treat large numbers of patients will have a huge advantage." From his perspective, the prospects for the regenerative medicine sector are bright. "With cell therapies, we have seen much higher success rates going between each phase of clinical trials than with small molecules and biologics," he says. "Initially we're going to see small changes in patients, and as we get better with the cells, we'll see a gradual emergence of efficacy, but it takes time," he says. "I'm convinced that 10 years from now there will probably be 10 or 20 new products, which have gotten full FDA approval. And 20 years from now, the cell therapy industry will be where the monoclonal antibody industry is today."

George S Mack, ***Columbia, South Carolina***

Cephalon splashes out on mesenchymal stem cells

As mesenchymal stem cell (MSC) transplantation has yet to deliver a commercial product, it takes a certain amount of chutzpah to forge a $1.7 billion deal around the approach. In early December, Frazer, Pennsylvania–based Cephalon made an up-front payment of $130 million to Melbourne, Australia–based Mesoblast to develop and commercialize adult mesenchymal precursor cell therapies for a multitude of disorders, ranging from congestive heart failure and neurodegenerative diseases to cancer. The collaboration will provide funding for Mesoblast to run a phase 2a trial; Cephalon will oversee phase 2b and 3 trials if the MSC therapy is taken forward and retain global commercialization rights. Cephalon has also paid $220 million for a 19.99% equity stake and a seat on the board of Mesoblast. In its due diligence process, Cephalon had access by a confidential agreement to data from a randomized placebo-controlled phase 2 congestive heart failure trial of 60 patients who had received injections of Revascor, Cephalon's adult allogeneic off-the-shelf MSC therapy. The product, delivered through a catheter to the ischemic myocardium, reduced the overall monthly rate of major adverse cardiac events by 84% compared with controls. "We had a great deal of difficulty in explaining that data away," says new Cephalon CEO Kevin Buchi. "It had a placebo, and all the endpoints seemed to be moving in the same direction," he says.

Cephalon's $350 million cash investment, with milestone payments potentially adding up to $1.7 billion, is certainly substantial for an early-stage platform, but one specialty pharma analyst, who wants to remain anonymous, calls it a "smallish transaction" that won't really produce any meaningful phase 3 data until some years away. Venture capitalist and managing partner Daphne Zohar of Boston-based PureTech Ventures also stops short of saying the deal is too rich. "But the up-front payment is higher than most we're seeing," she says. "Most recent deals are structured as earnouts that are more backloaded, but Cephalon must have thought it was worth it."

The big question is whether Mesoblast's phase 2 efficacy data will translate to larger trials. Another company, Osiris Therapeutics of Columbia, Maryland, also had compelling phase 2 efficacy data for its MSC therapy, Prochymal, in severe refractory graft-versus-host disease (GvHD), but failed to translate that efficacy into phase 3. In 2009, on the basis of the phase 2 data, Genzyme of Cambridge, Massachusetts, struck a deal with the Maryland biotech, paying $130 million up-front for rights to Osiris' MSC products: Prochymal for GvHD and Crohn's disease, and Chondrogen for knee cartilage repair (*Nat. Biotechnol.* **27**, 966–967, 2009). It should be noted, however, that although Osiris' and Mesoblast's products are both MSC therapies, the target indications and heterogeneity of the clinical populations studied are different. The methods of preparation for the two companies' products are also different: Osiris' cells are prepared by density gradient separation of bone marrow mononuclear cells and then purified on the basis of the (>90%) presence of CD73, CD90 and CD105 markers and absence of CD34, CD45, CD14 and CD3 markers (*The Lancet* **371**, 1553–1554, 2008). Mesoblast's MSCs are $CD34^+CD117^+$ cells obtained by sorting granulocyte colony stimulating factor-mobilized bone marrow–derived cells (*Nat. Med.* **7**, 430–436, 2001).

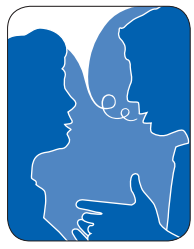
If the Mesoblast cell therapy does show efficacy in large-scale trials, the market opportunity with congestive-heart failure alone is substantial, with 1.1 million hospitalizations and 300,000 deaths each year in the US alone and as many as 20 million patients globally. "We're a pharmaceutical company, and we didn't spend a whole lot of time focusing on the fact that this was a stem cell technology, *per se*", says Buchi. "We focused on the fact that it's a manufactured, off-the-shelf product, and from our perspective it feels very much like a biologic that can be stocked in a cath lab and used for patients as needed by the physician." *GM*

IN brief

Fabry drug march-in denied

Three people affected by shortages in Genzyme's drug for Fabry disease failed to convince the National Institutes of Health (NIH) to use 'march-in rights' to break manufacturing patents held by the Cambridge, Massachusetts–based biotech and grant a new license to third parties to deal with the problem. The enzyme replacement therapy Fabrazyme (agalsidase β; rh α-galactosidase A) is the only treatment available for individuals with this disorder, and ongoing manufacturing problems at Genzyme's plants (*Nat. Biotechnol.* **27**, 681, 2009) have curtailed supplies for over a year. March-in right is granted to the government under the Bayh-Dole Act to issue a new license or revoke an existing patent in cases where a federally funded invention has not been adequately developed. Two of the drug's patents, owned by Mt. Sinai Hospital School of Medicine in New York, are based on inventions funded by NIH and exclusively licensed to Genzyme. But in December, NIH declined to hold a hearing on the issue, stating that a march-in proceeding would not increase the supply of Fabrazyme in the short term. Given that Genzyme expects to return patients to normal dosing during the first half of 2011, the real interest of the petitioners may lie more in inducing the biotech to lower the price of Fabrazyme, which costs hundreds of thousands of dollars per patient per year. That strategy succeeded for Knowledge Ecology International (KEI), a nongovernmental organization dealing with intellectual property issues related to public health, based in Washington, DC. KEI obtained a march-in hearing on the antiviral drug ritanovir in 2004. Although they lost the case, "Abbott Labs did make concessions," says KEI director James Love, who assisted the Fabrazyme plaintiffs. "But these Fabry's patients will never have their day in court and won't be able to push Genzyme." The plaintiffs are appealing the decision. Opening up the Mt. Sinai patent license could spur development of a biosimilar, which would put price pressure on Fabrazyme. But in the 30 years since Bayh-Dole was enacted, NIH has never asserted march-in rights. "It's often perceived that one of the missions of the NIH is to keep the biotech community as happy as possible, so innovation continues," says Love. But when taxpayers put up the money for research, not industry, "patent law protection is not relevant," he contends. *Mark Ratner*

IN their words



"We're like a biotech company in the context of big pharma."

CEO Mary Haak-Frenscho on the San Francisco facility of Takeda Pharmaceuticals that now has 70 employees. (JP Morgan Healthcare Conference, San Francisco, 11 January 2011).