WILLKIE FARR & GALLAGHER LLP

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INTELLECTUAL PROPERTY NEWSLETTER

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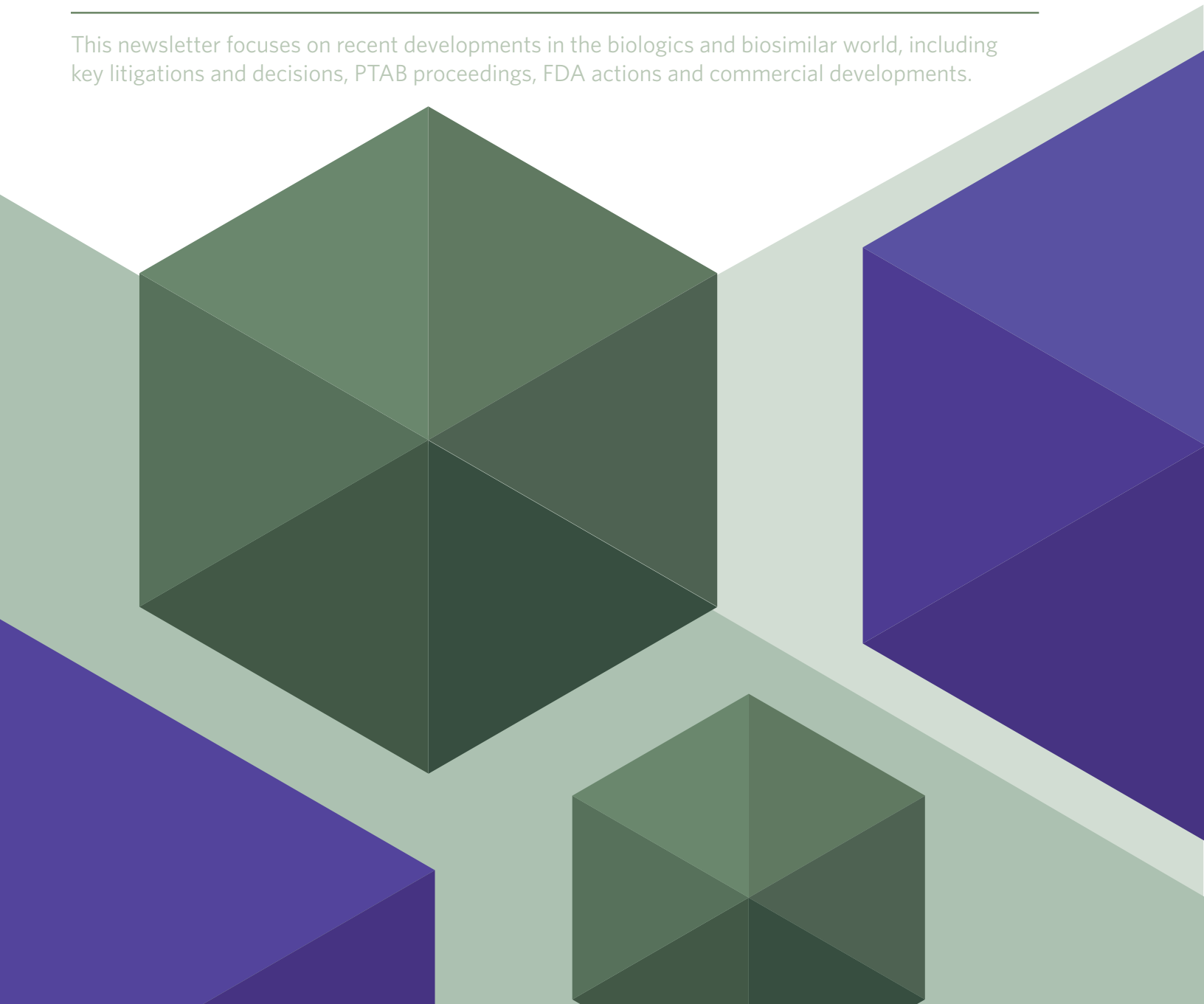
THE BIO-QUARTERLY:
WILLKIE'S BIOLOGICS AND BIOSIMILARS NEWSLETTER

This newsletter focuses on recent developments in the biologics and biosimilar world, including key litigations and decisions, PTAB proceedings, FDA actions and commercial developments.



Contents

This article provides an analysis of various trends observed in Biologics Price Competition and Innovation Act ("BPCIA") litigation to date.

FEATURED ARTICLE

Should I Stay Or Should I Go?: An Article III Standing Dilemma

The Leahy-Smith America Invents Act of 2012 created a statutory scheme under which any party can challenge a patent in an *inter partes* review ("IPR"). Since then, the IPR system has proven to be a common approach for a biosimilar applicant to challenge the validity of some patents covering a reference product before filing an abbreviated Biologics Licensing Application ("aBLA"). But what happens when the Patent Trial and Appeal Board (the "Board") decides that the patent is valid and the challenger has yet to file its aBLA? Does the challenger have Article III standing to appeal to the U.S. Court of Appeals for the Federal Circuit? The Federal Circuit may answer this particular question when it issues its long-awaited decision in *Momenta Pharmaceuticals, Inc. v. Bristol-Myers Squibb Co.*

In 2015, Momenta filed an IPR challenging Bristol-Myers Squibb's ("BMS") patent to a formulation of ORIENCIA® (abtacept) which is used in the treatment of rheumatoid arthritis. The Board ruled in BMS's favor, holding the patent valid, and Momenta timely appealed the determination. Under the broad language of 35 U.S.C. Section 319:

> A party dissatisfied with the final written decision of the Patent Trial and Appeal Board under Section 318(a) may appeal the decision pursuant to sections 141 through 144. Any party to the *inter partes* review shall have the right to be a party to the appeal.

However because Momenta's aBLA has not yet been accepted for review, BMS has yet to sue and has not threatened to sue Momenta for infringement. As a result, BMS argued that due to a lack of Article III standing, Momenta's appeal should not even be considered on the merits. More than seven months ago, on December 5, 2017, the Federal Circuit heard oral arguments in which BMS laid out this position.

Ordinarily, a party does not have standing to challenge a U.S. patent in an Article III court unless the party is sued or is threatened with a suit for infringement. *See Sandoz Inc. v. Amgen Inc.*, 773 F.3d 1274 (Fed. Cir. 2014) (holding that Sandoz lacked Article III standing to sue under the Declaratory Judgment Act before it filed its aBLA); *see also Celltrion Healthcare Co., Ltd. v. Kennedy Trust for Rheumatology Research*, 2014 WL 6765996 (S.D.N.Y. 2014) (dismissing Celltrion's declaratory judgment suit for lack of subject matter jurisdiction before Celltrion filed its aBLA). In order to establish Article III standing, an appellant must have suffered an injury-in-fact that is fairly traceable to the challenged action and that is

likely to be redressed by a favorable judicial decision. To establish an injury-in-fact, an appellant must show that he or she suffered a concrete and particularized invasion of a legally protected interest that is actual or imminent, not conjectural or hypothetical. A concrete injury must actually exist and may be either "tangible" or "intangible." "Particularized" is defined as affecting an appellant "in a personal and individual way." Based on these standing requirements, a party is not generally allowed to challenge *any* patent, at *any* time – except through IPR.

Not surprisingly, BMS argued that Momenta has not yet suffered a concrete and particularized injury sufficient to establish an Article III injury because Momenta does not market a product covered by the patent claims and has yet to file an aBLA to market any such product. In response, Momenta asserted that it has, in fact, suffered a concrete and particularized harm because the development of its product was at a crucial point, and it would incur costs associated with changing the direction of its R&D efforts. Lastly, the IPR system contains an estoppel provision, codified at 35 U.S.C. § 315(e), which prohibits an IPR petitioner from asserting that a patent "claim is invalid on any ground that the petitioner raised or reasonably could have raised during that inter partes review." Thus, Momenta argued that if it cannot appeal the patentability of the claims on the grounds raised in the IPR, it will not be allowed to do so in the future.

There have been only a few decisions addressing the standing requirements for IPR appeals, and the Federal Circuit has previously highlighted the different standing requirements between appellants and appellees in decisions from the Board. In a recent decision, the Federal Circuit decided that an ***appellee*** does not have to establish Article III standing when the Federal Circuit reviews the Board's final decision in an IPR. In *Personal Audio, LLC v. Electronic Frontier Foundation*, 867 F.3d 1246 (Fed. Cir. 2017), the Federal Circuit held that because it was not EFF who was invoking judicial review, there was no constitutional exclusion against EFF appearing in court to defend the Board's decision.

In contrast, the Federal Circuit has held that appellants *do* have to establish Article III standing when appealing the Board's final decision of patentability in an IPR. In *Phigenix, Inc. v. ImmunoGen, Inc.*, 845 F.3d 1168 (Fed. Cir. 2017), the Federal Circuit dismissed an appeal for lack of standing where appellant Phigenix did not manufacture products, but purportedly was developing an extensive intellectual property portfolio, including one patent that allegedly covered ImmunoGen's KADCYLA® product (also covered by the ImmunoGen patent that was the subject of the IPR). Phigenix stated Immunogen rejected the offer to license its patent which prompted Phigenix to challenge ImmunoGen's KADCYLA® patent in an IPR. To establish standing on appeal, Phigenix asserted that it had suffered an actual economic injury because the patent at issue increased competition between itself and ImmunoGen, and this increased competition represented a cognizable Article III injury. Specifically, Phigenix argued that the existence of ImmunoGen's patent encumbered Phigenix's efforts to license its patent. The Federal Circuit was not persuaded and determined that Phigenix failed to show that it suffered an injury-in-fact from the Board's decision sufficient to establish Article III standing.

Similarly, the court has determined that a nonprofit organization failed to establish an injury-in-fact when it did not show any involvement in researching, commercializing, or licensing the patented technology at issue. *Consumer Watchdog v. Wisconsin Alumni Research Foundation*, 753 F.3d 1258, 1262 (Fed. Cir. 2014), *cert. denied*, 135 S. Ct. 1401 (2015). The Federal Circuit rejected the appellee's argument that its injury was the burden on taxpayer-funded research in California allegedly caused by the patent. As in *Momenta*, Consumer Watchdog identified the estoppel provisions of the *inter partes* review statute as establishing an injury-in-fact, but the court rejected that argument, as Consumer Watchdog had not performed any activity that could result in an infringement suit.

In contrast, the Federal Circuit *has* found that the threat of imminent litigation was sufficient to establish

Article III standing. *See Altaire Pharms., Inc. v. Paragon Bioteck, Inc.*, 889 F.3d 1274 (Fed. Cir. 2018). Altaire and Paragon entered into an agreement to pursue FDA approval for Altaire's phenylephrine hydrochloride ophthalmic solution products, but Paragon later filed a patent application covering the products. Altaire filed a complaint against Paragon alleging breach of contract, and requesting that the contract be terminated and seeking a declaratory judgment of invalidity of the Paragon patent. Altaire then filed an IPR petition to invalidate Paragon's patent. The Board found the patent to be valid. On appeal, the Federal Circuit found that Altaire established Article III standing because it showed: (1) imminent harm by threat of infringement litigation, where it planned to resume selling its formulation after the agreement with Paragon was terminated, and where Paragon refused to stipulate that it would not sue Altaire for infringement; (2) that the injury was concrete and particularized because the agreement between the parties prevented Altaire from manufacturing its products; and (3) that the injury was also compounded by the likelihood that Altaire would be estopped from arguing that the Paragon patent would have been obvious over its own development work.

Likewise, in *PPG Indus., Inc. v. Valspar Sourcing, Inc.*, 679 F. App'x 1002 (Fed. Cir. 2017), the Federal Circuit found that Article III standing was satisfied where: (1) by the time the appellant filed its notice of appeal, it had launched a commercial product implicating the subject matter of the patent challenged in the underlying IPR; and (2) the appellant had received at least some indication "that [the patentee] intended to pursue infringement litigation against" appellant.

The Federal Circuit's decision in *Momenta* could have a major impact on the biosimilar industry's strategy for bringing a biosimilar to market. Under the current landscape, applicants may file an aBLA and attack any asserted patents both through the BPCIA litigation and in an IPR challenge, guaranteeing that standing is not an issue. Alternatively, prospective applicants can file a preemptory challenge to the patents in an IPR process before filing an aBLA. If the Federal Circuit rejects *Momenta*'s appeal, however, that second pathway poses a risk. If the Board holds the challenged patents valid before an aBLA is filed, that decision may be both unappealable and create an estoppel. The petitioner may have no choice but to hope that an aBLA is filed and its product approved in time to create standing. Alternatively, the Federal Circuit may well determine that Article III standing is established when the appellant's arguments of immediate injury-in-fact rest on concrete plans to submit an aBLA-a showing of millions of dollars of investment in the development of a biosimilar-even if the threat of litigation is not imminent.

In short, should a biosimilar applicant seeking to clear the patent roadblocks to commercialization wait to file an aBLA or go ahead with an IPR challenge? The forthcoming *Momenta* decision will likely provide much-needed guidance.

For a copy of the briefing, please contact us here.

The information below will keep you up to date on key appellate decisions, district court decisions, new suits, and settlements, in addition to any other notable events that have taken place in the courts during the last quarter.

Litigation Quarterly Update

I. Key Appellate Decisions

There have been no major appellate decisions handed down regarding biosimilar products or the BPCIA this quarter.

II. Key District Court Decisions

Celltrion v. Genentech. As reported in last quarter's Litigation Quarterly Update, Celltrion and Teva filed a pair of declaratory judgment actions in the Northern District of California on January 11, 2018, seeking declarations of noninfringement and invalidity for multiple patents related to their proposed biosimilars to Genentech's RITUXAN® (rituximab),[1] and HERCEPTIN® (trastuzumab).[2] Genentech moved to dismiss both suits for lack of subject matter jurisdiction under Rule 12(b)(1) and failure to state a claim under Rule 12(b)(6). On May 9, 2018, the District Court for the Northern District of California granted Genentech's motions to dismiss, and, after Celltrion and Teva declined to amend their complaints, entered final judgments terminating both suits on June 11, 2018. Celltrion filed notices of appeal to the Federal Circuit in both cases on July 11, 2018.

The court dismissed the complaints under Rule 12(b)(6). Celltrion's complaints failed to allege that it had completed the disclosures and exchanges required by 42 U.S.C. § 262(l)(5), and the suits were thus barred by Section 262(l)(9)(B), which precludes declaratory judgment actions by applicants who begin the patent dance by providing notice of their aBLA under Section (l)(2)(A), but who fail to comply with subsequent exchange and negotiation provisions of the BPCIA. In so ruling, the court rejected Celltrion's argument that it was absolved from the Section (*l*)(5) requirements because it indicated at the outset of the "good faith negotiations" under Section (*l*)(4) that it wished to litigate all the patents on Genentech's 3(A) list. Similarly, the court also rejected Celltrion's contention that, because it had filed its declaratory judgment actions nine days before the end of Section (*l*)(4)'s 15-day negotiation window, no obligations under Section (*l*)(5) had yet arisen to bar its suit. The court dismissed this argument as "an unpersuasive legal Catch-22."

Finally, Celltrion argued that, by serving its notices of commercial marketing pursuant to 42 U.S.C. § 262(*l*)(8)(A), it was relieved of its obligations under the other BPCIA provisions. In rejecting this argument, the court noted that Section (*l*)(9) contains three distinct bars to

[1] *Celltrion, Inc. v. Genentech, Inc.*, No. 18-cv-00276 (N.D. Cal. Jan. 11, 2018).
[2] *Celltrion, Inc. v. Genentech, Inc.*, No. 18-cv-00274 (N.D. Cal. Jan. 11, 2018).

declaratory judgment suits. While service of a notice of commercial marketing may remove the bar under Section (*l*)(9)(A), the court held that it does not have any effect on the separate bars under Section (*l*)(9)(C), which bar declaratory judgment filings by BPCIA applicants who have not begun the patent dance by providing a 2(A) Disclosure, or under Section (*l*)(9)(B), which bars declaratory judgment actions by applicants who, like Celltrion in these cases, begin the patent dance, but fail to complete it.

Notably, despite dismissing the complaints, the court rejected Genentech's argument that "Celltrion's failure to perform the BPCIA's 'patent dance' deprive[d] this Court of jurisdiction," construing the BPCIA's "patent dance" requirements to be "claim processing" rules that must be met before a suit can be filed, rather than provisions conferring jurisdiction. This creates a potential split among the district courts, as the Central District of California, in dismissing *Amgen v. Genentech*,[3] held that the BPCIA's exchange and negotiation provisions are jurisdictional in nature in granting Genentech's Rule 12(b)(1) motion in that case.

For a copy of the decisions, please contact us here.

Genentech v. Amgen.[4] There was a significant order issued on April 17, 2018 in this case, which concerns Amgen's MVASI™, its proposed biosimilar to Genentech's Avastin® (bevacizumab). Amgen had moved to dismiss count 1 of this case and count 30 of *Genentech, Inc. v. Amgen Inc.*[5] (which has been consolidated with this case for trial), for lack of subject matter jurisdiction under Rule 12(b)(1) and failure to state a claim under Rule 12(b)(6). The District Court for the District of Delaware found that it lacked subject matter jurisdiction and granted Amgen's motions, dismissing both counts.

The two counts both sought declaratory judgment of infringement, and an injunction barring Amgen from marketing MVASI™ before December 18, 2018, the date identified in Amgen's May 2017 3(B) response as the earliest launch date for MVASI™. However, in October 2017, Amgen had served Genentech with its notice of commercial marketing, which stated that it would not launch before April 4, 2018—considerably earlier than the date it had previously identified. In its complaints, Genentech asked the court to enforce the December date.

The court noted that this presented "a novel legal theory not yet addressed by any court," but sidestepped the issue by noting that, in order for a federal court to have subject matter jurisdiction in a declaratory judgment case, there must be an actual controversy "of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." Since the April 4, 2018 date had already come and gone without any sign that a launch was imminent, the court held that the claims were not yet ripe enough "to warrant the issuance of a novel declaratory judgment."

For a copy of the decision, please contact us here.

AbbVie v. Boehringer Ingelheim.[6] There have been a number of important decisions regarding discovery disputes in this suit, which concerns BI 695501, Boehringer Ingelheim's proposed biosimilar version of AbbVie's HUMIRA® (adalimumab). After its discussions with AbbVie over the scope of discovery reached an impasse, Boehringer Ingelheim filed multiple motions to compel, which met with varying degrees of success.

In the first order, issued on May 23, 2018, the District Court for the District of Delaware denied AbbVie's motion for a protective order staying responses to eight third-party subpoenas issued pursuant to an order from the court on May 10, 2018, which compelled production of clinical trial documents for three HUMIRA® studies purportedly relevant to Boehringer's public use defense. Notably, the court held that the subpoenaed researchers were not "customers" in any ordinary sense and should anticipate that document production for patent litigation

[3] No. 17-cv-07349 (C.D. Cal. Oct. 6, 2017); see last quarter's issue for additional information.
[4] *Genentech, Inc. v. Amgen Inc.*, No. 17-cv-01407 (D. Del. Oct. 7, 2017).
[5] No. 17-cv-1471 (D. Del. Oct. 18, 2017).
[6] *AbbVie Inc. v. Boehringer Ingelheim Int'l GmbH*, No. 17-cv-01065 (D. Del. Aug. 2, 2017).

is a foreseeable risk in conducting pharmaceutical clinical trials.

On May 30, 2018, the court granted Boehringer's motion to compel production of distribution, supply, and manufacturing agreements. Boehringer noted that some patents-in-suit had issued as late as 2013, and might be invalid if HUMIRA® products produced under the agreements included the inventions claimed by those patents. In siding with Boehringer, the court noted that not only executed agreements, but also proposed ones, could be relevant to the on-sale defense, and ordered AbbVie to produce all such agreements dated from January 31, 2003 to December 31, 2011.

On June 4, 2018, the court granted Boehringer's motion to compel production of documents related to its unclean hands defense, which alleged non-fraudulent anticompetitive behavior (the use of a "patent thicket" of weak or invalid overlapping patents).

For a copy of the decisions, please contact us here.

III. New Litigation

On June 21, 2018, Genentech filed a patent infringement suit against Amgen relating to Amgen's aBLA filing for its biosimilar candidate to Genentech's HERCEPTIN® (trastuzumab).[7] In its complaint, Genentech asserted 37 patents, and sought declaratory judgment that Amgen's biosimilar product will infringe, entitling Genentech to injunctive relief and monetary damages.

On July 2, 2018, Genentech also filed a suit accusing Eli Lilly's TALTZ® (ixekizumab), an IgG monoclonal antibody that binds to interleukin 17 and is FDA-approved for treatment of plaque psoriasis and psoriatic arthritis, of infringing a newly issued drug substance patent.[8] The asserted patent 10,011,654, issued at midnight on July 3, 2018 and Genentech filed suit immediately thereafter. This is not a BPCIA litigation, however, as TALTZ® was approved pursuant to its own BLA on March 22, 2016, has been on the market since mid-2016, and is not a biosimilar of any Genentech biologic product.

Finally, on July 18, 2018, Amgen filed suit against Hospira, accusing Hospira's proposed biosimilar to Amgen's NEUPOGEN® (filgrastim) of infringing one of its bioprocess patents.[9] The asserted patent, No. 9,643,997, claims a method of protein purification which Amgen alleges will be infringed by Hospira's production process.

IV. Settlements and Stipulations

Immunex v. Sandoz.[10] On June 7, 2018, the District Court for the District of New Jersey entered an amended stipulation to a Consent Preliminary Injunction, pursuant to which Sandoz Inc. (the U.S. subsidiary of Sandoz International GmbH) "shall not make, use, import, offer to sell, or sell Sandoz's etanercept product, except as allowed by 35 U.S.C. § 271(e)(1)." This stipulation does not terminate the proceeding, however. Oral arguments on the parties' *Daubert* motions and motions *in limine* were heard on June 29, 2018 and a jury trial is scheduled to begin on September 11, 2018.

[7] *Genentech, Inc. et al. v. Amgen Inc.*, No. 18-cv-00924 (D. Del. June 21, 2018).
[8] *Genentech, Inc. v. Eli Lilly and Co.*, No. 18-cv-01518 (S.D. Cal. July 3, 2018).
[9] *Amgen Inc. v. Hospira Inc.*, No. 18-cv-01064 (D. Del. July 18, 2018).
[10] *Immunex Corp. v. Sandoz Inc.*, No. 16-cv-01118 (D.N.J. Feb. 26, 2016).

In this section, we will provide a quarterly summary on key developments that occurred at the Patent Trial and Appeal Board ("PTAB") regarding patents related to biologics.

PTAB Quarterly Update

The information below is intended to keep you updated on filings, institutions, and final decisions, in addition to any other notable events, that took place at the PTAB in the last quarter.

Senator Hatch Files Amendment to Limit IPR Challenges for Biosimilars

On June 13, 2018, Senator Orrin Hatch, co-author of the Hatch-Waxman Act, filed the Hatch-Waxman Integrity Act of 2018 (the "Amendment") in the Senate Judiciary Committee. Senator Hatch's proposal would force a biosimilar applicant to choose between relying on the BPCIA pathway or filing IPR/PGR petitions, and preclude them from taking both paths to invalidate asserted patents.

Under Section 5(d)(1) of the Amendment, a 262(k) applicant would have to file a certification that the applicant has not filed, and will not file, a petition to institute an IPR or PGR of patents included on the reference product sponsor's 3(A) list. Section 5(d)(2) of the Amendment further requires that the Secretary of Health and Human Services make a determination that the biosimilar application fully complies with the above certification requirement prior to licensing the product.

At the Senate Judiciary Committee hearing, Senator Hatch stated that *inter partes* review "is a critical tool for fighting patent trolls and is of particular importance to the tech community. But it also threatens to upend the careful Hatch-Waxman balance by enabling two separate paths to attack a brand patent." According to Senator Hatch, the Amendment "would force a party that wishes to challenge a brand patent to choose: the party can file a Hatch-Waxman suit, which carries the benefits of being able to rely on the brand company's safety and efficacy studies for FDA approval, or it can file an IPR proceeding, which is cheaper, faster, and easier to win. But it can't do both."

For a detailed summary of the Amendment, please contact us here.

Trastuzumab (HERCEPTIN®):

On March 29, 2018, the PTAB instituted two petitions filed by Boehringer-Ingelheim, IPR Nos. IPR2017-02031 and IPR2017-02032, each challenging Genentech's Patent No. 6,407,213 directed towards a humanized antibody variable domain comprising non-human CDR amino acid residues. Boehringer-Ingelheim filed on grounds "essentially identical to those already instituted in" previous IPRs against the same patent filed by other

parties, although Boehringer-Ingelheim declined to join those pending IPRs. The PTAB exercised its discretion under Section 325(d) and denied the petition with respect to the identical grounds, but instituted review on the remaining grounds.

On May 8 and May 18, 2018, the PTAB heard oral arguments regarding four Genentech patents directed towards a method of treating cancer patients with an anti-ErbB2 antibody (U.S. Patent Nos. 6,627,196 and 7,371,379, IPR Nos. IPR2017-00804/805 and IPR2017-01139/1140; U.S. Patent Nos. 7,846,441 and 7,892,549, IPR Nos. IPR2017-00731/737 and IPR2017-01121/1122).

On June 14, 2018, Pfizer filed IPR No. IPR2018-01219, challenging claims 1-5, 10-12, and 20 of Roche's patent directed towards a nucleic acid encoding a glycine-lysine dipeptide in an antibody heavy chain. (No. 8,314,225)

On June 18, 2018, the PTAB denied institution of Samsung Bioepis's IPR challenging Genentech's patent directed towards a method of treating a human patient with a malignant progressing tumor (U.S. Patent No. 7,846,441; IPR No. IPR2018-00192). The PTAB denied institution under Section 325(d) because it had previously instituted an IPR against the same patent based on the same primary prior art.

Rituximab (RITUXAN®):

On April 19, 2018, the PTAB denied institution of Pfizer's IPR challenging Biogen's and Genentech's patent directed towards a method of treating chronic lymphocytic leukemia ("CLL") by administering a 500 mg/m2 dose of rituximab (U.S. Patent No. 8,206,711; IPR No. IPR2017-02127). Although the Petitioner identified prior art that disclosed the claimed dosage of rituximab for the treatment of non-Hodgkin's lymphoma ("NHL"), the PTAB found it had not established a reasonable expectation that a dosage used to treat NHL would work to treat CLL.

On May 31, 2018, the PTAB denied institution of Pfizer's IPR No. IPR2018-00086 challenging Biogen's patent No. 8,545,843 directed towards a method of treating vasculitis in a human who does not have rheumatoid arthritis or cancer by administering rituximab. Despite Petitioner's reliance on prior art related to vasculitis associated with systemic lupus erythematosus ("SLE") and with granulomatosis with polyangiitis ("GPA"), the PTAB found that none of the references described a study for the use of rituximab to treat SLE or GPA.

On June 14, 2018, the PTAB instituted Pfizer's IPR challenging Biogen's and Genentech's patent directed towards a method of treating low-grade or follicular non-Hodgkin's lymphoma (U.S. Patent No. 9,296,821; IPR No. IPR2018-00186). Although two of the asserted grounds were already asserted in a previous IPR filed by Celltrion, the PTAB applied *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 148 (2018) and found that the Petitioner presented new arguments that established a reasonable likelihood of prevailing.

In addition, on April 25, 2018, Petitioners Pfizer and Celltrion appealed to the Federal Circuit the Final Written Decision in IPR No. IPR2016-01614 challenging U.S. Patent No. 7,820,161, in which the PTAB upheld validity as reported in further detail in last quarter's issue. Moreover, on June 6, 2018, the PTAB granted Pfizer's unopposed motion to dismiss its IPR No. IPR2018-00231, challenging Biogen's patent No. 9,504,744, directed towards a method of treating a 60-year-or-older patient with diffuse large cell lymphoma.

Adalimumab (HUMIRA®):

On May 3, 2018, the PTAB denied institution of Sandoz's IPR challenging AbbVie's patents directed towards a method of treating psoriasis by administering adalimumab (U.S. Patent No. 9,512,216; IPR No. IPR2018-00002). The PTAB opined that the Petitioner merely asserted, without further elaboration, that two HUMIRA® labels were "prior art FDA approved label[s],"

and held that the labels were not printed publications for purposes of 35 U.S.C. Sections 102(b) and 311(b). On that same day, the Board also denied Sandoz's request for rehearing of the decision denying its earlier-filed IPR petition on the '216 patent, which had similarly found that the Humira Label was not prior art, despite the Petitioner's attempt to raise new arguments in the request. (IPR No. IPR2017-01824).

On June 5, 2018, the PTAB denied institution of Sandoz's IPR No. 2018-00156 challenging AbbVie's patent No. 9,187,559 directed towards a method of treating idiopathic inflammatory bowel disease using a loading and maintenance dose of adalimumab. There, Sandoz established that the HUMIRA® Package Insert was a prior art printed publication, offering evidence from the Internet Archive and the Wayback Machine, an affidavit from the Office Manager of the Internet Archive, and testimony regarding the accessibility of the drug product inserts (or labels) on the FDA website. However, despite that evidence, the PTAB found that the package insert did not disclose or suggest a baseline dose to calculate the appropriate induction dose as recited in the claims.

For copies of any decisions, petitions, or briefings, please contact us here.

In this section, we will provide a quarterly summary on key developments that occurred at the FDA regarding biologics and biosimilars.

FDA/Regulatory Quarterly Update

The information below is intended to keep you up-to-date on recent FDA developments, such as new biologics and biosimilars approvals, and new guidance, compliance and regulatory information issued related to biologics and biosimilars.

Breaking News

On July 17, 2018, the FDA announced that biosimilar applicants will be able to use European drugs as the reference product to demonstrate analytical similarity, eliminating the need to obtain U.S. samples from biologic manufacturers who have, at times, refused to provide them.

Additionally, on July 19, 2018, FDA Director Scott Gottlieb introduced a new Biosimilars Action Plan in an effort to "create more competition in the market." The Plan calls for, among other initiatives, increasing clarity for applicants by publishing FDA guidance on interchangeability and labeling, and improving the efficiency of the product development and application process. The Plan also seeks to develop communications to educate patients, providers, and insurers on biosimilars, and to develop measures aimed at reducing gaming of FDA requirements or other attempts to delay market competition.

FDA Withdraws Draft Guidance on Statistical Approaches to Evaluate Analytical Similarity

On June 22, 2018, the FDA announced that it was withdrawing a draft guidance document, "Statistical Approaches to Evaluate Analytical Similarity," after consideration of public comments. The draft guidance was released in September 2017 and was intended to provide advice to biosimilar developers in regard to how the FDA evaluates analytical similarity between a proposed biosimilar and a reference product.

FDA Commissioner Scott Gottlieb said that "[w]e're taking a fresh look at our draft recommendations for evaluating analytical studies in order to ensure our guidance takes into consideration the most current and relevant science. We'll continue to work directly with biosimilar developers on their programs as we develop new draft guidance in this area."

The agency noted that a future draft guidance will reflect state-of-the-art techniques in the evaluation of analytical data to assist the biosimilar developer in demonstrating the similarity between a proposed biosimilar and its reference product.

According to the on June 22 FDA press release "[t]he goal is for future draft guidance to address potential challenges faced by biosimilar sponsors in designing studies that are intended to demonstrate that a proposed biosimilar product is highly similar to a reference product, including consideration of appropriate methods to analyze analytical data to account for potential lot-to-lot variability of the reference product."

Recent FDA Approvals

FDA Approves CRYSVITA® (burosumab-twza)

On April 17, 2018, the FDA granted approval to Ultragenyx Pharmaceutical Inc.'s CRYSVITA® (burosumab-twza), the first drug approved to treat adults and children ages one year and older with x-linked hypophosphatemia (XLH), a rare, inherited form of rickets. CRYSVITA® was granted Breakthrough Therapy, Orphan Drug, and Priority Review designations. CRYSVITA® also received a Rare Pediatric Disease Priority Review Voucher under a program intended to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases.

FDA Approves RETACRIT® (epoetin alfa-epbx)

On May 15, 2018, the FDA approved Pfizer's RETACRIT® (epoetin alfa-epbx) biosimilar to Amgen's Epogen®/Procrit® (epoetin alfa), for the treatment of anemia caused by chronic kidney disease, chemotherapy, or use of zidovudine in patients with HIV infection. RETACRIT® is also approved for use before and after surgery to reduce the chance that red blood cell transfusions will be needed because of blood loss during surgery.

FDA Approves AIMOVIG™ (erenumab-aooe)

On May 17, 2018, the FDA approved Amgen Inc.'s AIMOVIG™ (erenumab-aooe), the first FDA-approved preventive migraine treatment in a new class of drugs that work by blocking the activity of calcitonin gene-related peptide, a molecule that is involved in migraine attacks.

FDA Approves PALYNZIQ™ (pegvaliase-pqpz)

On May 24, 2018, the FDA approved BioMarin Pharmaceutical Inc.'s PALYNZIQ™ (pegvaliase-pqpz) for adults with a rare and serious genetic disease known as phenylketonuria (PKU). Patients with PKU are born with an inability to break down phenylalanine (Phe), an amino acid present in protein-containing foods and high-intensity sweeteners used in a variety of foods and beverages. PALYNZIQ™ is a novel enzyme therapy for adult PKU patients who have uncontrolled blood Phe concentrations on current treatment.

FDA Approves FULPHILA™ (pegfilgrastim-jmdb)

On June 4, 2018, the FDA granted accelerated approval to Mylan GmbH.'s FULPHILA™ (pegfilgrastim-jmdb), the first biosimilar to Amgen's NEULASTA® (pegfilgrastim), to decrease the chance of infection as suggested by febrile neutropenia in patients with non-myeloid (non-bone marrow) cancer who are receiving myelosuppressive chemotherapy that has a clinically significant incidence of febrile neutropenia.

FDA Approves MIRCERA® (methoxy polyethylene glycol-epoetin beta)

On June 7, 2018, the FDA approved Vifor Pharma's MIRCERA® (methoxy polyethylene glycol-epoetin beta) for the treatment of pediatric patients five to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.

Biosimilars Under Development

On June 5, 2018, Celltrion announced that it has resubmitted to the FDA its aBLA to obtain its marketing approval for CTP10 (rituximab), a proposed mAb biosimilar to Genentech's Rituxan®. Celltrion also announced that in June 2018 it will resubmit the aBLA for the approval of CT-P6, a proposed biosimilar to Genentech's Herceptin®. In accordance with FDA regulations, Celltrion expects approval of the two proposed biosimilars this year.

This section will provide quarterly highlights on new biologic and biosimilar launches, major industry events, and corporate, regulatory, and legislative developments that may impact the marketplace for biologic and biosimilar drugs.

Market Quarterly Update

Pricing and Reimbursement Updates

As part of an announced effort by the Trump administration to reduce drug pricing, Health and Human Services Secretary Alex Azar announced on May 14, 2018, a plan to strengthen Medicare Part D and Part B negotiating powers to bring drug discounts through those programs closer to private-market plans for "protected" drug classes. Secretary Azar also hinted that the administration would be "very interested in the next company that takes a price increase not justified by inflation or change in clinical benefit." In a July speech at the 340B Coalition conference, Secretary Azar argued that more oversight was needed over the 340B program – which requires drug manufacturers to provide outpatient drugs to certain providers at reduced prices. The announced reforms were bifold: first, to improve transparency as to how discounts are used, and second, to reduce the gap between discounted prices and provided reimbursements.

Also in May, FDA Commissioner Scott Gottlieb suggested that the federal government "re-examine" rebates offered by drug companies to insurers. Commissioner Gottlieb suggested that the government should consider whether those rebates ought to retain a safe harbor under the Anti-Kickback Statute, stating that doing so could "boost affordability and competition" in drug pricing by aligning list and negotiated prices. Testifying before a Senate committee in June, Secretary Azar furthered those comments, suggesting "a need to move toward a system without rebates." These statements generally align with a push, both from FDA and a number of Democratic senators, to require drug companies to include pricing information in advertisements, floated as an option by President Trump in May as a means of reducing costs.

In July, following statements from President Trump, Pfizer announced that it would roll back previously announced price hikes on about 40 drugs, including its breast-cancer biologic Ibrance®, delaying their implementation until the Trump administration reveals a drug-pricing blueprint or until the end of the year.

Also in July, Novo Nordisk, Roche, Novartis, and Gilead confirmed that they would cancel previously planned price increases on 10 medications, including biologics such as Novartis's Cosentyx®, due to a recently implemented California statute. The statute requires companies to give a 60-day warning before raising prices, and justify such price increases.

New Biologic Launches

In June, Portola Pharmaceuticals launched ANDEXXA® (coagulation factor Xa (recombinant), inactivated-zhzo), an antidote for uncontrolled bleeding associated with latest-generation blood thinners, although initial supplies were limited by a required manufacturing changeover. The wholesale price of ANDEXXA® is $27,500 per patient dose, with some forecasts suggesting that it may have peak sales of up to $1 billion.

In May, Amgen and Novartis launched AIMOVIG™ (erenumab-aooe), a monthly self-injection for the prevention of migraines. AIMOVIG™, which was approved on May 18, carries an official list price of $6,900 per year. A similar anti-migraine medication from Eli Lilly, galcanezumab, is awaiting FDA approval. The biologic drug is generally expected to reach blockbuster status, with peak sales forecasted between $1 and $2 billion.

On May 24, BioMarin Pharmaceutical received FDA approval for PALYNZIQ™ (pegvaliase-pqpz), indicated for treatment of phenylketonuria (PKU). PALYNZIQ™ is currently available only through a restricted Risk Evaluation and Mitigation Strategy (REMS) program, and carries an annual price tag of $267,000, or $192,000 after discounts. Industry projections suggest five-year forecasts of approximately $430 million.

On April 30, Ultragenyx and Kyowa Kirin launched CRYSVITA® (burosumab-twza), indicated for the treatment of X-linked Hypophosphatemia (XLH) – an inherited form of rickets – in children and adults. Pricing for CRYSVITA® is set at approximately $160,000 annually for children and $200,000 for adults, depending on patient weight.

Other Market Developments

On May 15, 2018, TapImmune, Inc. announced that it had entered into a merger agreement with Marker Therapeutics, Inc., which had been spun off from the Baylor College of Medicine. Marker is a developer of a multi-antigen T-cell therapy platform, which reported positive clinical trial results in lymphoma, acute myeloid leukemia, and multiple myeloma.

On May 10, 2018, Eli Lilly announced that it had acquired ARMO BioSciences, Inc., a Silicon Valley-based immuno-oncology company, in a deal worth approximately $1.6 billion. ARMO's lead candidate, pegilodecakin, is currently in a Phase 3 clinical trial in pancreatic cancer, as well as earlier-phase trials in lung and renal cell cancer, melanoma, and other solid tumor types.

On May 2, 2018, Johnson & Johnson announced its purchase of Rockville, Maryland-based BeneVir Biopharm., in a transaction worth $140 million up front with up to $900 million in milestone payments. BeneVir is the developer of an oncolytic immunotherapy program dubbed "T-Stealth," which is currently in the preclinical stage - designed to overcome the barrier of the body's immune system.

On April 10, Promethera Biosciences announced its acquisition of Baliopharm AG, a Swiss biopharmaceutical company developing TNF-R1 antibodies. Baliopharm's pipeline includes two TNF-R1 antagonists, Atrosab and Atrosimab, and an antibody construct, Novotarg. Atrosab is currently in Phase I clinical trials, while Atrosimab is in the preclinical stage, and Novotarg remains in discovery. Financial terms of the acquisition were not disclosed.

On April 9, Novartis announced an $8.7 billion acquisition of Bannockburn, Illinois-based AveXis, Inc, whose lead candidate, AVXS-101, is a one-time gene replacement therapy for spinal muscular atrophy. AVXS-101 has received orphan drug and breakthrough therapy designations, and AveXis has enrolled patients for Phase 3 clinical trials.

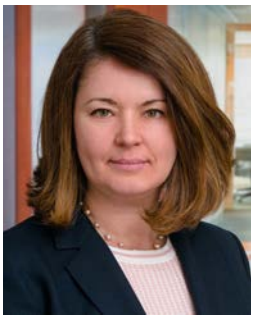
Contacts

Thomas J. Meloro

Chair, Intellectual Property

+1 212 728 8248

tmeloro@willkie.com



M. Diana Danca

Associate, Intellectual Property

+1 212 728 8692

ddanca@willkie.com

Michael W. Johnson

Partner, Intellectual Property

+1 212 728 8137

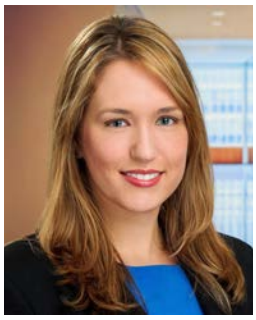
mjohnson1@willkie.com

Ronald A. Lee

Associate, Intellectual Property

+1 212 728 8943

rlee@willkie.com



Tara L. Thieme

Associate, Intellectual Property

+1 212 728 8489

tthieme@willkie.com

Devon W. Edwards

Associate, Intellectual Property

+1 212 728 8650

dedwards@willkie.com

If you have any questions regarding this newsletter, please contact Michael or Tara.

WILLKIE FARR & GALLAGHER LLP

NEW YORK WASHINGTON HOUSTON PARIS LONDON FRANKFURT BRUSSELS MILAN ROME

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