Schering AG tentatively enters gene therapy

Schering AG, the Berlin-based pharmaceutical and agrochemical concern, and the German technology transfer company CellGenix (Freiburg, Germany) have formed Metreon, a new cell and gene therapy development company based in Freiburg that will focus on cancer therapy. The two founding companies each hold a 50% share in the new joint venture, the long-term goal of which is the development and commercialization of cell and gene therapies in oncology, central nervous system, endocrinology, and cardiovascular disorders.

This is Schering's first joint venture for cell and gene therapy, and appears to be somewhat experimental, as Klaus Pohle, vice chairman of finance and administration of Schering AG, explained at a UBS conference in London (March 19–20, 1996). He said the venture would allow Schering "to assess what the market will be like for gene therapy, and how . . . [the company] would deal with therapies that consist of cells rather than tablets." The financial arrangements also seem tentative: The initial term of the venture is three years, but payments will be assessed on a case-by-case basis as therapies emerge.

According to Christine Thor-McCarthy, a spokesperson for Schering AG, the venture is part of Schering's strategy "to enrich its research pipeline through external collaborations" in Europe, the United States, and Japan. Currently, Schering specializes in diagnostics and hormonal products such as oral contraceptives, and its only biotechnology-based product on the market is Betaseron (interferon-β), licensed from Chiron (Emeryville, CA) for multiple sclerosis. Schering's sales of Betaseron in 1995 were $270.9 million, of which Chiron received $67.7 million in license fees. Biotechnology accounted for 7% of Schering's research and development budget for 1995, with the money being spent primarily in the United States and Germany.

The company has set up several collaborations in the past three years with biotechnology companies, including ImmuLogic (Waltham, MA)—for development of a peptide to treat multiple sclerosis, and Pharmacopeia (Princeton, NJ)—for combinatorial chemistry and screening technology. Although Metreon is the first gene therapy joint venture for Schering, the company already has an interest in cell and gene therapy research as an investor (with the German government and other private investors) in a quite separate collaboration established in 1993 with the Clinic of Tumor Biology in Freiburg.

Since its inception in May 1994, CellGenix has been involved in the production of good manufacturing practice grade (GMP-grade) peripheral blood stem cells for transplantation, using techniques that include expansion of cells using cytokine treatment, for use after high-dose chemotherapy. Now Metreon will take over this cell processing area, and there are plans to set up similar production sites elsewhere in Germany and internationally, according to Thor-McCarthy. The management board of Metreon consists of Gregor Schultz (CellGenix) as managing director, Felicia Rosenthal (CellGenix), and Klaus Menken (Schering) as finance director of Metreon.

Freiburg is a focus for gene therapy in Germany. In 1992, Freiburg researchers, led by Roland Mertelsmann, were the first to receive approval for a cancer gene therapy trial in Germany. The trial, which largely involves melanoma or renal cell carcinoma patients, did not actually begin until 1994. The current protocol—one of five gene therapy trials in Germany—involves mixing tumor cells from patients with allogeneic fibroblasts genetically altered to produce interleukin-2. The cell mixture is then injected back into the patient. Further development of the technique will involve modifying the tumor cells directly: Tumor cells will receive either a gene for interleukin-2 or for the costimulatory molecule B7. A mixture of the resulting cells will then be administered to HLA-matched patients with renal cell cancer.

Neither CellGenix nor Schering is directly involved with any of these trials at the moment. Cell and gene therapy research and early-stage development will continue to be conducted at Freiburg University. But if the techniques look worth pursuing, CellGenix will undertake the next clinical phase; Metreon would be involved later still in development. CellGenix's Rosenthal notes that Metreon could also develop cell and gene therapy from centers other than Freiburg University.

Sylvia Davidson

FDA race to reform gets frantic

The US Food and Drug Administration's (FDA, Rockville, MD) aggression in the face of industry criticism of its record continues. At the end of March, it announced measures designed to get more drugs more quickly to cancer patients. The reform of the FDA—a potentially ponderous process—seems to have become a frantic relay race, with the US Congress on the one hand promising legislative improvements, and the Clinton administration and FDA officials on the other implementing specific preemptive reforms of their own. And in the background, FDA Commissioner David Kessler continues to insist that FDA is outperforming all competition for the "best regulator" laurels.

The FDA's cancer initiatives largely resemble the streamlining measures that the agency already has in place for speeding approval of new drugs for treating AIDS. Thus, for example, FDA officials will now give considerable weight to signs of drug efficacy, such as tumor shrinkage, that are easier and quicker to attain, instead of insisting that an experimental drug extend the life spans of patients before it can be approved. It remains to be seen, however, whether the FDA's advisory committees will find such data as readily acceptable; their preference in the past has been to judge efficacy on the quality or extension of life criteria. Another of the administration's reforms will allow the appointment of patient representatives to the advisory committee.

Two other changes may help make cancer drugs available earlier to US patients. The first is that drugs that are already approved outside the US (in countries with "FDA-like" drug approval bodies and mechanisms) will be allowed on a "compassionate use" basis. The second is an easing of the restrictions on "off-label" use of drugs—the application of compounds approved for one condition in other indications.

Meanwhile, the Labor and Human Resources Committee of the US Senate recently sent Nancy Kassebaum's (R-KS) "FDA Performance and Accountability Act" forward to the full Senate. The bill for the act, introduced late in 1995, seeks to institute tighter review deadlines, extend the access for patients to still-unlicensed products, and create an atmosphere among agency officials, industry representatives, clinical researchers, and patients (*Bio/Technology* 14:138, Feb. '96) that is more collegial than adversarial. When (or whether) the bill will actually come before the Senate will depend heavily on the priorities of the legislation schedulers. In the year of a US election, issues other than FDA reform may attract attention. Similar measures are being crafted in the US House of Representatives.

To be sure, political huffing and puffing