# Genta seeks French okay for acne drug

Genta hopes revenues from its in-licensed acne drug will help fund development of its oligonucleotide products.

FORT COLLINS, Colo.—Though oligonucleotides represent the future for Genta (San Diego, CA), the firm's present rests on a handful of in-licensed compounds that treat acne, psoriasis, eczema, and other dermatological problems. Indeed, Genta recently completed phase III clinical trials in France for the topical acne medication G-101—it hopes to begin U.S. trials on the compound this fall—and plans to file for marketing approval with the French Ministry of Health later this month. Genta hopes to receive French marketing approval by the end of this year and to have the product on the French market next year. The firm has four other topical dermatological products—called G-201, G-202, G-203, and G-301—in various stages of clinical trials in both the U.S. and Europe.

In the 577-patient French trial, G-101—an erythromycin salt of acetylcysteinylsalicylate—produced marked improvement in mild to moderate cases of acne when applied twice a day for 12 weeks. In addition, the drug proved effective at treating a more severe form of acne accompanied by nodules and cysts, a surprising finding since currently available topical medications have little or no effect on nodules and cysts. Based on these results, Genta is optimistic that it can capture at least a chunk of the $1 billion worldwide market for prescription acne medications. According to Kenneth Brown, Genta's director of business development, the company is "currently looking for a European marketing partner in anticipation of French regulatory approval" of G-101. He adds that Genta plans to do its own marketing of G-101 in the U.S.

Analysts see Genta's dermatology product line, and its expected revenues, as playing a crucial role in the firm's ability to parlay its oligonucleotide technology, tradenamed Anticode, into products. Genta acquired the rights to its dermatology lineup when it hired William Bliss as president and chief operating officer and purchased his company, Visna Pharmaceuticals. Bliss had started the company in 1990 to commercialize in-licensed dermatology products—those with potential markets of less than $100 million—that he had identified during a five-year stint as vice president of licensing and acquisitions at the Rorer Group, now part of Rhône-Poulenc Rorer (Collegeville, PA). With much of the preclinical testing done by the compounds' original developers, Genta's expense for taking these compounds through clinical trials should be relatively small. Analysts at Alex Brown & Sons (New York) predict that the total clinical-trial costs for all five dermatological products will come to less than $20 million. Jeffrey Kraws, a biotech analyst at Montgomery Securities (San Francisco, CA), projects that earnings from G-101 will climb from $5.5 million in 1995 to $36 million in 1999, with revenues from the dermatology line topping $100 million by 2000.

"We'll be profitable before our first Anticode product hits the market," says Thomas Adams, Genta's chairman and chief executive officer. Yet Genta is being careful not to shortchange its future by committing too much of its limited resources to short-term projects. "We haven't shifted any personnel or other resources from the Anticode projects. And we're relying on a clinical research organization, instead of using in-house talent, to do the necessary testing to get regulatory approval for the dermatology products," says Genta's Brown.

Genta is also counting on near-term revenues from a patented drug-delivery system, Geomatrix, that it developed in a joint venture formed in 1992 with Jagotec (Basel). The venture, Genta-Jagotec, has identified more than 20 major drugs that have gone off patent, or will soon go off patent, that could be reformulated with the Geomatrix system into once-a-day formulations, including cimetidine, acyclovir, and tamoxifen. The Geomatrix system uses a polymer matrix that swells and gels when it reaches the stomach, dramatically prolonging the formulation's transit time through the gastrointestinal tract. Genta-Jagotec has already licensed the Geomatrix system to Gensia (San Diego, CA), which hopes to market a Geomatrix-nifedipine combination sometime in 1995 as a generic alternative to Pfizer's (New York) Procardia XL, a cardiovascular compound with annual worldwide sales of $1.5 billion. Genta's royalties from this product could top $167 million by 1999, according to Montgomery Securities.

By that time, Genta hopes to have its first Anticode products on the market. Genta's Anticode technology involves the use of two identical single strands of oligonucleotide that bind to a targeted region of messenger RNA, creating a molecular knot that prevents protein expression. For example, Genta's Anticode cardiovascular drug—aimed at preventing arteries from reclosing, or restenosing, after balloon angioplasty—targets two proteins involved in controlling the cell cycle. These two proteins, a cyclin and a cyclin-dependent kinase, form a complex that enables the cell cycle to proceed. Inhibiting production of both proteins in vascular smooth muscle cells, through local application of Anticode oligonucleotides, shuts down proliferation and migration of such cells for two weeks in a rat model of coronary artery disease. "If we can demonstrate the same effectiveness in a pig model, which we're working on right now, then we should be filing an investigational new drug (IND) application for the oligonucleotide by the end of the year," says Donald Picker, Genta's senior vice president for research and development. Restenosis affects 40 percent of patients who undergo angioplasty or vascular grafting, an estimated $2 billion annual problem in the U.S. alone.

Genta also hopes to file an IND application this year for its Anticode cancer product, which down regulates production of the protein BCL-2. This protein, present in abnormally large amounts in tumors resistant to radiation and chemotherapy, inhibits cell death. Shutting down BCL-2 production with oligonucleotides either triggers cell death itself or renders the cell vulnerable to chemotherapy. Genta is completing tests of an Anticode oligonucleotide in animal lymphoma and prostate-cancer models, and plans to start tests in animal breast-cancer models. **—Joseph Alper**