

UNLOCKING IL-2'S BUSINESS POTENTIAL

Lymphokines have always been the glamor-child of biotechnology. First, interferon bore the standard for a promising but fledgling industry. When this biological response modifier seemed to lose some of its magic in the clinic, another lymphokine, interleukin-2 (IL-2), stepped into the hope-and-hype spotlight as a potential treatment for two of mankind's most dreaded diseases, cancer and AIDS. But the lymphokines do not stop there. Interleukins now number IL-1 through IL-4 (with IL-1 divided into α and β subclasses); other lymphokines include a host of colony stimulating factors and a pair of tumor necrosis factors (TNFs).

Although biotech-derived products are coming to market in ever-increasing numbers, company executives, Wall Street analysts, and the general public still await the "home run" that will once-and-for-all establish the commercial credibility of biotechnology. Many believe that IL-2, with its well-publicized clinical trials against cancer by Steven Rosenberg at the National Cancer Institute (NCI), represents just such an opportunity. In a favorable stock market that has been particularly fond of biotech companies, firms emphasizing interleukin-2 have done particularly well (see chart)—especially since the end of last year, when Rosenberg's preliminary successes came to light.

Previously and more descriptively termed "T-cell growth factor," IL-2 stimulates the growth and increases the function of T cells and other cells in the immune system. These lymphocytes help the body protect itself against tumors; T cells are depleted, however, in AIDS victims.

According to Technology Management Group (TMG, Stamford, CT), commercial sales of IL-2 should become significant by 1987 or 1988. Total sales, virtually all for cancer treatment, should reach around \$400 million annually by 1990, TMG predicts, and they could rise to \$560 million by 1995. TMG president Manny Ratafia stresses that the biggest uncertainty centers on the actual dates that companies receive regulatory approvals. Of total IL-2 sales, Ratafia predicts that 30% will be in the U.S., 35% in Europe, 20% in Asia, and 15% elsewhere.

Peter Drake, biomedical technology analyst at Kidder, Peabody (New York, NY), agrees with TMG's 1990

market estimate. He predicts that dual 40-percent market shares will be garnered by Cetus Corp. (Emeryville, CA) and by Immunex Corp. (Seattle, WA, with its partners Hoffmann-La Roche, Nutley, NJ, and Ajinomoto, Tokyo). Drake expects that the team of Amgen (Thousand Oaks, CA) and Johnson & Johnson (New Brunswick, NJ) will achieve a 10-percent share, as will Biogen (Cambridge, MA) and its Far East partner Shionogi (Osaka).

Also, recombinant IL-2 has been or is being targeted by companies like Genetics Institute (Cambridge, MA) with Sandoz (Basel, Switzerland), Genzyme (Boston, MA), Chiron (Emeryville, CA), and Genex (Rockville, MD) in contract research for Yoshitomi Pharmaceutical Industries (Osaka). Other Japanese companies reported to be developing IL-2 include Takeda Chemical Industries (Osaka) and Suntory (Osaka).

At least two companies, Collaborative Research (Lexington, MA) and Interleukin-2 (Alexandria, VA), are trying to commercialize natural forms. According to Collaborative founder and president Orrie Friedman, the firm hopes to decide by the end of the summer whether it can indeed develop a commercial production process. "If the recombinant material does everything that the natural material does, then I think we'd bow out of this," he says. "But we're betting that the natural substance may have some very special characteristics." Whether the natural glycosylation found in non-engineered IL-2 will have any advantage *in vivo* remains to be shown.

Interleukin-2, the company, represents Wall Street's only "pure-play"

on natural IL-2, and the stock's recent performance demonstrates the confidence felt by investors. The company is sponsoring phase I studies in London against cancer and AIDS, and is in the process of formulating phase II protocols. The company terms its product "an IL-2 rich preparation," and it hopes that its mix of natural interleukins will yield clinical superiority over highly purified, recombinant IL-2.

Although IL-2 has enormous potential, its commercialization requires more than a string of impressive clinical trials. Robert Kupor, biotech analyst at Cable Howse & Ragen (Seattle, WA), points out that IL-2's "efficacy-to-effort" ratio must be increased before it can generate profits for its developers. Right now, he says, "you have an embryonic situation in which extraordinary anti-cancer activity has been demonstrated using a cumbersome technique." He says that the adoptive immunotherapy practiced by NCI's Rosenberg, in which the researcher cultures a patient's white blood cells *in vitro* in the presence of IL-2, does not represent a very marketable approach. Kupor points out that less involved procedures may be applicable for earlier-stage cancer patients and for post-surgical situations. Other promising possibilities for IL-2, he notes, include using stimulated white blood cells from donors instead of the patient himself, using IL-2 in combination with TNF or cytotoxic drugs, and treating patients with additional drugs to alleviate IL-2's sometimes devastating side-effects.

—Arthur Klausner

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REASONS

Indexed closing price analysis of five companies that have emphasized interleukin-2. Base date is Dec. 8, 1983.