Amgen's NESP victory cuts out Johnson & Johnson

An arbitration panel in Chicago has awarded Amgen (Thousand Oaks, CA) exclusive rights to its next-generation anemia drug, novel erythropoiesis-stimulating protein (NESP), rejecting the claim of Johnson & Johnson (J&J; New Brunswick, NJ) that the drug falls under a 1985 license agreement between the two companies for erythropoietin (EPO). As well as giving Amgen a monopoly over the expected blockbuster drug (except in Japan and China), the decision sent Amgen stock price surging 23% and averted what some observers saw as a potential hostile takeover by J&J.

NESP is an improved version of α-EPO (*Nat. Biotechnol.* **15**:940, 1997). It has been granted patent protection in Europe until 2004 and in the US until 2012. NESP is currently in a 1,000-patient phase III trial for kidney dialysis patients in Europe, the US, and Australia, and preliminary data seems to confirm that NESP's serum half-life and its effective biological activity are three times greater than those of EPO. Since it needs to be administered less often, NESP is expected to replace EPO when it enters the market in 2001. "Patients need subcutaneous injections once a week or, at best, once biweekly instead of three times a week," confirms investigator Roland M. Schaefer of the department of nephrology at Münster University (Münster, Germany).

J&J's involvement with erythropoietin began in 1985 with a license from Amgen that gave it marketing rights to all treatments in the US except kidney dialysis or any indication in Japan and China (where Kirin Breweries in Tokyo has the rights). When NESP emerged, J&J claimed that it was similar enough to EPO for it to fall under this original agreement. However, the Chicago court has ruled that NESP's extra sugar residues make the two molecules biochemically different, and that Amgen has sole rights to NESP.

The binding arbitration decision will allow Amgen to sell NESP anywhere (except in Japan or China), significantly increasing its $1.35 billion share of the lucrative anemia market, which generates annual worldwide sales of more than $3 billion. In Europe, EPO sales for all indications in the areas of nephrology, oncology, and surgery (still out of reach for Amgen) run to $750–800 million in 1998, according to statistics collected by Amgen. (Unofficial sources suggest that Amgen's NESP is looking at a market share of 30–40% in its first year.) And in the US, according to the Amgen stats, the nondialysis market in 1998 amounted to approximately $600 million—making the total available to Amgen at least $1.35 billion.

The December ruling, which sent Amgen stock to a record high, will help ensure Amgen's independence. Stock analysts had been disappointed in the company's performance in the last three years: Amgen's earnings per share (the net income divided by the number of shares outstanding) fell from $2.42 in 1996 to $2.35 in 1997 (*S&P Stock Report*, 31 December 1998), and the share price dropped dramatically in October 1997 to below $50, a three-year low. In addition, the consensus buy/hold/sell recommendation of Wall Street analysts declined in 1997 from "hold" to "sell" in March 1998.

Richner: Amgen will remain independent.

Amgen itself seemed to be nervous about its performance and the consequences for its independence. During the third quarter of 1997, it substantially completed its authorized stock repurchases of $450 million, and announced additional $1 billion stock repurchase programs for 1998. According to Goldman Sachs' (New York) analyst Gabrielle Napolitano, repurchase plans—which increase earnings per share by reducing the number of shares outstanding—are often used to thwart takeover attempts.

Indeed, according to Amgen spokesperson David Kaye, Amgen management was reacting to a potential J&J takeover. "In 1997, it [Amgen] adopted a 'poison pill' plan. If Amgen had lost the arbitration, a takeover would have been the likely scenario," adds an Amgen insider who does not wish to be named.

Since February 1998, Amgen's share price has been performing well, climbing from a low of $47.13 to reach $109 on the first day of trading after the company won the J&J arbitration. "Amgen will stay independent," says Daniel Richner, fund manager of the Immunology fund, at Lombard Odier (Zurich, Switzerland). "No one [of the pharmaceutical companies] can afford to pay $30 billion to acquire it."

NESP has the potential to become Amgen's third best-selling drug, after granulocyte colony-stimulating factor (a protein that stimulates neutrophil production in cancer patients) and EPO. "With three blockbusters, Amgen is on a bed of roses," says Richner. Of its arbitration victory over J&J he says, "Amgen has got rid of J&J by a clever move."

Amgen now faces competition from Boehringer Mannheim (part of Roche; Basel, Switzerland), which sells Genetics Institute's (Cambridge, MA) β-EPO under the name of Recormon mainly in Europe; and Elanex (Bothell, WA), which markets EPO under the name of Epoietin-omega in Latin America, India, and the Eastern Bloc.

Meanwhile, J&J itself is developing new longer-acting formulations of erythropoietin. In collaboration with Alkermes (Cambridge, MA), using its "ProLease drug delivery system," J&J is working on a version of EPO that could be given as infrequently as once or twice a month. (It is assumed that Amgen will sue for patent infringement once the phase III trials are complete.)

Further out in the future, competition may come from Avigen (Alameda, CA) and Ariad Pharmaceuticals (Cambridge, MA). Both biotechnology companies are currently conducting gene therapy trials in animals using the adeno-associated viral vector to deliver an EPO gene that could stay in the body and produce EPO for over a year.

A more immediate threat comes from Transkaryotic Therapies' (TKT; Cambridge, MA) gene-activated erythropoietin (GA-EPO), which is currently in phase III trials. According to analysts, although GA-EPO offers no therapeutic advantage over conventional EPO, the way it is manufactured—large-scale production of therapeutic proteins without the need for cloning structural genes and subsequent insertion into nonhuman cell lines—means GA-EPO will cost less than EPO, which is produced in recombinant mammalian cells. In direct contrast to its arguments in its litigation with J&J, Amgen has filed suit for patent infringement of EPO by GA-EPO against TKT and its partner Aventis (Strasbourg, France), claiming that the two molecules are not biochemically distinct.

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