Sense and antisense for investors

Tom Jacobs, of the Internet site Motley Fool (http://www.fool.com/), provides his angle on biotechnology investments. As Jacobs points out, "Industry insiders may know about biotechnology, but (as the song should go) 'it don't mean a thing, if you haven't learned sound investing principles.'" 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. At press, Tom Jacobs owned shares in Isis Pharmaceuticals.

Is investing in antisense for you? The Sitting Pretty Investment Club was so intrigued by a leading journal's feature on biotechnology companies working in the antisense field (*Nat. Biotechnol.* **20**, 121–124, 2002) that it devoted its most recent meeting to them.

This ruffled a few feathers: interim president Paisley McTort objects to unprofitable companies, but he could not oppose the club's rule permitting 20% of the total portfolio value to be in high-risk investments. So when young techie Clyde Goforth volunteered to lead the analysis, McTort showed his support—hopeful that a little magnanimity might win Goforth's vote to drop the "interim" from his title.

The leaders

With Palm Pilot at left, silenced cell phone at right, and laptop front and center, Goforth maneuvered his PowerPoint presentation like a commander deploying his troops. This earned both the attention and admiration of General (Rtd.) Blatzworthy, who quickly regretted muttering, "you might as well take the money to the betting parlor, like we did with Jellybabies.com."

Clyde identified the three leading antisense companies as Isis Pharmaceuticals (Carlsbad, CA), Genta (Berkeley Heights, NJ), and Hybridon (Cambridge, MA). Without mercy, he dispatched Hybridon, a stock trading for about $1.00 a share on the over-the-counter *Pink Sheet*. "After all," he quipped, "most investors should find themselves between them, not invested in them." Research indicates that the majority of "penny companies"—companies, such as Hybridon, whose stocks sell for less than $5.00 a share and that sport market capitalizations of under $250 million—are bankrupt within ten years.

Genediction

"Until late April, you can see that Isis was the clear leader, with 8 drugs in 12 clinical trials. It had cash not only from a $200 million research and development deal with drug giant Eli Lilly (Indianapolis, IN), which included the licensing of Isis's phase 3 lung cancer drug, but also from new share offerings that capitalized on Lilly's vote of confidence.

"Genta has less cash and a shallower drug pipeline than Isis, claiming only one (albeit very hot) drug in phase 3 trials, Genasense, a potential blockbuster against a range of blood-related cancers and solid tumors. Many big pharmaceutical companies were reportedly fighting over this prize, but Aventis recently won in a $480 million deal (*Nat. Biotechnol.* **20**, 533–534, 2002)—the second-largest single drug licensing deal ever penned after Bristol-Myers Squibb's $2 billion (later reduced) deal for ImClone's ill-starred Erbitux. Now, Genta will definitely live to play another day."

Cash burn

The club members insist that the first task in evaluating any unprofitable company is to determine whether it has enough cash to survive until it can make a profit. If you need money in bad times, you may not find it. Even worse, you may find it, but on terms hardly better than those offered by the neighborhood loan shark. Here, Goforth shone even brighter.

"Isis announced that it had $290 million in cash as of March 31, 2002, but since then the company has sold $125 million in bonds at a quite favorable 5.5% interest rate, convertible to common stock at $16.625 a share. Management sensibly used the proceeds to pay off $74 million in pesky 14% interest–bearing debt, the only terms available back in 1997 and 1998 when the company had poorer prospects. That leaves Isis with $343 million in the bank. With a cash burn rate of $150 million a year as of December 31, 2001, Isis could survive for 2.5 years without needing to raise additional funds."

"By contrast, at the end of last year, Genta sported $54 million in cash and had a cash burn rate of about $9 million a quarter. Accounting for the first quarter of cash burn during 2002, which reduces the $54 million to $43 million, and adding the $60 million that Aventis will pay up front in licensing and development fees and convertible debt, Genta has a 2.33-year survival term. If it meets a near-term milestone, Aventis pays another $75 million, which further prolongs Genta's survival." (For more details on computing cash burn and survival term, e-mail TomJ@Fool.com.)

Not the whole story

Clyde paused, then added, "But these survival terms mean nothing by themselves. Will these companies be profitable in the next several years, if ever? All drug makers deal with the odds being firmly against success. Research shows that there is an 80–90% failure rate for drugs in human clinical trials."

The odds are that Isis will earn additional payments from partners as its research and drug candidates advance, but investors willing to undertake the risk will want to see that one, if not both, of Isis's two drugs in phase 3 earn approval and significant revenue in a few years. Lilly's vote for one of them helps, but does not guarantee, US Food and Drug Administration (FDA; Rockville, MD) approval. And while Isis, unlike Genta, has several drugs in phase 2 trials, none of them is likely to hit the market within four years.

"Genta's future depends on Genasense, and Aventis's investment also hardly guarantees FDA approval. According to Genta, its soon-to-be-marketed drug Ganite, which is used to treat cancer-related blood problems, has limited market potential, and there are no other Genta drugs in trials beyond phase 1. The Aventis deal buys Genta more time, but it will certainly have to spend much of the proceeds of the deal to fatten its pipeline. Investors may profit in the short term, but beyond a few years, the outlook is fuzzy.

The club decides—not

While debate and dessert ensued, the club considered the prospects. Isis has the deeper pipeline and longer-term partnerships, but Genta—as long as Genasense is approved and marketed—provides more near-term opportunity for investor gains. Both present significant risk. Club members agreed to put Isis and Genta on the candidate list and continue their search for possible high-risk investments.

McTort also congratulated Goforth on his astute financial analysis, but assured other members that they need not aspire to his ambitious production standards to be warmly received.

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