30-year-old individuals. The cells are first isolated by density gradient separation and further purified by a selective adherence technique to eliminate non-MSC contaminants to 99.5% purity. From here, Osiris expands the culture to yield 10,000 doses of Prochymal from a single donor. According to University College's Mason, the company's novel method for expanding MSC cells, their experience in processing and packaging marrow-derived MSCs into an off-the-shelf product, was instrumental in clinching success. "The cells are high quality, the material is reproducible and the results excellent," Mason adds. From the investor point of view, it makes for a highly scalable and efficient business model.

When infused into the patient, the MSCs are drawn to the sites of damage and inflammation, whether it is ischemic tissue in the myocardium immediately after a heart attack or the mucosal crypts in the colon of patients with Crohn's disease or the tissues affected by GvHD, which occurs in ~50% of bone marrow transplant patients. In fact, the colitis of Crohn's disease can resemble the histopathology of the GvHD-affected colon, which is what originally prompted investigators at Osiris to explore and develop the product in the former indication.

Because Prochymal and Chondrogen are allogeneic, some degree of immune response might be expected, but to date it appears that MSCs are either immune privileged or they turn off or disable immune cells. Of ~850 patients treated with Osiris's MSCs over the past decade, with some GvHD patients having received as many as 12 consecutive doses, there have been no infusion reactions either on initial or subsequent administration, even with doses given months later. "It's an innate property, not something we do to them," says Osiris CEO Randal Mills. "It's the stem cell equivalent of O-negative blood. They just lack the cell surface antigens."

MSCs seem to achieve their therapeutic effects by working as anti-inflammatory agents. Although the complete mechanism remains uncertain, MSCs down-modulate the immune response by suppressing tumor necrosis factor α and interferon γ production while boosting interleukin (IL)-10 and IL-4 secretion by T-helper 2 cells. Because of their pluripotency, MSCs might be expected to engraft the tissues they are intended to regenerate, but in the case of infused MSCs, engraftment appears to be transient. "In Crohn's, we do see the MSCs go to the intestine," says Mills. "They will engraft at the site of inflammation, but they don't persist there." The cells act more as a drug than as a reconstructing agent. "This is not strictly 'regenerative medicine', but it has that effect and the results are excellent," Mason points out.

Whatever the reason, Prochymal appears to work. Phase 2 results in 32 adult patients with acute GvHD showed an overall response rate of 94%, with a complete remission or response rate of 77% representing 24 patients. And results for end-stage refractory GvHD in 12 children, ranging from infant to 15 years, showed a 100% response rate with a complete remission or response in 58% or 7 children.

> "Do I think the MSC therapy will be effective at counteracting a broad range of autoimmune diseases? Absolutely."

Osiris is also pursuing MSC formulations for type 1 diabetes, chronic obstructive pulmonary disease and the prevention of heart failure following acute myocardial infarction, all of which are in phase 2 clinical trials. And there's probably more on the way. "There's a lot of animal data suggesting multiple sclerosis as a target," says Mills. Rheumatoid arthritis, acute organ rejection and scleroderma are also targets. "Do I think the MSC therapy will be effective at counteracting a broad range of autoimmune diseases? Absolutely."

George S. Mack *Columbia, South Carolina*

New product approvals

RoActemra (tocilizumab)/F. Hoffmann-La Roche (Basel) and Chugai (Tokyo)

The European Commission approved RoActemra for adult patients with moderate to severe rheumatoid arthritis (RA) who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs or tumor necrosis factor antagonists. RoActemra is the first humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody developed for RA.

Stelara (ustekinumab)/Janssen-Cilag (Beerse, Belgium) and Centocor (Horsham, Pennsylvania)

The European Commission approved Stelara for moderate to severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate and PUVA (psoralen plus ultraviolet A light). Stelara is a human monoclonal antibody that targets the p40 sub-unit of cytokines interleukin-12 (IL-12) and interleukin-23 (IL-23). Centocor (a Johnson & Johnson subsidiary) discovered the drug and has exclusive marketing rights in the U.S.

IN brief

GM poplars to grow next door

Researchers at the Ghent, Belgium–based Flanders Institute of Biotechnology (VIB) have gained ground in a long-running battle over the planting of genetically modified (GM) poplar trees by applying for permits to plant the trees across the border. The Belgian government initially refused VIB's application to run field trials on home turf, but now the Dutch government, which has already issued a 'positive opinion', may grant them permission. The transgenic poplars are deficient in the enzyme cinnamoyl-CoA reductase, which reduces the lignin content making them more suitable for bioethanol production, although so far their benefits have only been demonstrated in the lab. The VIB had hoped for a green light from the Belgian Biosafety Council to run the trials closer to its research facilities and pilot-scale biorefinery. Instead, researchers will be forced to make regular trips to neighboring Holland to monitor and harvest the trees. Willy De Greef, secretary general of EuropaBio, the Brussels-based association for European bioindustry, says, "VIB is a public institute, which doesn't have the resources of a multinational. I don't even dare to think about what it does to their annual research budget." He says if European laws governing the planting of GM field trials were more consistently adhered to across member states, such situations wouldn't arise. A final decision from the Dutch government is due in spring 2009. *–Hayley Birch*

FDA goes public-friendly

In an effort to reach out to the American public, the US Food and Drug Administration (FDA) in December announced a collaboration with online health information provider WebMD to disseminate health and drug safety information. The deal gives the FDA pages within WebMD's website and print magazine. WebMD.com reaches a far larger audience than the FDA's website with nearly 50 million unique visitors each month compared with the FDA's 6 million. "It's important to put the information where the people are going, and not expect them to come to us," says FDA's Jason Brodsky, director of consumer health information. The WebMD-FDA site http://www.webmd.com/fda/ links to the agency's guides to reporting adverse events and understanding product recalls, and offers safety tips on drugs, medical devices, food and cosmetics. The agency plans to add multi-media content and features on the safe use of products. For example, the agency will offer a guide to parents on vaccines, warn consumers about unlawful distribution of unapproved drugs and answer questions such as, What are biologics? European agencies are also attempting to improve online access to health information. The UK's National Health Service (NHS) plans to launch in April NHS Evidence, a web-based service that consolidates clinical data and experience, prescribing and safety information, and technology appraisals. And the European Commission in December adopted a legislative proposal aimed to improve patient access to information about drugs. *–Emily Waltz*