clinical trials with Norcalcin in the U.S. Kirin pledged up to $25 million in licensing fees, research support, and milestone payments in exchange for exclusive rights from NPS to develop and sell Norcalcin and other compounds for the treatment of HPT in Japan, China, Korea, and Taiwan.

Without a doubt, Japanese pharmaceutical executives believe that they have to be up to speed in biotechnology to be in business in the 21st century. Though they may have been slow starters, it now seems clear that they have the will and the stamina to catch up.

—Mike Ward

U.S. skin-replacement market could heat up

ALLENTOWN, Penn.—The U.S. market for skin-replacement products designed to treat severe burns and chronic wounds could be heating up. Currently, two such products are on the market, one produced by Genzyme Tissue Repair (GTR, Cambridge, MA) and the other by LifeCell (The Woodlands, TX). Also, two other skin-replacement products—made by Advanced Tissue Sciences (ATS, La Jolla, CA) and Organogenesis (Canton, MA)—recently received expedited-review status from the U.S. Food and Drug Administration (FDA, Rockville, MD).

Skin is largely made up of two layers, the outer epidermis and the underlying dermis. The epidermis—a thin layer composed mostly of keratinocytes—forms a physical barrier against the environment. The dermis—which is about three times thicker than the epidermis and is vascularized—is composed predominantly of fibroblasts locked in a collagen matrix.

The two skin-replacement products already on the market—both of which focus on treating severe burns—did not require FDA approval, because they are derived from human skin cells. GTR, for its part, acquired its skin-replacement product, Epicel, when it acquired BioSurface Technology late last year. Epicel, which was first introduced in 1988, is manufactured by harvesting a small sample of a patient's own epidermis and growing in cell culture enough new epidermis in three to four weeks to cover the patient's entire body. Epicel, however, sees only limited use, because it doesn't contain a dermal layer and, thus, doesn't reduce wound contracture or improve wound durability as well as conventional skin grafts. In fact, Epicel—which sells for $15,000 a square foot—racked up sales of just $5.4 million in 1993 and $6.3 million in 1994.

LifeCell's skin-replacement product, AlloDerm, was introduced last year. LifeCell produces AlloDerm by first removing the epidermis from human cadaver skin and then by removing the fibroblasts from the cadaver-skin dermis, leaving intact the collagen bundles of the dermal matrix, as well as the dermis' basement membrane, which anchors the epidermis' keratinocytes to the dermis. Patient keratinocyte-supplying epithelial grafts are applied to the grafted AlloDerm's surface.

AlloDerm—which costs $10,000 a square foot—had 1994 sales of just $93,940, which LifeCell largely attributes to a hesitation among burn surgeons to try new approaches. So, during the second half of 1994, LifeCell embarked on an aggressive marketing program, shipping a lot of AlloDerm free of charge or at reduced cost and expanding its sales force from two to five people. "We're seeing the results now in increasing orders and in the development of specific procedures where AlloDerm is especially beneficial," such as grafting on hands and on areas around joints, as well as in treating children, who have thinner skin than adults, observes Jane Lea Hicks, LifeCell's vice president of business development. And, indeed, AlloDerm's sales for the first half of this year have climbed to $227,951. Moreover, though LifeCell is marketing AlloDerm to the burn sector itself, it is looking for partners to market the product to the periodontal market and the plastic-surgery market.

"Burn surgeons tend to be cautious in adopting new technologies, due to the complexity of the comprehensive approach to burn care," says Harvey Himel, director of the DeCamp Burn Center at the University of Virginia Hospital (Charlottesville, VA). "Whereas AlloDerm has a firm theoretical foundation, and early anecdotal reports are encouraging, I think some burn surgeons are waiting to see how it performs in a randomized clinical trial. In this era of cost consciousness, the preference is for innovations to be cost neutral, and all skin-replacement technologies will be evaluated by this criterion, in addition to their clinical performance."

Organogenesis' skin-replacement product, Graftskin, recently completed pivotal trials for treating venous ulcers. The product—which contains both a dermal and an epidermal layer—is made up of bovine collagen, human dermal fibroblasts, and human epithelial keratinocytes. Graftskin's pivotal trial involved 233 venous-ulcer patients, and results showed that the product was 60% more effective than standard compression therapy in achieving complete wound closure, according to Organogenesis, and that it achieved wound closure in a median time of 57 days, compared to 181 days in the compression group. Also, among patients with venous ulcers that had persisted for more than a year, 57% of Graftskin-treated patients attained complete wound closure, compared to 17% of patients receiving standard therapy. Furthermore, Graftskin—a price for which has yet to be set—was not rejected by patients.

ATS's skin-replacement product, Dermagraft-TC, should complete pivotal trials this year for use as a transitional covering for severe burns. The product consists of human dermal fibroblasts seeded onto a nylon mesh, which is attached to a plastic membrane that acts as a protective covering. "Dermagraft-TC ensures an adequate vascular supply when the autograft is put on. It also delivers matrix proteins, which are secreted by the fibroblasts, to the wound," says Gail Naughton, ATS's chief operating officer. The product is expected to cost $3000 a square foot.

—Vicki Glaser

Vicki Glaser is a freelance science and medical writer in Allentown, PA.

Currently, two skin-replacement products are on the U.S. market, and two more recently received expedited-review status from the FDA.