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Just say no

After delivering a 50% gain in 2012, the Nasdaq Biotechnology Index has leapt by 60% in the 11⅓ months of 2013. In November, 75% of the respondents to a poll by the ISI Group said they expected another banner showing in 2014. Herewith a dissenting opinion and a short-sale candidate. (Spoiler alert: Keryx Biopharmaceuticals is the name of that candidate.)

To make a clean breast of it, nobody on the staff of *Grant's* so much as passed an organic chemistry course, let alone took the Hippocratic oath. We pretend to no special pharmaceutical knowledge. What we do bring to the analysis is a working relationship with a thoroughly credentialed biotech investor. Our source, who insists on anonymity, is successful enough to have remained in business (profitably so, he reports) as a short-seller of biotech stocks during the recent melt-up. Insofar as this publication brings a proprietary store of knowledge to the table, it derives from long experience with a non-institutionalized psychiatric patient called Mr. Market.

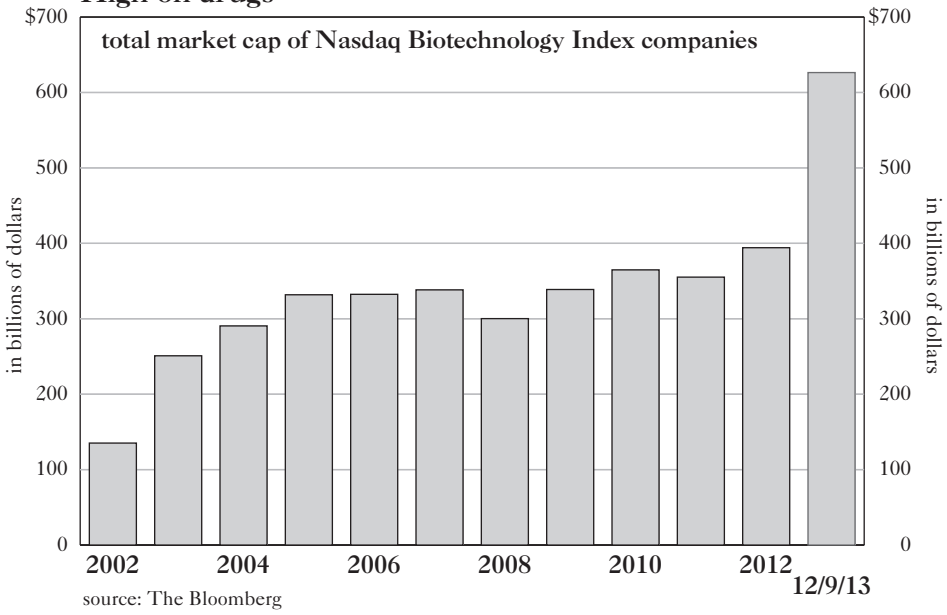
The theme of this unfolding essay reprises the themes of its predecessors in the issues of *Grant's* dated May 3 and Oct. 4—to wit, biotech stocks, now with an aggregate market cap of more than $600 billion, are on a bender. When *Grant's* was a little quicker on the predictive trigger, we might have added, self-confidently, that biotech has peaked. The fact is, we have no idea whether biotech has peaked. What we do believe is that risk seems vastly to outweigh reward.

The market appears to be only partly on board with this proposition. Isis Pharmaceuticals and Sangamo Biosciences, both panned in our May 3 analysis, subsequently climbed by 67% and 21%, respectively. Coronado Biosciences, also disparaged in May, has fallen by 84%. Sarepta Therapeutics, a short-sale candidate from the Oct. 4 issue of *Grant's*, has fallen by 63% since publication date.

Making money imparts its own feeling of optimism, but the biotech bulls give other reasons for being confident. Respondents to the ISI poll indicated that research and development productivity has permanently improved, and that the Food and Drug Administration is newly inclined to listen to reason, as a pharmaceutical manufacturer might define reason. "The biopharma industry leads with innovation," Alice Avanian, associate director of research for the biotech-centered investment bank, Leerink Swann, sums up the bullish case: "Scientific advances such as immuno-oncology [an approach to fighting cancer that mobilizes the immune system] and genomics enhance our understanding of disease and lower clinical risk. Combined with a more transparent and efficient regulatory process, new molecular entity approvals rose in 2012 and have stayed at this higher level in 2013." Then, too, Avanian adds, there's support for the biotech industry both in American demographic trends and in the promise for continued growth in emerging markets.

There's no gainsaying some of these points. Twenty-six new molecular entities have passed regulatory

High on drugs



source: The Bloomberg

muster this year, a significant follow-on to the 39 approved in 2012. It's true, as well, that the FDA's "orphan drug" exemption has cleared a regulatory path for therapies intended to treat small patient populations. We can agree that aging Americans need more and better drugs. One can even make the argument that, by certain bespoke metrics, biotech stocks are fairly valued. For example, the NBI carries a price to *positive* earnings ratio of 33.1 times—i.e., those companies that show any earnings trade at a multiple of 33.1. The ratio was as low as 17.6 times in 2010 and as high as 164 times in 2001. Then, too, a visionary might demand, what are mere earnings compared to such news as that out of Organovo Holdings (ONVO on the NYSE Mkt)? You may recall that Organovo disclosed in October that it had "bio-printed" human liver tissue, and that this digital creation functioned like nature's own for 40 days. No wonder a long-serving T. Rowe Price portfolio manager, Hugh Evans III, is leaving the money management business for the frontiers of 3-D printing. "Very few people have the chance to be part of an industry that is going to change the world," Evans was quoted as saying by the *Baltimore Business Journal*.

Very few people may have that particular opportunity. But everyone with a brokerage account may avail himself of the public investment opportunity. And to judge by some elevated alternative measures of biotech valuation, many an investor has.

For instance, observes colleague Charley Grant, among the top 20 performing companies within the NBI in 2013, just five expect to report positive net income. As a multiple of price-to-book value, the NBI trades at 7.2 times, the highest such reading since the 5.46 times registered in 2001.

More easily than Organovo can materialize human liver tissue, Wall Street can create stock certificates. Thirty-four biotech IPOs have come to market this year for proceeds of $2.04 billion. The last time more money was raised in this fashion was in 2007. The last time more biotech deals were done (not counting the 11 in the investment-banking queue) was in 2005.

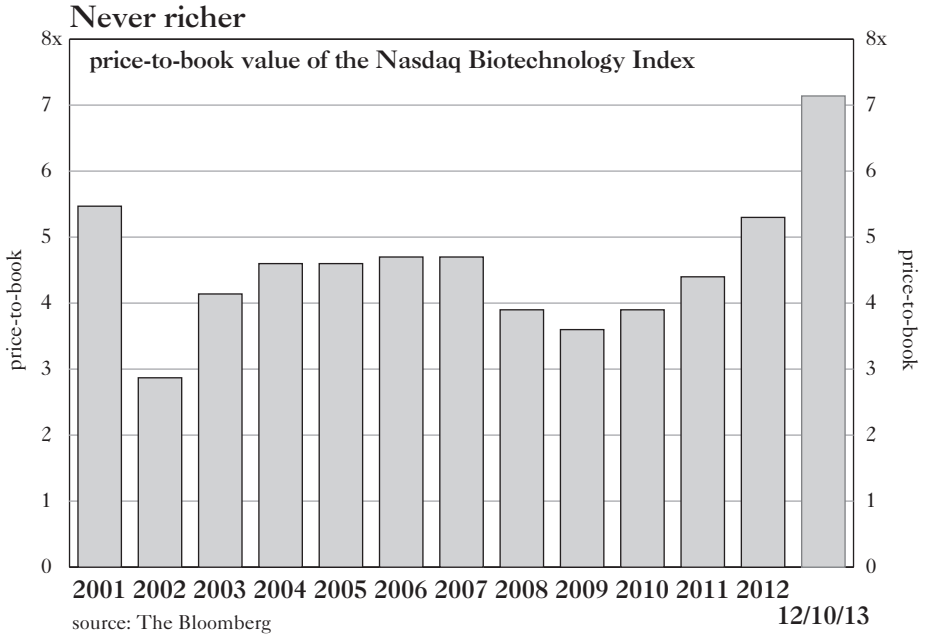
The wonder is that there aren't more. Last week, Celgene, the world's fourth-largest biotech company by market cap, announced a partnership with newcomer OncoMed Pharmaceuticals; the parties valued the tie-up at $177.25 million. OncoMed, whose drugs target the stem cells of cancers, went public only in July. News of the Celgene transaction sent the OncoMed share price up by 98% two Tuesdays ago.

Another sign of the excitable times: Last month, Shire Plc, the Dublin-based biotech giant, agreed to buy ViroPharma, a maker of antiviral pharmaceuticals. The price was $4.2 billion, which represents 58 times ViroPharma's EBITDA in the 12 months through Sept. 30. According to Bloomberg, acquirers have paid a median price equivalent to 23 times EBITDA in biotech transactions valued at more than $100 million over the past five years. "Clearly at an eye-watering multiple," Bloomberg News quoted one analyst as saying, "but strategically very sound."

"But scientific breakthroughs are not the only kind of innovation for which biotech companies are known," Grant relates. "Some are pioneering in the art of behavioral finance. Consider the case of Oculus Innovative Sciences (OCLS on the Nasdaq), a tiny manufacturer of products designed to treat infections and so reduce the need for antibiotics. Founded in 1999 and public since 2007, Oculus is capitalized at just $29 million. That's down from $80 million in March 2008. In the 12 months through September, operating cash flow was minus $4.6 million; as of Sept. 30, net cash stood at $2 million.

"What to do? Oculus had hoped to spin out its new, wholly owned subsidiary, Ruthigen Inc., via an IPO announced in October. The IPO hung fire. Fast forward to last Wednesday. Investors cheered as Oculus announced that the FDA had granted approval for the parent's anti-scar treatment. A breakthrough! Never mind that the agency had actually approved the treatment on Nov. 15. In reaction to the not-so-new news, the price of a share of OCLS doubled, closing at $4.74 on Wednesday, up from $2.33 on Tuesday. Following which, late Wednesday evening, the company issued 550,000 new OCLS shares at $4 each. The FDA described the product as 'substantially equivalent' to existing therapies. Asked about that characterization, Oculus replied to me in an e-mail: 'It is the only product available that contains our proprietary Microcyn® Technology, which has been shown in studies to reduce inflammation and increase blood flow to a wound site.'"

"Biotech allows you to craft a story," our biotech authority maintains. "It's kind of like modern art. People can see in it whatever they want to see in it. . . . It's what hopes and dreams are made of. But what it comes down to is, if your stock has gone up on the rising tide, well good for you. You're on



the right side of the market. But the probability of that drug working in its clinical trial has not changed one iota."

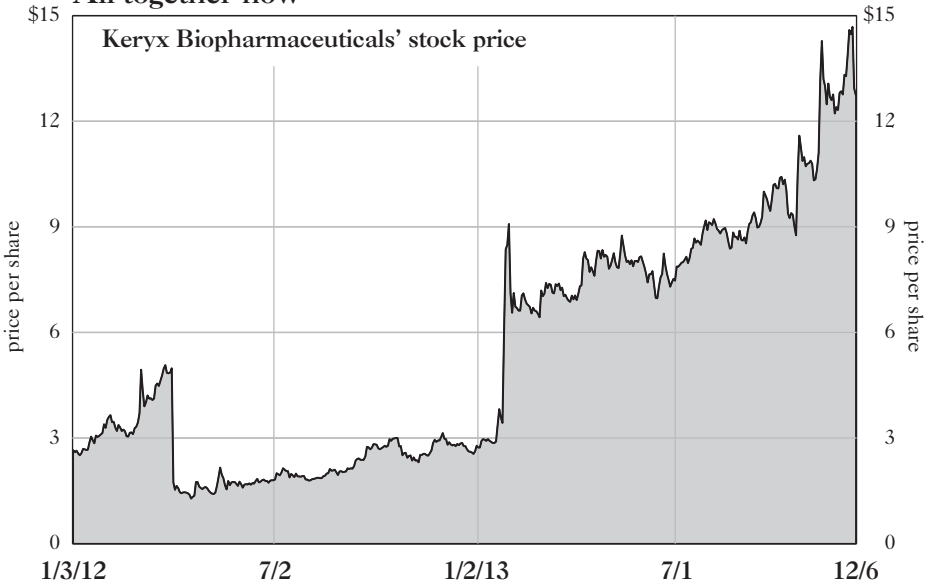
Which prompts us to ask our source about research and development. Has it, as the bulls contend, reached some kind of permanent high plateau of scientific and economic efficiency?

"People said a similar thing back in the genomics era [1998-2000]," he replies. "Back then, it was hard to find drug targets. It was hard to find proteins that drugs would go after. What happened was that people said there are advances in our ability to find targets and to screen drugs against those targets. But all that did was to move the bottleneck in drug development forward a little bit. Because you still had to synthesize the lead molecule, and there's no easy way to do that, other than by the way it's currently done. You still need chemists to look at these things and make them and try different variants and whatnot, and then you put them in mice and see if they work. There's no speeding that up right now, and you still have to study the drug in the clinic. Companies don't say, 'We're going to take our best four drugs forward in to clinic.' They take the best one, because clinical trials are expensive. So I don't think R&D productivity is permanently higher."

There's a contrary contention: No fewer than 83% of the respondents to the November ISI survey indicated that, in their opinion, R&D has, in fact, arrived at a kind of new era of heightened productivity. On the evidence, that belief would seem to be priced into the market.

It doesn't matter how many dollars the Federal Reserve produces, our source points out. QE might raise up the stock market, but it won't improve the odds on success for a given therapy in a clinical trial. "If your company has got one drug in the pipeline," our man goes on, "and that drug is going to report out data at some point in the future, with the index up 60% this year and the dreck is up even more than that. But … fundamentally, what's happened? Nothing. The drug has still got to work, it still has got to get approved, they still have to sell it. If there was ever a sector insulated from macroeconomic issues, it's biotech. All of these events are idiosyncratic. But yet they've all gone up."

All together now



source: The Bloomberg

One that especially doesn't deserve to go up, in our mole's opinion and ours, is the aforementioned Keryx Biopharmaceuticals (KERX on Nasdaq). Keryx is the developer of KRX-0502, a.k.a. Zerenex, an oral iron supplement that binds to phosphate. Keryx is developing Zerenex to treat patients with hyperphosphatemia, or elevated levels of phosphate in the blood. It's a condition from which victims of chronic kidney disease, or CKD, are likely to suffer. In January, Keryx announced a successful phase 3 clinical trial for patients with CKD who are on dialysis. A clinical trial for a different indication for Zerenex, the treatment of iron deficiency in patients with anemia and stage three to five CKD (for patients not on dialysis) is in phase 2.

That announcement, together with news of a licensing partnership with Torii Pharmaceutical Co., a subsidiary of Japan Tobacco, caused the Keryx share price to triple. Next day, Jan. 29, management monetized the excitement by issuing $55 million in new stock. To date in 2013, shares of Keryx have climbed by 387%. Debt-free, the company is also virtually sales-free: $7 million in 2013 revenue to date derives from licensing. The market cap stands at $1.1 billion. There is $67 million in cash on the balance sheet.

In raising his price target to $22 from $14 on November 6 (the stock closed Tuesday at $12.76), J.P. Morgan analyst Cory Kasimov projects that the hyperphosphatemia indication has a 75% chance of regulatory approval, the iron deficiency indication a 70% chance of approval. He forecasts annual product sales of $520 million by 2017. Kasimov is not alone in his positive reading of the situation; nine of 10 sell-side analysts tracked by Bloomberg rate KERX a buy (the one dissenter says "sell"). Then, again, the last recorded insider purchase of KERX occurred in April 2012, at a price of $1.28; maybe management is as incredulous as we are.

Threshold question No. 1 is whether the FDA will give Keryx the green light. Say it will. Question No. 2 is whether these products can generate a half-billion dollars in revenue. Our authority is skeptical. The market for drugs to reduce phosphate is already well established, he says. Existing products include Phoslo (a generic), Renagel (by Genzyme), Fosrenol (by Shire) and Velphoro (by Galenica in partnership with Fresenius Medical Care), which the FDA approved on Nov. 28. How does a patient choose? "If you have something that has a lower pill burden and a lower side effect, that's what you take," says our informant. "Because their efficacy is basically fungible, they all do the same thing. Velphoro is basically a flavored gummy bear that you take, one pill, with meals. Zerenex is at least six pills a day."

How does a payer choose which drug to supply? The decision tree, whatever its current configuration,

will change in September 2014 when Genzyme's patent on Renagel expires.

"Then the dialysis providers are going to say, 'We're going with the cheapest one that works,'" our source predicts. "[I]t's cost-driven, right? If your choice is Renagel vs. Zerenex, and Renagel is a generic, which it will be very shortly, then you go with Renagel."

Keryx bulls insist that because their therapy has been shown to enhance a patient's iron levels, a cost-conscious dialysis center will net the higher cost of the Keryx drug with savings realized by the reduced need for intravenous iron infusions.

"Here's the fallacy of that argument," our authority ripostes. "Let's assume that Keryx somehow replaces 100% of the IV iron use in the country for dialysis that's paid for by the government. The budget for this year, the amount the Centers for Medicare and Medicaid Services expect to pay for IV iron supplements, is $226 million. The market leader in IV iron is Venofer, and it's going generic in 2015, so that price is probably coming down. IV iron is dirt cheap and injecting it is not a problem. Even if [Keryx] took the whole market, they would save the dialysis centers $226 million. I don't think the dialysis centers are giving them the entire savings."

Though Keryx Biopharmaceuticals is a relatively cheap and easy stock to borrow, it has been—needless to say—a brutally unprofitable stock to short. Maybe that will change. Our informant's parting comment concerns the above-quoted ISI survey. More than half of the respondents admitted to being "generalists." "I'm thankful for it," he says, "because they don't know anything. But I also think that they're weak hands; they're the first to leave when things blow up or threaten to." Then, too, our helpful friend conjectures, biotech "is just infested with retail."

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