collaborative development financing is pretty expensive. Biotech companies might get better financing options that allow them to control their compounds when the biotech equity markets heat up again. And the real danger to the companies is not in failure of a compound or its success, but in mediocre trials. Because Symphony buys the compounds outright, if the trials are not a home run, the companies would have to buy back the compounds to use the intellectual property (IP) for other purposes after they have already spent many millions in investor money to develop that IP.

Despite these potential drawbacks, Mark Kessel, a managing director and cofounder of Symphony, believes that the benefits of the deal for biotech companies are many and obvious. He thinks that such a deal often means more objective validation for biotechs than a standard licensing deal with a big pharma. And in a big pharma deal, Kessel warns, the due diligence may not be as extensive nor the commitment as solid from a pharmaceutical company. Indeed, he adds, big Pharma might do a biotech development deal for more complex reasons than just the promise of success that the covered compounds may hold.

In addition, collaborative financing could prevent a biotech company from losing quality control of its compounds at the most critical moment in the product's development. Indeed, Kessel claims Symphony's approach could prevent biotech companies from having to go through what he calls "early licensing." That happens when companies license their compounds right after their most important scientific validation (phase 2a trials), in return for more money to continue trials. Such a phenomenon, he feels, causes biotech companies to dilute the value of their investment in a compound, just at the moment the value is going to go up the most. "That's the theory," says Wittenberg. "But whether [project financing] makes sense depends on what they think they can get from a licensing deal with a pharmaceutical company."

This type of financing arrangement, previously known as 'special purpose entities,' has been around for a while and has benefited Amgen and Genentech in the past (*Nat. Biotechnol.* **22**, 271–277, 2004). But it has lost popularity because it no longer holds the tax advantages that it did in the 1980s, which allowed companies to pass through losses from partnerships like these, according to Wittenberg. Nor does it hold the accounting advantages of more recent memory that allowed companies to keep development costs off their balance sheet. Unfortunately, the accounting legerdemain that was used with this type of financing led to the accounting scandals at Enron. The practice of 'off balance sheet' accounting has since been largely curtailed.

So why has Symphony had such a warm reaction in the biotech marketplace? "We offer better deals than either private or public equity," says Kessel. Wittenberg agrees: "These types of financing arrangements are a function of low valuations in the market." Companies that may have used a secondary offering of stock to fund mid-stage research are finding it more attractive to borrow the money, even at 27% interest.

However, the clear implication is that when the equity markets return to their love affair with biotech—which they have in the past—this type of financing deal will have to either cut their return substantially or look at lesser compounds with more risk—both unlikely options. For now, though, it's likely that more biotechs will take advantage of similar arrangements rather than wait for equity markets to heat up again.

John Ransom, Lone Tree, Colorado

Tysabri back on market

The return of the multiple sclerosis (MS) drug Tysabri (natalizumab) to the US market, sanctioned by the US Food and Drug Administration (FDA) on June 5, and its first-time approval in the EU, announced on June 29, was welcomed by investors. The move should also eventually lead to a clearer understanding of the association between the immunosuppressive monoclonal antibody and the risk of developing progressive multifocal leukoencephalopathy (PML). But, as officials from the drug's developers, Biogen Idec of Cambridge, Massachusetts, and Elan of Dublin, have warned, more cases of PML and more fatalities are expected before a proper risk-management plan can be developed to provide treating physicians with a fuller understanding of the danger involved in its use. The drug was initially approved by the FDA on November 23, 2004 as a first-line treatment for relapsing forms of MS, on the basis of one-year data from two phase 3 clinical trials. It was voluntarily withdrawn from the market on February 28, 2005, after the development of one confirmed and one suspected case of PML among patients who had received Tysabri along with Avonex (interferon β-1a) in a combination trial (*Nat. Biotechnol.* **23**, 397–398 2005).

Tysabri has now gained US and EU approval as a second-line monotherapy for MS patients with actively remitting disease who have either an inadequate response to, or are unable to take, alternative therapies. Access to Tysabri will be strictly controlled in the US through a mandatory patient registration program, called Touch. Only authorized infusion centers will be permitted to administer the drug to qualifying patients under controlled conditions, designed to promote early detection of PML. In the EU, the core elements of the risk-management plan will be replicated, although, because of the absence of a centralized authority like the FDA, a pan-European patient registry will not be put in place.

Some 5,000 patients from the US and Europe will be enrolled in a five-year post-marketing safety study called TYGRIS (Tysabri Global Observation Program in Safety), which is expected to provide a firmer understanding of the association between Tysabri and PML. In its early stages, however, the risk-management framework that Biogen Idec and Elan have put in place is, inevitably, limited by a lack of data. "I think it's really about quantifying what the risk is and identifying patterns in the future that might help minimize the risk," says Eric Schmidt, managing director and senior research analyst at investment bank SG Cowen in New York.

Despite the safety concerns, the drug still has blockbuster potential, because the MS market remains poorly served by existing therapies. Schmidt has forecast $1.1 billion in sales by 2010, whereas Cannacord Capital has forecast sales of $1.65 billion by 2011. "The current standard of care is not much better than placebo," says Schmidt.

Cormac Sheridan, Dublin