
# A Report on Patent-Based Event-Driven Investing For 2016

## *The Rise of Biologics and Biosimilars*

**March 2016**
**New York, New York**

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Dear Clients and Friends:

At Markman Advisors, we actively consult members of the investment community—institutional investors, hedge funds, family offices—on the intersection of patent litigations and the markets. As a patent-consultancy, we are not industry-specific, but rather embrace any industry where patents, and disputes over patents, are material to the ongoing valuations of public companies. In the past, those industries fell generally into three categories: non-practicing entities (NPEs), small-molecule pharmaceuticals, and high-tech.

We are issuing this newsletter to our clients and friends to comment on the dawn of a new industry where patents and the markets intersect, one that may soon come to eclipse the scope and range of opportunities to date.

That industry is **biologics and biosimilars**. Biologics have been licensed by the FDA and marketed to consumers for years. However, 2015 witnessed the FDA's first approval of a "biosimilar" for an existing biologic. This first approval was accompanied by a number of other pending biosimilar applications. And those applications were accompanied by the first major wave of patent lawsuits brought by innovator companies in their attempt to keep biosimilars at bay through enforcement of their patents.

At the same time, we witnessed a new trend in patent cases between competitors in the pharmaceutical industry. These cases involve one biologics producer attacking another seeking royalties for infringing biologics patents. In the small-molecule sector, this would correlate to one brand pharmaceutical company suing another brand for royalties due to patent infringement—something that has rarely to never occurred.

Biologics and biosimilars have created entirely new vehicles for event-driven investors, and patents are set to play a leading role. Markman Advisors is already out in front of the intersection between biologics/biosimilar patent lawsuits and the market.

We have been quoted twice by the ***Wall Street Journal*** in articles related to biologics patent issues. (See P. Loftus, Panel Recommends FDA Approval of Remicade Knockoff, Feb. 9, 2016; P. Loftus, Gilead Tries to Block Merck's Patent Claims on New Hepatitis C Drugs, Mar. 9, 2016).

We have published extensive commentary on some of the major patent events affecting current biologics, including HUMIRA, REPATHA and PRALUENT, and ENBREL.[1]

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[1] See citations below.
[2] http://seekingalpha.com/article/3756696-humira-will-abbvies-patents-keep-biosimilars-tnf-

And we have received increased interest from clients about the new patent landscape being set by biologics and biosimilars and what their impact will have for investors.

We hope you find this newsletter informative and helpful, and we welcome any and all inquiries. In addition to commenting on biologics and biosimilars, the newsletter concludes with additional comments on the status of the traditional industries for event-driven patent-investing, namely, NPEs, small-molecules and high-tech.

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**Biosimilars Sector Set To Expand**

Biologics were approved by the FDA and marketed to consumers for years, but it was not until 2010 that Congress provided a mechanism for firms to apply for license to distribute a generic or "biosimilar" version of existing biologics. That mechanism came in the form of the Biologics Price Competition and Innovations Act (BPCIA). Much like the Hatch-Waxman Act for small-molecule drugs, the BPCIA provides an abbreviated approval pathway for biosimilar versions of biologics drugs.

Although the BPCIA was enacted more than five years ago, 2015 saw the first wave of patent lawsuits under the BPCIA. The filing of a biosimilar application triggers a patent litigation commenced by the innovator company in federal district court under the BPCIA. As more biosimilar applications are filed, more patent cases are likely to be filed.

BPCIA cases are likely to yield increased trading opportunities over the traditional sectors marking an intersection between patent cases and the market, including Hatch-Waxman cases. First, the stakes are typically bigger. Biologics are high-priced and high-revenue drugs, which means they are more likely to be material to companies selling biologics. Second, because the revenue at stake is so large, the outcome of the BPCIA cases will likely impact both sides of the dispute, namely, the innovator and the biosimilar applicant. Third, the companies with the financial and technical wherewithal to participate in the biologics or biosimilar market are typically large-cap, deeply liquid companies (e.g., Amgen, AbbVie, Sandoz, J&J (Janssen), Hospira, Apotex, Regeneron.)

Below is a list of some cases under the BPCIA that are currently pending or expected to be filed shortly:

- **HUMIRA**: Amgen ($AMGN) filed its biosimilar application with the FDA in November 2015, and numerous other biosimilar applications are not likely far behind. This will trigger a patent suit under the BPCIA. Depending on whether the parties choose to engage in the "patent dance," we expect the case to be filed by Q3 of 2016. AbbVie ($ABBV) claims to have 70 patents protecting its HUMIRA product. We published an in-depth overview of patent issues facing HUMIRA.[2]

- **REMICADE:** Janssen (JNJ) commenced a patent suit against

[2] http://seekingalpha.com/article/3756696-humira-will-abbvies-patents-keep-biosimilars-tnf-blocker-blockbuster

Celltrion ($CONIF) and Hospira ($PFE) over a biosimilar Remicade in March 2015. Janssen originally asserted six patents against Celltrion, but we view only one patent to be material to the outcome. Celltrion recently filed a motion for summary judgment to invalidate that patent, and the outcome of that motion in the next several months will likely be material to both companies.

- **ENBREL:** Amgen ($AMGN) reaps a quarter of its annual revenue from Enbrel (~$5B). In March 2016, Amgen commenced a patent suit under the BPCIA against Sandoz's ($NVS) proposed biosimilar. Amgen is asserting numerous patents, but two in particular are not set to expire until ~2030. We previously wrote about these two patents and how material they are to Enbrel.[3] The case is just getting started, but likely to be closely watched.

- **NEUPOGEN, NEULASTA, EPOGEN:** Amgen is currently prosecuting several other patent suits against proposed biosimilars of its other biologics drugs, including Neupogen, Neulasta and Epogen.

A noteworthy trend among biologics is the filing of petitions for *Inter Partes* Review (commonly known as "IPRs".) prior to the filing of any biosimilar applications. In the small-molecule context, it is rare for a generic to file an IPR against an Orange Book-listed drug prior to filing its ANDA. The reasons are that that would telegraph the generic's plans, and generics prefer to design-around a patent, but leave it intact to keep out other generics. Yet, in the biosimilar context, pre-FDA submissions IPRs is what exactly prospective biosimilar applicants are doing.

In June 2015, prior to submitting its biosimilar application to FDA, Amgen filed two IPRs against formulation patents covering HUMIRA, but those petitions were denied institution. Coherus Biosciences ($CHRS) and Boehringer have yet to submit biosimilar applications to FDA for HUMIRA, but they have already filed IPRs challenging method of treatment patents for the drug. The institution decisions are anticipated in July 2016. Momenta Pharmaceuticals (MNTA) has filed an IPR challenging a patent covering Bristol Meyers Squibb's ($BMY) fusion-protein ORENCIA, even though Momenta has yet to file any applications with FDA.

Prospective biosimilar applicants are availing themselves of IPRs for a number of reasons. They are alternatives to district court litigation that carry a lower standard of proof for success. And, unlike district court litigation, IPRs can be filed long before lodging any biosimilar application with FDA. And if successful, they can prospectively clear a significant obstacle to launching a biosimilar far in advance of FDA submissions. In the case of ENBREL, an IPR challenging one of two patents protecting the drug until approximately 2030 could have had a material impact on Sandoz's anticipated biosimilar, even though the IPR was filed by Kyle Bass, rather than Sandoz. The IPR was denied institution in early March.

To date, the success rate for IPRs challenging biologics patents have been

[3] http://seekingalpha.com/article/3468906-kyle-basss-latest-ipr-missile-ventures-biologics-threatens-amgens-5b-enbrel-drug

mixed. That may be because developing and designing a biologic drug is generally regarded as technologically much more complex than small-molecule drugs. Yet, rather than auguring a slow-down in the strategic use of IPRs by prospective biosimilar applicants, we anticipate these companies will grow increasingly keen on what is required by the Patent Office to successfully invalidate a biologics patent through an IPR, as well as which types of patents (formulation, method-of-treatment, manufacturing, etc.) are most likely to be successfully invalidated.

We intend to follow these cases and IPRs as well as others as they are filed.

**The Rise of Competitor Biologics Cases**

A corollary to the rise of biosimilar cases is the rise of competitor pharmaceutical patents cases over existing biologics. In the small-molecule industry, it is very rare for one brand pharmaceutical company to sue another brand over infringement of patents. Yet, that is what is happening in the context of biologics. In addition to cases under the BPCIA, this is creating an entirely new class of patent disputes between companies that provide attractive trading opportunities.

These cases fall generally into two categories.

In the first category, different innovator companies are receiving FDA approval to market biologics for the same new class of drugs at the same time. In the summer of 2015, both Amgen and Sanofi ($SNY)/Regeneron ($REGN) received approval to market their version of a new PCSK9 inhibitor for cholesterol (Repatha and Praluent, respectively). Amgen sued Sanofi/Regeneron for infringement of its patents. The case just went to trial in Delaware, where Amgen prevailed on liability. Now, Amgen is seeking a significant royalty as well as a possible injunction, which will be decided shortly. The outcome of the case could be material to both companies, and regardless of the outcome of the trial, we anticipate further post-trial motions and appeals. We published commentary on this case shortly after the claim construction order issued.[4]

In the second category, the enormous revenues for biologics are incentivizing competitors to attempt to grab some of that revenue by pursuing royalties for patent infringement. Bristol Meyers has sued Merck ($MRK) for infringing its patents for anti-PD1 antibodies through the sale of Merck's Keytruda drug. Bristol Meyers recently survived a motion to dismiss under *Alice* grounds, and thus the case is likely to continue on for some time.

Competitor pharmaceutical patent cases are a relatively new category of patent cases not seen before. Overlapping biologics research by innovator companies seeking to break out with new classes of biologics drugs has yielded arsenals of patents everywhere. Even when companies fail to make it to the FDA's door first, they may nevertheless have patents covering the drugs that do. While patent lawsuits between brand-competitors in the small-molecule sector are rare to non-existent, we predict that the revenue at stake for the sale of protein-inhibitors will make them more frequent in the context of biologics. This is a new and unique patent-specific sector that event-driven traders should continue to watch.

[4] http://seekingalpha.com/article/3724596-repatha-vs-praluent-will-amgens-patents-decide-race-prevailing-pcsk9-inhibitor

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As explained above, the intersection of patent lawsuits and the markets has traditionally centered around three industries: NPEs, small-molecule, and high-tech. The remainder of the newsletter addresses the status of these sectors in light of developments in patent law.

**NPE Sector Contracts Significantly**

During 2012 through 2014, we witnessed numerous event-driven opportunities in the NPE space. These trades were driven primarily by Vringo ($VRNG), VirnetX ($VHC), Parkervision ($PRKR), Rovi ($ROVI), Acacia Research ($ACTG), Marathon Patent Group ($MARA) among others. Pending trials and appeals created significant volatility around these names.

Yet, 2015 saw the NPE sector significantly contract. Many previously volatile NPEs faced losses or considerable setbacks in their cases, and valuations dropped significantly. Vringo's ($VRNG) petition for *certiorari* to the Supreme Court was denied after the Federal Circuit eviscerated its trial win and found its patents obvious. Parkervision ($PRKR) has struggled to resurrect its case after the trial judge overturned its jury verdict, and short-sellers pressed IPRs against its patents. Rovi ($ROVI) suffered material damage to its licensing potential after its center-piece patents were invalidated as directed to ineligible subject matter. VirnetX ($VHC) remains one of the few contenders, but it has been on the defensive, back to trial in an attempt to resurrect the decimation of its $378M verdict by the Federal Circuit. The two NPEs that have traditionally taken a more diversified strategy have also slowed down. Acacia's ($ACTG) strategy of enforcing a smaller number of supposedly high-quality marquee portfolios suffered a major setback after losing its Adaptix cases involving a portfolio acquired for eight-figures. Marathon ($MARA) continues to bring patent cases, but was unable to return any considerable victories in 2015 that allowed its share price to break away.

This contraction has been due to significant changes in patent law and the way that patent litigations are managed by district courts and the Federal Circuit. Among these changes, the Supreme Court issued a landmark decision in the *Alice Corp. v. CLS Bank* case, which indirectly invalidated scores of software patents among the ilk typically asserted by NPEs. The rise of IPRs, as well as the rate at which they have invalidated patents, has short-circuited many patent litigations that, in the past, would have raged for years. Finally, the Federal Circuit has taken an increasingly hard-line on damages, and significantly raised the bar and rigor required to prove them. This has made it much harder for NPEs enforcing software patents to build a successful case for verdicts worth hundreds of millions of dollars.

Overall, our prediction is that 2016 will not witness a reemergence of the hype and volatility that has trailed many of the NPE patent cases in the past half-a-decade. Practically none of the publicly traded NPE companies propped up on the promise of large patent-jury awards has fulfilled the expectation of their investor base. And the changes to patent law are too inescapable to make these promises any more believable today than three or four years ago. There remains a rich market for acquiring patents and enforcing them through litigation, but we predict the strategy of

utilizing public companies to do so will fade.

**Small-Molecule Sector Increases Slightly**

Unlike the NPE-sector, which witnessed a spike in activity in 2012-2014, only to drop significantly in 2015, the Hatch-Waxman sector remained relatively unchanged in 2015. The changes to patent law described above have not, for the most part, impacted patent-litigation disputes under the Hatch-Waxman Act. First, pharmaceutical patents are rarely susceptible to invalidation under *Alice*. (There are exceptions to that for "diagnostic" patents, as witnessed in the case of Jazz's ($JAZZ) Xyrem dispute.) Second, Hatch-Waxman cases rarely comprise the pursuit of damages, which makes them immune from the Federal Circuit's increased constraints on proving them.

IPRs, however, have increased the trading opportunities in the Hatch-Waxman sector. This is due, in part, to the emergence of the "hedge-fund" petitioner in 2015, the most noteworthy being Kyle Bass' Hayman Capital (see discussion below).

Yet, IPRs are not only filed by "hedge funds" and other non-generic entities alone. ANDA filers were originally palpably more hesitant to file IPRs compared to high-tech defendants involved in patent litigations. Apple ($AAPL), Samsung, Google ($GOOGL) and other high-tech defendants quickly embraced IPRs, but at the beginning of 2015, there remained considerably fewer IPRs filed by ANDA defendants. That has slowly changed. As ANDA defendants have slowly embraced filing IPRs (particularly those ANDA defendants that are not first filers,) this has changed the dynamics of many Hatch-Waxman cases and afforded greater trading opportunities.

Event-driven trading opportunities for Hatch-Waxman cases continue to arise most typically around mid-cap brand companies where the drug at issue comprises a significant portion of the company's overall revenue. We are not aware of any patent-law-based reasons that 2016 should witness a diminishment in the number of such cases filed.

Finally, though not indicative of a trend, a set of unique cases in this space, which is likely to have further trading opportunities through 2016, include Merck's and AbbVie's cases against Gilead ($GILD). Merck has alleged that Gilead's blockbuster Sovaldi is infringing its patents. Merck is seeking a 10% royalty, which Gilead has described as "prohibitive." The case is currently in trial, but has the potential to be clearly material to both companies. In a similar case, AbbVie has also claimed that Gilead's Sovaldi infringes two of AbbVie's patents. Given the size of Sovaldi, we anticipate more companies emerging from the wings with patents they claim are infringed by the blockbuster.

**High-Tech Remains Constant**

High-tech cases refer to those patent disputes outside of the pharmaceutical context where one competitor sues another in pursuit of both an injunction and damages. The plaintiff is typically a larger, more established entity seeking to box out a smaller, but growing competitor. Likewise, the smaller defendant company typically has much to lose, which translates into volatility in that stock built around milestones in the case.

In 2014, Juniper's patent lawsuit against Palo Alto Networks ($PANW) reaped rich trading opportunities. In 2015, Samsung's ITC action against NVIDIA ($NVDA) was a closely watched competitor case. Similarly, Cisco's ($CSCO) patent lawsuit against Arista Networks ($ANET) yielded several event-driving opportunities in 2015, and will continue to do so in 2016. That dispute involves the rarely witnessed trifecta of being waged in three separate tribunals—district court, the International Trade Commission and the Patent Office (via IPRs filed by Arista.)

While these cases provide rich trading opportunities for investors, their frequency has remained relatively low year on year. The changes in patent law have not, generally, slowed down the pace of these cases, given that they were not terribly frequent to begin with. IPRs have ironically provided more milestones within the cases that are filed, and thus more trading opportunities.

While Apple and Samsung appear to be diffusing their lengthy patent disputes, we do not predict a decrease in the frequency of high-tech competitor patent disputes. Rather, the most recent high-tech disputes have generally resulted favorably for the plaintiff (Juniper settled with Palo Alto, Samsung prevailed over NVIDIA, Cisco is prevailing over Arista.) We anticipate that new upstarts in the quickly commoditizing networking and IT fields will increase—modestly—the incidence of high-tech patent cases worth following.

**A Note On Kyle Bass**

No newsletter issued by a patent-consultancy would be complete without a comment on Kyle Bass.

Mr. Bass' Hayman Capital filed numerous IPR petitions against scores of pharmaceutical companies in 2015. He created volatility and trading opportunities around companies that would not likely have arisen under the Hatch-Waxman cases alone. He clearly broke ground on an investment strategy that, even if not transparent and not successful, was innovative and peaked the interest of the investment and patent communities. Our blog post making observations on Mr. Bass' investment strategy published on IAM Media was one of IAM's most widely read blog posts of 2015.[5]

Mr. Bass' success rate has been less successful than predicted, and we estimate that his institutions are around 50%. He has purportedly returned capital to investors and will not be filing any more IPR petitions. That said, Mr. Bass' IPRs that were actually instituted will be decided in 2016. These remain worth watching.

Regardless of his success, however, he clearly left a lasting mark. First, he forced the issue of whether filing IPRs as an investor is somehow improper. In connection with his IPRs against Celgene's ($CELG) Revlimid patents, the Patent Office held that filing IPRs to short-sell stocks is not improper.

Mr. Bass has also created uncertainty in the pharmaceutical sector where there was not before. Though Hayman Capital may be out of the IPR business, it remains to be seen whether other non-traditional strategic filers will continue to take advantage of the IPR process. Prior to Mr. Bass, the presumption among brands and generics was that as long as they settled their differences with respect to

[5] http://www.iam-media.com/blog/detail.aspx?g=167f0df5-ddc9-4d42-b7d6-183d47af62d3

the patents at issue, no one else would be interested. A big question for 2016 will be whether that presumption continues to hold, or whether even without Mr. Bass, the IPR process will create uncertainty around pay-for-delay settlements and first-filer status.

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