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Could Big Pharma's Patent Collapse Sink Your Portfolio?

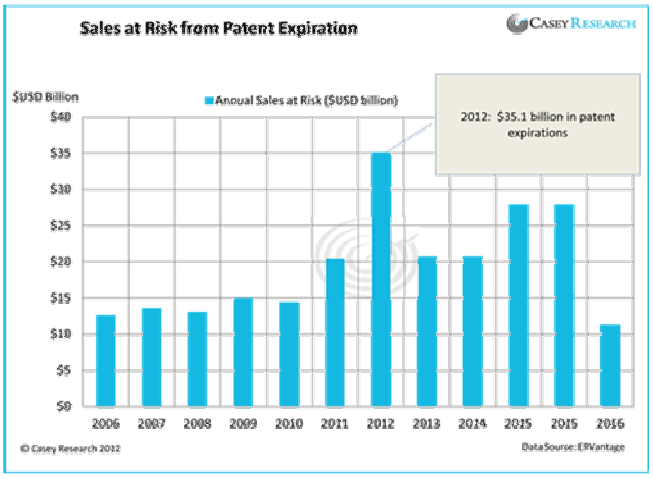
By Alex Daley, Chief Technology Investment Strategist

Like it or hate it, prescription drugs are **big** business. The pharmaceutical and biotechnology companies of the world rake in billions of dollars per year in revenues and proportionately large numbers in profits. A large part of that power to make great profits comes from investing in proprietary intellectual property, i.e., brand-name drugs that the companies can patent and sell exclusively for a fixed period of time.

When those patents expire, generic drugmakers are quick to bring out cheaper versions of the drugs. Without having absorbed all of the high research and development costs that the original manufacturers fronted, these generic drugs tend to be much cheaper and eat up a large portion of the market.

Every year on average, a few billion dollars' worth of brand-name drugs drop from patent protection and find themselves with generic competition. But 2012 is record setting. More of the most profitable drugs are coming out of patent protection than ever before, by a long shot.

Better than *$35 billion* in annual sales is at risk. Nine blockbuster drugs account for the majority of those sales – over $27 billion – with blood-thinner Plavix leading the pack. Plavix raked in more than $7 billion last year for Bristol-Myers, but is expected to see its sales fall by half or more in 2012, thanks to generic competition. Antipsychotic Seroquel and asthma medicine Singulair follow with $4 and $3.5 billion in sales, respectively.



The numbers would have been even higher if Pfizer had not won a high-stakes court battle against Teva last year, defending Viagra from generics until 2019 (that decision is still up for appeal, however).

With 401(k)s and pension plans around the world heavily invested in pharmaceutical companies – and many individuals relying on the steady dividends and, until now, rock-solid valuations – this spells an entirely new risk for portfolios across the board. Many of the world's largest drugmakers will see declines of 50% or more in their core revenues over the next few years, and that could spell significant trouble come earnings time.

Leading the downward charge is Eli Lilly. In 2011, the company saw global sales of $21.5 billion. In 2012, $7.2 billion worth of its products face patent expiration, followed by another $8 billion worth over the next three years. This means that some 71% of Lilly's total revenues will be pressured by generic competition. AstraZeneca, with $32 billion in annual revenue, also has more than 70% of its sales at risk over three years.

Nor is this problem unique to one or two companies. Takeda will see 67% of its revenue at risk. Pfizer, 66%. Bayer, 63%. Johnson & Johnson, 58%. The list goes on and on.

In a normal year, a few billion dollars in patent-protected drugs would be facing expiration, and the expectation would be for each company to have a rich pipeline of replacement drugs to fill the void created by those older therapies falling out of patent protection. This isn't likely in 2012. Not only is the number of expirations large, but the big pharmaceutical companies have also seen a considerable decrease in their research and development throughput over the past decade.

Where Is the Next Generation of Drugs?

Casual observers of the pharma industry, upon seeing the data on the massive number of patent expirations on the horizon right now, could easily conclude that company executives have been asleep at the switch. Maybe they failed to invest in research and development. Maybe they took too much in profits out of the business.

But it's not that simple. A number of factors have conspired to create the shortfall. One of the most commonly cited factors among pharmaceutical executives is the rapid increase in recent years in the amount of time and money it takes to bring a new drug to market.

With major lawsuits over the past few decades stemming from side effects of drugs like Accutane, Fen-Phen, and Vioxx resulting in multibillion-dollar settlements and fines, regulators have been feeling pressure for some time to increase the burden of proof that drugs are not just effective but also safe. The result is that the cost to bring the average drug to market has now soared to over $1 billion. And the length of time to market has been increased – by some estimates to as much as double what it once was. While costs and timelines vary greatly depending on the therapy and the disease targeted, it is clear to any industry observer that the bar is now higher.

Pharmaceutical executives are quick to place the blame for this on the regulators. But they themselves must share some of it. In 2010 alone, at least a dozen pharmaceutical companies were successfully sued by the Department of Justice or state attorneys general and paid out of settlements in excess of $5 billion just for marketing drugs for "off-label" uses (i.e., when a drug is promoted to doctors to help cure a disease that regulators never explicitly allowed it to be marketed for; this is something that often arises organically after a drug has been readily available for some time and researchers have found other benefits). This kind of aggressive sales and marketing tactic has caused regulators to push back hard on drug companies, restricting labeling and rigorously enforcing prescription standards.

Nor is tighter regulation the sole culprit. These "big pharma" companies also have themselves to blame for supporting largely unsuccessful research and development programs for too long and failing to hold their developers accountable. In the past three years nearly every major pharma company has had to significantly reorganize its research and development efforts, lay off large amounts of staff, shutter programs, and in some cases dramatically reinvent the way they approach R&D.

The root of this big mess is that the science itself has changed, and the largest companies have failed to adapt.

The Year of the Small Guy

With the advent of entire new fields of study – like genomics or nanomaterials – smaller, more nimble companies have raced to the forefront… for instance, Curis Inc. This drug developer has been a pioneer in the field of pathway inhibitors. These biological drugs interfere with the replication pathways that enable cancerous cells to grow out of control. Pathway inhibitor research was born out of both academia and large commercial R&D labs like those in the pharmaceutical companies. And many major pharmaceutical companies have researchers working in that area, looking for biological treatments for cancer. However, instead it was a small company – Curis – that was the first to successfully commercialize the technology.

Companies like Curis have emerged due to a mass defection from both big pharma's labs and academic institutions. Our understanding of biological medicine in particular has increased greatly over the last 20 years, and that has led to a seismic talent shift from larger R&D efforts to small commercial development.

The reason is simple: incentive. As a researcher, you can strike proverbial gold with a valuable new approach, even if unproven, but you know it won't happen if you're lost inside a large organization. Better to concentrate solely on your narrower area of expertise, as the founder or early-stage member of a small private company with that specific focus. There are thousands of such biopharmaceutical startups in the United States alone, all of them aimed at producing drugs that serve a large – or even a small but now underserved – market. With a potential payoff that can run into the hundreds of millions or even billions of dollars in sales, the allure is clear.

And there is no shortage of venture capital available for the drug development industry. Companies seeking anywhere from $50 million to $250 million, on the back of promising early lab research, can usually count on finding enough money from private investors to fund the beginning stages of their work.

If they are successful and their drug shows promise in early human trials, even if it comes with a $1 billion price tag, there are ways to get a novel therapy to market. The two primary choices are: go public and raise the money from stockholders; or simply sell out to a large pharmaceutical company.

It is exactly this latter path that many small biopharmas want to follow. These small companies, in an environment where big pharma is starved for new products, hold a great deal of negotiating power. The formula *du jour* is to strike marketing partnerships, as opposed to wholesale acquisition. In these arrangements, small companies continue to work on the drug, using funds from their larger partners to sustain development, while giving their partners future rights to sell the drugs in one or more markets and keeping a royalty for themselves. This has transformed large pharmaceutical companies from drug developers into drug marketers. And it has created a massive market for entrepreneurs seeking the next Advair or Ambien.

With 2012's patent-bubble bursting, that market has more potential than ever. After a very successful decade, large pharma companies are flush with cash. Yet with their R&D pipelines comparatively dry, they know that the gravy train is slowing quickly. So the pressure is on for them to make use of that cash and quickly refill their pipelines with new drugs. The only way to do that is to partner with or acquire an even larger number of small biopharmaceutical companies.

On their end, the little guys are in need of cash, in large amounts. Plus, the little guys don't always have the political connections and necessary muscle to push something novel through a crowd of risk-averse regulators. It's a marriage made in heaven.

Making It Work for Your Portfolio

The question remains: what does all this mean for investors? And what is the most effective way to profit from it?

The patent problems highlighted above aren't news to the institutional traders on Wall Street and around the world. So, profiting from the major revenue hits is not as simple as shorting big pharma stocks and waiting for the market to turn. Long or short, the question for big pharma investors is which ones will pick the real winners from among so many new drugs. Those that place the right bets have a chance of stemming the bleeding – and maybe even coming out whole. But their desperation is likely to lead to a lot of bad decisions, and in addition it remains to be seen if the most promising of those small companies, the ones with the multibillion-dollar-per-year opportunities, are even willing to take big

pharma to the dance. While big pharma brings a lot to the table, their sales and marketing talent is just as vulnerable as their researchers were to the lure of a startup's money-machine potential.

Increasingly, startups are hedging their bets by partnering with a big pharma company on a handful of their therapies, using those paychecks to fund a number of proprietary research projects, and intending to take those other drugs to market themselves. It's a movie we've seen before, with companies like Amgen and Genentech having been formed on the backs of deals with larger distributors, only to parlay that success into building the next generation of billion-dollar pharmaceutical companies.

Thus, the key to investing success in this race is about picking the right horses. That means not only the companies with the best technology, but those who also really understand their business model and structure their company either for a major partnership or to go it on their own.

With the number of major drugs coming off patent in 2012 greater than ever before, the opportunity for small drug developers, and investors, has never been bigger. And the stakes for larger companies have never been higher.

[Our "Curing Cancer" portfolio features four innovative biotech firms that could save the lives of millions… and create a brand-new generation of millionaires. Learn more.]

Bits & Bytes

Congress Questions Apple over Path Debacle (***The Next Web***)

A privacy debacle that started with social startup Path has unfurled into a firestorm over the past week. The company, which was following usual industry practices (as many observers have pointed out), stored address book data from application users on the iPhone on its servers and then used that data for making recommendations. Since that information was revealed, Apple (whose APIs allow it to store data without any kind of notice to users), Twitter (whose application does basically the same as Path's), and even the US Congress (whose members know how to get on TV when they butt their noses in where they don't belong) have become embroiled in the mess.

New LED Burns Ten Times Brighter (***Technology Review***)

In a sort of follow-up to last week's article on the lighting wars, here's a story about Fremont, California-based startup Soraa, which thinks it can make LEDs cheaply enough to replace regular bulbs. The company's new MR16 LED is a 12-watt bulb that supposedly matches the output of a 50-watt halogen while using 75% less energy.

Doing Biotech in My Bedroom (***Technology Review***)

Its practitioners call it "DIYbio." But due to similarities of this movement to computer hackers and their culture, outsiders have dubbed the practice "biohacking" and the practitioners "biohackers." Biohackers are do-it-yourself biologists who conduct their experiments outside the traditional university and corporate laboratory setting – instead taking to basements, dorm rooms, kitchens, and even closets to fiddle with genomes, conduct biotech research, and even develop novel cures for disease. DIY biologists come in all shapes and sizes – from the formally trained, seasoned scientist and biotech founder to the self-taught hobbyist whose daily life has nothing to do with science. In this case, 26-year-old Cathal Garvey dropped out of a Ph.D. program at a big cancer lab to prove that important biotech can be done by just about anyone in an open-source fashion and on a shoestring budget.

Coffee App Finds Caffeine's Safe Zone (***Futurity***)

A new software app from Applied Cognitive Systems called Caffeine Zone 2 Lite can help tell you when a cup of coffee will give you a mental boost and when it will keep you awake.

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