

Just mad about mAbs



Tom Jacobs, of the Internet site Motley Fool (<http://www.fool.com/>), provides his angle on biotechnology investments. Read on and become "Foolishly"

informed*. He can be contacted about biotechnology and investing at TomJ@Fool.com. Jacobs cannot give individual investment advice but welcomes any.

The members of the Sitting Pretty Investment Club recently returned from their summers in Brighton, Cape Cod, and the back porch, greeting each other at the Bull & Bear with good-natured fellow suffering: "Oh, the agony!"; and "When will this madness end?"

The club reviewed the past two issues of *Nature Biotechnology*, which exhorted them to stay focused on sound personal finance principles while the market endures it malaise. "Malaise?" General (Retd.) Blatzworthy harumphed. "I knew Malaise. She was a friend of mine. And this is far worse than Malaise."

But he and the other members remained resolutely optimistic about a brighter future. For months, they had pored over some particularly interesting research on monoclonal antibody (mAb) drugs developed during 1980–2002 (*Nat. Biotechnol.* 19, 819–822, 2001; *Curr. Opin. Mol. Ther.* 4, 110–118, 2002). Interim club president Paisley McTort would have preferred to browse the latest issue of *Punch*, but once he started reading these articles he was completely absorbed. So, an entire meeting would be devoted to it.

Clyde Goforth began the night's work, a pint of lager and lime in hand. "According to this article in *Nature Biotechnology*, there were 77 mAb drugs either in human trials or under review by the US Food and Drug Administration (FDA; Rockville, MD) as of February 2002. Around 22% of the mAbs entering human trials during this period secured FDA approval, versus the 10% figure that is often cited for small-molecule drugs. And FDA review times for mAbs beat those for other drugs."

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The assembled knew that these were excellent numbers. Hortense Convertible-Bond, secretary–treasurer, offered a rationale for the better performance of mAbs. She had consulted the website of Abgenix (Fremont, CA), one of the two companies producing fully human mAbs. Here she found some answers: "Faster product development, fewer unwanted side effects as a result of [mAbs'] high specificity for the disease target; greater patient compliance and higher efficacy as a result of favorable pharmacokinetics; ability to deliver various payloads, including drugs, radiation, and toxins, to specific disease sites; and ability to elicit a desired immune response."

Convertible-Bond concluded, "All else being equal, this means that a company with more mAbs in its drug development pipeline has a more valuable pipeline. Naturally, you have to adjust for safety and effectiveness of an individual drug, market size, competition in that market, and other drugs in development, but the power of mAbs cannot be denied."

Lower risk options

General (Retd.) Blatzworthy made the case for a more conservative investment in mAbs. He noted that the healthcare giant Johnson & Johnson (JNJ; New Brunswick, NJ) forked out \$4.9 billion for mAb pioneer Centocor in 1999. That proved a smart move when Centocor's anti-clotting agent ReoPro and its therapy for Crohn's disease, Remicade (now also approved for treating rheumatoid arthritis), each began to generate more than \$500 million a year in revenue. Remicade is in phase 3 trials for several other indications, and the company has other mAbs in phase 1 and 2 trials, although no others in phase 3.

JNJ dependably increases its quarterly revenue at low double-digit and high single-digit rates. More importantly, it has turned those rising revenues into free cash flow at a much higher rate over the past four years, and pays a not insignificant 1.5% dividend. Even if its growth rate should slow, the company's enterprise-value to free cash-flow (EV/FCF) ratio (see *Nat. Biotechnol.* 20, 219, 2002, for explanation) of 20 offers room for steady—not spectacular—value creation for shareholders in the future, along with a margin of safety on the downside. JNJ is therefore ideal for a dividend reinvestment plan or dollar-cost average investing.

Moderate risk

The General admitted that venturing into somewhat riskier territory put him on edge. He pointed out that Genentech (S. San

Francisco, CA) dominates the world of mAbs today. Of the 11 mAbs on the market, Genentech has licensed, developed, and marketed three of them, two of which—Herceptin and Rituxan—have provided much of the fuel for the company's 27%, 24%, and 22% gains in revenue over the past three years. And Zevalin, its newest mAb-based product, co-marketed with IDEC Pharmaceuticals (San Diego, CA), delivers a radioisotope to non-Hodgkins lymphoma that is not responsive to Rituxan.

But even with a 36% fall in stock price this year, Genentech's EV/FCF ratio is 58, so far beyond the company's current revenue, profit, or free cash-flow growth that investors face a considerable downside risk. And that growth has been further threatened this year: the FDA has held up the company's next mAb hopefuls, requiring more data on asthma drug Xolair and addressing manufacturing concerns about psoriasis treatment Xanelim. Genentech may be a better prospect for investors the closer it gets to \$20 a share and under, at or below a \$10 billion enterprise value.

High risk, high reward

Next, Convertible-Bond examined the riskiest group. First, she explained that to date all mAbs approved are murine, chimeric, or humanized. Of these three, humanized mAbs promise the greatest effectiveness, and Protein Design Labs' (Fremont, CA) "humanizing" mAb technology is licensed for all humanized mAbs marketed today and a large chunk of those in clinical trials (*Nat. Biotechnol.* 19, 395–396, 2001). Although Protein Design Labs is not yet profitable, it has plenty of cash and a relatively low annual cash-burn rate.

Close on their tails are the fully human mAbs, which could be safer and more effective than "humanized" mAbs. Almost all are produced by, or licensed from, Medarex (Princeton, NJ), Abgenix, and Cambridge Antibody Technology (Melbourne, UK). All three companies are unprofitable, and although they have a lot of cash they also have substantial annual cash-burn rates. These companies should interest only those investors willing to take on considerable risk, and even then with only a small part of their portfolios. "That is to say," Convertible-Bond quipped, "these companies come with label warnings."

The group raised their glasses in praise of summer and the glory of mAbs. The literary McTort swelled with sudden Shakespearean inspiration, but the group had already dispersed when he retorted: "I see Queen Mab hath been with you."

Tom Jacobs owns shares in Medarex.

