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Stuart J. Sweet, President February 21, 2007

# WASHINGTON BIOTECH AND PHARMA WARS: ATTACK OF THE CLONES

With the Democratic takeover of Washington last fall, traditional pharma investors have braced themselves for rough times in Washington. However, biopharma investors may not realize that they are, in fact, more at risk. After years of talks, Washington politicians may end special patent protections biopharma has enjoyed for decades.

In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act, commonly known by the names of its primary authors, "Hatch-Waxman." Under Hatch-Waxman, the generic drug industry can reverse engineer patented drugs before patent expiration. After expiration, any generic company can apply to the FDA for permission to sell a copy cat drug. The experience of the past twenty years has shown that within two the three years after generic companies enter a market, prices of off-patent drugs fall by 50 to 80 percent. The FDA routinely approves the application of confirmed copy cats of conventional pharmaceuticals but almost never approves "biogenerics," sparing biotech companies from considerable financial pain. After years of grousing, the 110th Congress probably will compel the FDA to approve generic biotech products; biopharma patents may no longer be immortal.

## Why Have Biologics Received Exceptional Treatment from the FDA?

The FDA believes that it lacks the legal authority to approve most potential biogeneric drug applications because the Hatch-Waxman law was written before biologics were an important category that required Congress' attention. A few biogenerics have won approval, using exceptions to the Hatch-Waxman law that are not widely applicable.

In addition, the FDA has expressed concern that it is much more difficult to confirm a company has made a "copy cat" biogeneric. Companies produce traditional generics by synthesizing active chemical compounds. The FDA can confirm these processes, and therefore it can rely on the safety and efficacy testing of the innovator companies that produced the originals, allowing generics to hit the market with confidence. Biological products, however, are derived from living cells that are induced to express large proteins which are often 500 times the molecular weight of standard drugs. Companies wishing to make copy cat biologicals cannot literally do so without stealing the cell lines and duplicating the entire environmental package used to turn the cell factories "on."

However, enough information is available from the U.S. patent office to produce "biosimilar" products, using similar cells that have been tweaked in a similar fashion to produce nearly the same large proteins. The FDA has been leery about letting these on the market and has insisted that current law usually prevents it from doing so unless the biosimilar products go through rigorous multi-year testing, comparable to what the originator drugs had to do. It is this requirement that has given off patent biologicals their immortal lives. Such exhaustive testing is

prohibitively expensive, although in many cases the FDA would never order the entire roster of tests if current law did not require it.

**The Biologic Pioneers' Loss will be Generic Manufacturers' Gain**

Since all of the more that 250 biologic products now on the shelf, as well as 418 in clinical trials, will enjoy many fewer years of monopoly pricing power if Hatch-Waxman changes become law, the entire biopharma industry could be harmed. The earliest sales impacts would fall on companies making biological products who's patent lives are over or will soon end. They could face head-to-head competition by 2010. Each company listed below appears to derive between 8 percent and 50 percent of its revenue from patent-expired, or patent-expiring, biologics.

| Company | Patent-Endangered Biological Products |
|---|---|
| Amgen | Epogen<br>Neupogen |
| Biogen | Avonex |
| Eli Lilly | Humulin<br>Humatrope |
| Schering-Plough | Intron |
| Genetech | Nutropin<br>Activase |
| Genzyme | Protropin |

Several generic drug manufacturers believe they have the capability to manufacture biogenerics, and they are eager to fight for market share, as soon as the law allows. The names most often mentioned are: Barr, Teva, and Sandoz, a division of Novartis.

**Show Me the Money!**

Congressional Democratic leaders plan to destroy biopharma's regulatory monopoly that is boosting profits by expressly giving the FDA the authority to:

- Approve biosimilar products
- Tailor the amount of testing needed before it approves a biosimilar drug for sale.

Granting discretionary authority to the FDA would open up the biopharma industry to competition and is similar to the approach already adopted by the European Union. H.R. 1038, the "Access to Life-Saving Medicine Act," was introduced in the House last week by seven Congressmen, including Henry Waxman (D-CA), Rahm Emanuel (D-IL), and Pete Stark (D-CA); read its description at www.henrywaxman.house.gov/issues/health/generic_biologics.htm.

Six Senators – Schumer (D-NY),Vitter (R-LA), Clinton (D-NY), Leahy (D-VT), Stabenow (D-MI), and Collins (R-ME) – have introduced S. 623, a Senate companion. The bill has a powerful array of supporters, including Aetna, the Generic Pharmaceutical Association, the PBM industry group known as the Pharmaceutical Care Management Association, Teva, General Motors, AARP, Consumers Union, and the AFL-CIO.

Congressional Democrats have a strong motive for doing this; they need to find ways to pay for an expansion in federally subsidized child health insurance or other high priority spending initiatives. If the prices of biologicals come down, the government will save money on Medicare and Medicaid costs. It may not be chump change, either, since the U.S. is expected to spend $50 billion on biologicals by 2010, with Uncle Sam picking up a third of the tab. Express Scripts released a study last week projecting multi-billion biogeneric savings. Read the report at http://www.express-scripts.com/ourcompany/news/outcomesresearch/onlinepublications/study/potentialSavingsBiogenericsUS.pdf . It conservatively suggests that health care payors would save $71 billion over ten years if biogenerics developed for just four diseases were authorized.

Governors are weighing in, too. Tired of paying more than they believe is necessary for state Medicaid bills, the governors of eleven states – including Kansas, Minnesota, Mississippi, New Mexico, Vermont, Virginia, West Virginia, and Wisconsin – have written the FDA urging the agency to take steps making biogeneric insulin available. Fifteen million Americans have diabetes.

**PDUFA must be Reauthorized This Year, So Biogeneric Advocates Have Leverage**

The likely vehicle for biogeneric reform is a complementary law, the Prescription Drug User Fee Act (PDUFA) which faces sunset at the end of September 2007. As Hatch-Waxman allows generic companies to compete with research pharmaceutical companies on an expedited basis, PDUFA provides a path to accelerate the FDA approval process for new innovator drugs. The Act was first passed in 1992, then reauthorized in 1997 and 2002, and its reauthorization is considered "must-pass" legislation by a research pharmaceutical industry anxious to maintain its fast track. Under PDUFA, pharmaceutical companies can pay a modest sum to have the FDA hire additional experts to place on its staff to review their drug application submissions on a fast track basis. This is very valuable since, even with expedited approval review, a typical innovator drug only is on the market for eight years before generic competition savages margins. Without fast track, the FDA would have to make do with its existing staff and companies might get only five years of pricing power due to work backlog. "Time is money" is never more accurate than when dealing with traditional drugs that will go off patent at a date certain.

As result, big pharma will be lobbying hard to have PDUFA reauthorized before the law sunsets on September 30, 2007. There is a 50 percent chance that a version of the Schumer-Waxman proposal will be incorporated into this must-pass bill, to the dismay of biopharma shareholders everywhere. If Schumer and Waxman miss this legislative train, they will wait for another one.

**Big Pharma May Swallow a Bitter Pill: Unwelcome PDUFA Amendments**

Knowing that the research pharmaceutical companies are eager to have PDUFA reauthorized, Congressional Democrats may end what they consider industry abuses by incorporating reforms into the renewed PDUFA. Three stand high on their list.

- The first is to end the practice of brand-name drug companies marketing "authorized generics" at the same time that the first independently manufactured generic version of a drug could be released for sale. Current law gives the first generic manufacturer a 180-day generic "exclusivity" period, time to market its product without other generic competition, in order to recoup its FDA application and approval costs. However, Hatch-Waxman also allows brand-name companies to release an "authorized generic" at the same time the first generic hits the market, undermining the motivation of generic companies to enter the market. Threats to issue "authorized generics" can lead to agreements by generic companies to delay their entry. *Since 2004, practically every drug with an expiring patent has been sold as an authorized generic.* Sen. Rockefeller's (D-WV) "Fair Prescription Drug Act" prohibits authorized generics.

- The second is to end "negotiated settlements," whereby brand-name manufacturers commence legal challenges against generic applicants, then conclude the disputes by paying the generic firms settlements in exchange for their agreements to terminate their applications. *Half of all 2006 filings resulted in payments to generic firms and deferral of the introduction of generic competition.* The numbers grow every year, as blockbuster drugs roll off patent. In 2001, the FDA received 307 generic applications, and by 2005 that number had more than doubled to 766. The Consumers Union estimates that just five 2006 generic applications – Zocor, Pravachol, Zoloft, Wellbutrin and Flonase – add up to potential annual savings of over $6 billion. Six months of generic deferral is real money. On January 17, the same day that Sen. Leahy (D-VT) introduced the "Preserve Access to Affordable Generics Act," he presided over a Senate Judiciary held a hearing titled, "Paying Off Generics to Prevent Competition with Brand Name Drugs: Should it be Prohibited?" The key witness, FTC Commissioner Jon Leibowitz, cited the example of Prozac to describe the impact of negotiated statements; Pfizer offered Prozac's generic applicant a $200 million settlement, which was declined, and consumers have since saved over $2 billion by having the choice to buy a generic alternative.

- The third is to eliminate frivolous "citizens petitions" which delay generic applications. On the first day of the 110th Congress, Sen. Kohl (D-WI) offered the "Citizen Petition Fairness and Accuracy Act," to "help speed the introduction of cost-saving generic drugs by preventing abuses of the FDA citizen petition process." These rules require the FDA to consider the petition of any person having concerns about the "safety or efficacy" of a pending generic drug and to delay ruling until the petitions have been evaluated. *Between 2001 and 2005, the FDA denied two-thirds of the generic safety and efficacy citizens petitions*, and the Director of the Office of Generic Drugs believes that a growing number have no merit, but are used to delay the entry date of generics on the market.

In the aftermath of Merck's Vioxx problems, Congressional Democrats likely also will insist that 2007 PDUFA contain expanded and expensive "phase IV" testing, the analysis of adverse drug reaction data after new innovator drugs come to market.

**No White House Rescue for Pharma/BioPharma**

Few expect President Bush to veto PDUFA reform. If Congressional Democrats follow through, and they have a significant incentive to do so, developing a way to pay for expanding child health insurance coverage, then the golden age of biopharma investing may be coming to an end. PDUFA reform also will diminish returns to traditional drug manufacturers by accelerating generic competition and adding new safety regulation burdens. Given rising political risks, this may be a good time to underweight both.

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For further analysis or information, contact Capitol Analysts Network, Inc. at:
2000 P Street, N.W.
Suite 615
Washington, D.C. 20036

Phone: 202-223-4014
Fax: 202-223-4243
Email: capnet@xecu.net

website: www.capitolanalysts.com