DARK FUTURE

SETBACKS SEND XOMA SOUTH

NEW YORK—Xoma's (Berkeley, CA) future is indeed dark. That's the consensus on Wall Street after the company's two flagship products—its E5 monoclonal antibody and its CD5 Plus immunoconjugate—suffered crippling blows. The U.S. Food and Drug Administration (FDA, Bethesda, MD) refused to approve E5 for gram-negative sepsis, ruling that two phase-III clinical trials failed to prove efficacy. And Ortho Biotech (Raritan, NJ)—which had acquired CD5 Plus worldwide marketing rights in 1990—returned the rights to Xoma without charge, except for rights for graft-versus-host disease (GvHD) in bone marrow transplants.

Several Wall Street analysts have given up on Xoma. Before the setbacks to its lead products, Joseph Edelman of Prudential Securities (New York) had expected Xoma to break even in 1994. He now projects annual losses well beyond 1996. And R. Brandon Fradd of Montgomery Securities (San Francisco, CA) believes Xoma isn't even an attractive acquisition candidate. "Xoma's products either have questionable futures or are in early development, so they lack significant fundamental value," says Fradd, adding that because of this "there's little prospect for a takeover" by another biotech company or a pharmaceutical company.

About all Xoma has of value is $110 million in cash, say several analysts. So at its current burn rate of $8 million a quarter, it at least has a few years of life, even without product approvals.

Regarding E5, Xoma is negotiating with FDA over whether to conduct further clinical testing. Yet even if FDA eventually approves E5, analysts believe it will grant a narrow indication for enhanced resolution of organ failure rather than a broad indication for improved survival. "The question becomes whether to spend additional dollars on a product with such a limited market," says Margaret McGeorge, an analyst at Sutro & Co. (San Francisco, CA).

FDA approval of E5 would probably come too late, moreover. "The likely presence of superior sepsis drugs would foreclose any significant market share for E5," says David Webber, an Alex Brown (New York) analyst. Among companies developing second-generation sepsis products are Chiron (Emeryville, CA), Genentech (S. San Francisco, CA), Immunex (Seattle, WA), and Synergen (Boulder, CO). Particularly promising, according to analysts, is Synergen's interleukin-1 receptor antagonist, which is now in phase III trials.

Xoma's Pipeline

Product	Indication	Status
Sepsis		
E5	Gram-negative sepsis	PLA
BPI	Gram-negative sepsis	Research
Anti-*Pseudomonas* MAbs	Gram-negative sepsis	Research
Immune System Disorders		
CD5 Plus	GvHD therapy	PLA
	GvHD prophylaxis	Phase III
	Rheumatoid arthritis	Phase III
	Type I diabetes	Phase II
	Inflammatory bowel disease	Phase II
	Lupus	Phase II
	Scleroderma	Phase II
	Organ transplant rejection	Phase I
CD7 Plus	Autoimmune disease/malignancy	Phase I
T cell receptor products	Multiple sclerosis	Phase I
Collagen antagonists	Rheumatoid arthritis	Research
Cancer		
XomaZyme-Mel	Melanoma	Phase II
XomaZyme-791	Colon cancer	Phase I
Bone Repair Proteins		
Ostein	Bone repair	Phase I
	Osteoporosis	Research
Low Calorie Sweetener		
Thaumatin	Flavor enhancer	Research

Source: Xoma (Berkeley, CA)

Xoma's CD5 Plus, for its part, has been awaiting FDA approval for GvHD in bone marrow transplants for over a year. The product—made up of a murine monoclonal coupled to ricin's A chain—targets the CD5 antigen on the surface of T lymphocytes. So it could treat diseases with T lymphocyte involvement, like GvHD. Xoma is currently conducting CD5 Plus clinical trials for organ-transplant rejection and a host of autoimmune diseases, including rheumatoid arthritis, inflammatory bowel disease, lupus, and scleroderma.

That Ortho returned CD5 Plus marketing rights to Xoma "indicates that Ortho has lost confidence in the market potential of CD5 Plus in autoimmune and organ-transplant indications," says Prudential Securities's Edelman. He believes CD5 Plus is too immunosuppressive and toxic to treat non-life-threatening diseases like rheumatoid arthritis, though it "could be marginally useful" for GvHD. He pegs the GvHD market in the U.S. at $20 million a year. **—B.J. Spalding**

KEY DISTRIBUTION QUESTIONS

WHOLESALER'S ROLE IN BIOTECH

NEW YORK—The race was on from the minute Amgen (Thousand Oaks, CA) received word that the Food and Drug Administration (Bethesda, MD) had approved Neupogen granulocyte-colony stimulating factor (G-CSF). That was on a Friday. By Monday, package inserts had been printed, vials labeled, and the drug bottled in Michigan by Amgen's packager Parke-Davis and flown back to the company's distribution center in Thousand Oaks. "We had product in patients's arms by noon the next day," recalls Edward Garnett, Amgen's director of logistics and materials management.

For its February, 1991, launch of Neupogen, Amgen relied heavily on traditional drug wholesalers. Today, those wholesalers handle 80 percent to 85 percent of Amgen's sales of