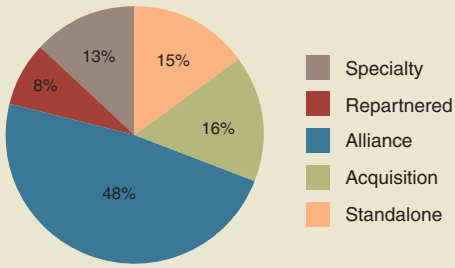
Box 1 M&A not the only solution

Data from Recombinant Capital suggest that the most value in drug development comes from alliances, not M&A, because alliances often end with the biotech junior partner regaining full rights to what is still a promising product. This rights reversion is often followed by either repartnering or commercialization of the compound by the originator biotech firm.



Percent of product sales in 2006 attributable to development paths.
Source: Recombinant Capital

Mark Edwards, from Recombinant, points out that of the 260 biotech drugs approved by 2006, 23 had been partnered, terminated and then repartnered in development. A further 14 were partnered, terminated and then developed independently by the originator. Repartnered drugs include big names, such as Betaseron (interferon beta-1b), Synagis (palivizumab), Cialis (tadalafil), Byetta (exenatide) and Tarceva (erlotinib). "Once investors realize this, they are likely to be much more favorably disposed to big ticket alliances, even compared with M&A," says Edwards.

Brothers' Peter Welford points out that last year, several such companies were searching for buyers—Biogen Idec, of Cambridge, Massachusetts; PDL BioPharma, of Fremont, California; and ImClone, of New York—but didn't accept the deals on offer. The intensifying pressure in 2008 combined with the closed capital markets might be too much to resist, forcing investors to accept a haircut in return for an exit. The process might be further catalyzed by currency effects: the weakness of the dollar may tempt European and even Japanese companies to become opportunistic acquirers in 2008, though European biotechs will look very expensive to potential US acquirers. Some of the big fish—notably Genentech—have already declared their intent to go hunting for good-value buys, says Eric Schmidt, managing director at Cowen & Co. in New York.

If merger and acquisitions (M&As) opportunities don't emerge, many cash-starved public biotechs will have to resort to unconventional ways of raising funds, says Schmidt. One possible resort is the committed equity financing facility. Here the finance company guarantees to buy equity in very small tranches from the cash-poor company and then dispose of it in a planned way so as not to destabilize the stock price. Leading players in this game are London-based Kingsbridge Capital and Azimuth Opportunity.

Another option is the collaborative development deal, a space dominated by Symphony Capital in New York. Here the bank identifies one of the biotech firm's specific products and offers to co-fund its development for a given period, after which the biotech firm must buy back the product rights at a fixed price. Deals of this kind have been done with Exelixis, of S. San Francisco, and Isis, of Carlsbad, California, and are getting more common all the time, says Schmidt. Interestingly, both these types of deals and plain licensing have a better track record for product success than M&As (**Box 1**).

Other more drastic options include bundling up a company's royalty streams and selling them for cash, or even sale-and-lease-back deals where a company disposes of its real estate to a cash buyer and rents it back.

But the best strategy for many small-caps might be waiting for now, and hoping. Robin Davison, senior analyst at Edison Investment Research in London, points out that pharma companies are bureaucratic organizations that take time to make decisions. "They are faced with a wealth of opportunity where they can acquire companies pretty much at the value of the cash they hold, but they have to think it through first." The second half-year could see them act on their thinking, says Davison.

That doesn't take away the current uncertainty. "Maybe this time round we will see the first real wave of biotech bankruptcies, of those lesser quality companies that can't find partnership agreements or acquirers and don't have good fund-raising prospects," says Schmidt. "But these companies do tend to have nine lives. In the past, the financing window has generally opened up just in time to bail them out."

Peter Mitchell *London*

IN brief

IL-1 trap go-ahead

The first drug based on 'Trap' technology, which fuses two receptor components and a portion of an antibody molecule called the 'Fc' region, has been given marketing authorization by the US Food and Drug Administration (FDA). On February 27, 2008, the Tarrytown, New York-based Regeneron Pharmaceuticals received approval for Arcalyst (rilonacept), a treatment for cryopyrin-associated periodic syndromes (CAPS), including familial cold auto-inflammatory syndrome and Muckle-Wells syndrome. Arcalyst is a first-in-class drug designed using Regeneron's 'Trap' technology. The drug is a fusion protein comprising the human interleukin (IL)-1 type 1 receptor (extracellular domain and accessory protein) and the Fc portion of human IgG1. Regeneron's drug is the only therapy approved for CAPS, a group of rare, incurable, inflammatory diseases, generally caused by inherited genetic mutations that result in alterations in the cryopyrin protein, which regulates IL-1 production and results in IL-1 overproduction and inflammatory disease. Arcalyst is also in development to treat other IL-1-driven diseases, including gout. "There are long lists of diseases hypothesized to be driven by IL-1," CEO Len Schleifer noted. "We are looking to test them relatively systematically over the years to come." The Regeneron drug is competing with other IL-1 targeting drugs including Kinaret (anakinra), an IL-1 receptor antagonist approved to treat rheumatoid arthritis from Amgen of Thousand Oaks, California, and ACZ 885 (canakinumab), a fully humanized monoclonal antibody directed at IL-1β, from Novartis of Basel, Switzerland, currently in phase 3 trials for Muckle Wells syndrome. (Under a collaboration agreement with Novartis, Regeneron has the right to opt-in to jointly develop ACZ 885.) *—Mark Ratner*

IN their words

"I've never seen a babassu nut, but it's amazing that it helped power an airplane the size of a 747."

President Bush, at the Washington International Renewable Energy Conference, commenting on Virgin Atlantic's 747 that flew from London to Amsterdam, fueled in part by coconuts and Brazilian babassu nuts.

"This is on the same level of catastrophe as the Challenger disaster"

Robert Gallo, co-discoverer of the human immunodeficiency virus and head of the Institute for Human Virology in Baltimore, likens the expensive, unsuccessful two-decade effort to produce an AIDS vaccine to the NASA space shuttle disaster. (*The Washington Post*, March 21, 2008)