Executive Overview

Rising like a phoenix from the ashes, the US biotech industry re-emerged in 2003, having fully recovered from the massive devaluation that took place during the last three years. Biotech turned in a stellar performance on Wall Street with the Burrill Biotech Select Index rising a whopping 66% in 2003 and the industry's market cap jumping 53%. In addition, the industry raised more than $16 billion, making 2003 biotech's second best year ever.

VC investment in US biotech was more than $2.8 billion, compared to $2.7 billion in 2002. What's more, after five consecutive quarters without a single traditional IPO, seven new biotech companies went public in 2003 raising a total of $453 million. By the end of December, there were 16 additional deals on file (four of which have withdrawn and may refile later in 2004)—the majority for companies with products that are generating significant revenues or in late stage clinical trials. This is wildly different from the IPO boom in 2000, which was fueled more by the excitement of genomics than revenues and pipelines.

Tremendous strides were made in the battle against cancer and AIDS as well as many other chronic and debilitating diseases. With a capable and dedicated commissioner in place, the FDA was able to improve both the quality and the efficiency with which drugs, devices and diagnostic tests are reviewed and approved. In all, some 25 new biotech therapies were approved along with 12 new indications for previously approved drugs.

The biotech industry was also successful at shaping the Medicare Prescription Drug and Modernization Act of 2003 to include reimbursement for biotechnology drugs, devices and diagnostics. Thanks to the lobbying efforts of the Biotechnology Industry Organization, the new bill also prohibits the future application of the controversial "functionally equivalent" mechanism for novel drug reimbursement and also mitigates the cuts that were made to the use of biotech products in outpatient settings earlier in 2003.

Not surprisingly, biotech is expected to have another big year in 2004 with Medicare resolved in the industry's favor, close to 400 drugs advancing through clinical trials, rekindled investor interest and a sizeable sum of money in the war chest. We believe that the equity markets will be robust during the year and that the industry will raise as much as $20 billion through PIPEs, secondaries, convertibles and IPOs, as well as venture investment. Having said that, we will not see another year on Wall Street where the industry rises as much as 50% again. However, while the increases in 2003 were mostly in the realm of "recovery," we'll see genuine gains in value in 2004 with industry returns in the realm of 25 to 40%.

Even though the IPO market will be choppy in the first half of 2004, we expect to see 25 to 30 IPOs getting done in 2004. We'll see a discriminatory period where a very large number of companies will be in the market—perhaps as many as 50—but not all the deals will fly. Early in 2004, the supply of deals will likely overwhelm market appetite . . . and the markets will be very challenging. But as the year progresses, the supply/demand situation will equalize and the markets will improve.

Our outlook for 2004 is very positive. It's entirely likely that the year ahead could be the best ever for biotech. For one, there are no more "boxcar" size issues looming in the wings that could get the industry off track. We've had the dot-com disaster, the technology bubble, the 9-11 bioterrorism phenomena, the "headless" FDA, the **ImClone** debacle and its ensuing ramifications and the war with Iraq. Now, as the economy continues in a positive direction and the industry is firmly on its feet, we'll see a very strong performance in the year to come.

The trends we see unfolding during 2004 include:

- Although in 2003, the lion's share of fundraising came through convertible debt, we'll see a shift away from that financing device and we'll see increased interest in secondaries, PIPEs and IPOs. Convertible debt is used when the markets are more challenging and investors are more interested in being "paid to wait."
- We'll see more Big Pharma consolidation among players such as **Bayer**, **Aventis**, **Schering-Plough** and **Eli Lilly**. In pharma's desperation to find more innovation, we'll see more partnerships where the values are greater and the terms more favorable to biotech. We'll continue to see deals done at substantial premiums to the marketplace (which speaks to the underlying strength of the biotech industry).
- We can also expect one or two marquee level biotech mergers at the level of **IDEC/Biogen** in 2003 as the larger cap biotech companies compete nose to nose with Big Pharma.
- With the resolution of Medicare and the associated reimbursement issues behind us, we'll see the focus on Capital Hill shift to other things. Drug re-importation will continue to be a challenging area and there are still aspects of Project BioShield that need ironing out. There's also a full court press to get the new energy bill passed so that bioenergy research and development will continue to be supported. The biotech industry is also urging congress to restore SBIR eligibility for venture-backed biotech companies.

- We can expect to see numerous important product approvals in 2004 as the FDA finishes streamlining the review process and continues to approve drugs early on signs of efficacy. Lining up on the runway are **Genentech's** cancer drug Avastin, **ImClone's** Erbitux, **Genta's** Genasense and **CV Therapeutic's** Ranexa, among others.
- Although we may yet hear a lot about healthcare and healthcare reform with the new Medicare and prescription drug legislation in place, the talk will be about productive ways to get the job done, rather than just the political rhetoric required to get the bill passed.
- In the diagnostics sector where there are now well over a thousand genetic tests available, we'll see more of a linkage between the Dx and the Rx side of the equation. Indeed, in 2004, we can expect to see more interest in pharmacogenomics and theranostics driven by the science. Regulators and payors who have a strong interest in trying to screen out adverse reactions and non-responding patients will continue to embrace molecular diagnostics with gusto.
- The nutraceuticals industry will continue to do well, although it's unlikely that we'll see another spectacular year like 2003 on Wall Street. Nonetheless, the pseudoscience that has dogged this industry has been exposed and we're seeing more and more companies reaching to the biosciences to get better clinical data and better correlation between diet and disease. The nutraceuticals side of biotech will swiftly matriculate into a stronger player in the overall healthcare scene in 2004 and one that has credentials and good science backing it.
- With some progress made on the EU GMO front and with Brazil embracing GM soybean seeds at last, agbio will do all right in 2004. Still, there are some difficult times ahead as the industry contends with the last of the GM hold outs. Output traits, rather than input traits will be emphasized and people seem more willing to accept and pay where they perceive a benefit, so that strategy is likely to pan out in agbio's favor.
- As for biopharming, we see a move towards using non-food crops to get around some of the perceived problems with containment and migration. While biopharming is clearly a longer term play, the economics are so compelling in many cases that we see this as an important component of the manufacturing armamentarium of providing lower cost antibodies and proteins.
- We will continue to develop new tools and technologies to support genomics, proteomics and systems biology. As we move from Genomics 'R Us and SNPs 'R Us models, we will bring protein medicine further, faster and hopefully cheaper with lower cost manufacturing options.
- Although biogenerics are inevitable, we believe there is still reasonable protection for biotech drugs because of the manufacturing issues. Still, it would be naive to assume that we won't have biogenerics selectively competing with biopharmaceuticals on the world stage in the not too distant future.

- Biodefense will continue to be a focus in 2004. Although the primary markets for countermeasures will be military, research will discover many useful things along the way about understanding the immune system, the way pathogens work, or how to detect miniscule amounts of dangerous materials in the air and water.
- We'll also continue to see nature's own bioterrorism in action in 2004. The onslaught of SARS and other infectious agents is a huge threat in this day and age of increasing urbanization and global mobililty. As a result, we'll see more interest in infectious diseases in 2004 and more companies participating in the search for solutions to everything from Ebola to malaria.
- Outside the US—China, India, Scandinavia, Eastern Asia, Australia and New Zealand—the biotech industry will be more robust. These countries will continue to contribute new technology and also become markets for biotech products themselves as biotech becomes an increasingly global industry.

In 2003 the biotech industry demonstrated not only its durability but also its ingenuity. Having survived the ravages of the bear market, the industry got back on track in 2003 and is poised for real growth in 2004. While technical and regulatory challenges abound and risk remains, biotech is no longer an industry of dreams—biotech products and revenue streams are real. But the most exciting news of all is that we've only just embarked on what is destined to be a very rewarding journey.

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