk and time that drug development takes. "They see that they've created an asset that is worth a lot, but actually it's not worth a lot because all of the risk is ahead of us—investment capital, development, technical risk."

But as grant funding proves ever harder to find, it's an opportune time for exploring new models. Plus, the venture capital industry is contracting significantly and is also shifting its focus, where possible, to more late-stage, downstream investments. The absence of an initial public offering market has made some of the investigators more realistic. "It's the right time for that kind of approach—getting them involved on a risk-sharing basis and setting some realistic near- to midterm milestones to achieve some value creation, even if it means then passing it on to Pfizer in exchange for a royalty," says Mack. The ability to hit the group running with a program and have immediate access to Pfizer's development resources may also be attractive to academics who are either uncomfortable or impatient with the venture capital process, where initial fund-raising could take years.

But more experienced academic entrepreneurs might not want to trade control or more potential upside in exchange for expediency. Paul Schimmel of the Scripps Research Institute in La Jolla, California, believes that "To preserve their freedom and work in an academic-like way, they'll probably want to turn to do that in the venture community and startups rather than the pharmaceutical industry, where it can get buried and disappear."

A tendency for people within companies to move is another ongoing issue. Regis Kelly, director of the California Institute for Quantitative Biosciences (QB3), a nonprofit institute spanning three University of California campuses in the San Francisco Bay Area, points to pharma's frequent management changes as a potential snag in making the partnerships thrive. For instance, in 2008, soon after Pfizer merged with Wyeth, it dissolved the Biotherapeutics and Bioinnovation Center (BBC)on UCSF's Mission Bay campus—set up in 2007 as a hybrid between academia and industry, to work on translational projects (*Nat. Biotechnol.* **27**, 308, 2009). For about a year, Kelly recalls, "there was a hiatus, where we couldn't start any new programs together."

Even as Pfizer focuses on decentralizing industry-academic partnerships, London-based GlaxoSmithKline (GSK) will soon adopt a virtual approach. GSK aims to create up to ten relationships with individual researchers throughout the world, forming a virtual project team with each of them in order to, like Pfizer, provide immediate access to GSK resources. "We're not talking about giving lots of money across to academia," says GSK's Patrick Vallance, who is leading the program. An experienced drug discoverer will work in tandem with the research group. "At the beginning it's very focused, with access to the whole of GSK's expertise," he says.

GSK is set to announce the first of its collaborations under the program, with Mark Pepys at University College, London (UCL), and Pepys' UCL spinout, Pentraxin Therapeutics, for the development of a small molecule to treat amyloidosis. GSK and Pentraxin are already working together to develop an antibody to treat the disease.

To some extent, Pfizer's CTI programs echo the spirit of Eli Lilly's Chorus initiative, started in 2007, in which a venture firm supplies the Indianapolis-based pharma with compounds for Lilly to rapidly advance through phase 1. But whereas both emphasize speed to the clinic from a similar preclinical starting point, the CTIs will also explore the biology around its targets in depth, at greater cost, but also presumably to its benefit. Indeed, although Pfizer is aware of the importance of targeted therapeutics and personalized medicine, "It's not an area we have invested a significant amount of time in," says Coyle. By focusing on translational medicine up front, "We're going to have a broader impact in the organization," he says.

Mark Ratner, *Cambridge, Massachusetts*

IN their words

"How many [new drugs] are approved each year—six, seven, eight, nine maybe? If the value of these few new drugs is worth 10, maybe 20 billion U.S. dollars, then where is the remainder of the $85 billion going?" Thomas Lonngren, outgoing chief of the European Medicines Agency, censures the industry for its profligate R&D spending. (*Wall Street Journal*, 15 December 2010)

"If I listened to you, I wouldn't be in this business. Without innovation, we are toast." Paul Hastings, CEO of Oncomed, responds to a question from the audience at 'Convergence' in San Francisco on 3 December on how his company can justify the high costs of its efforts. (*Xconomy*, 6 December 2010)