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INTELLECTUAL PROPERTY NEWSLETTER

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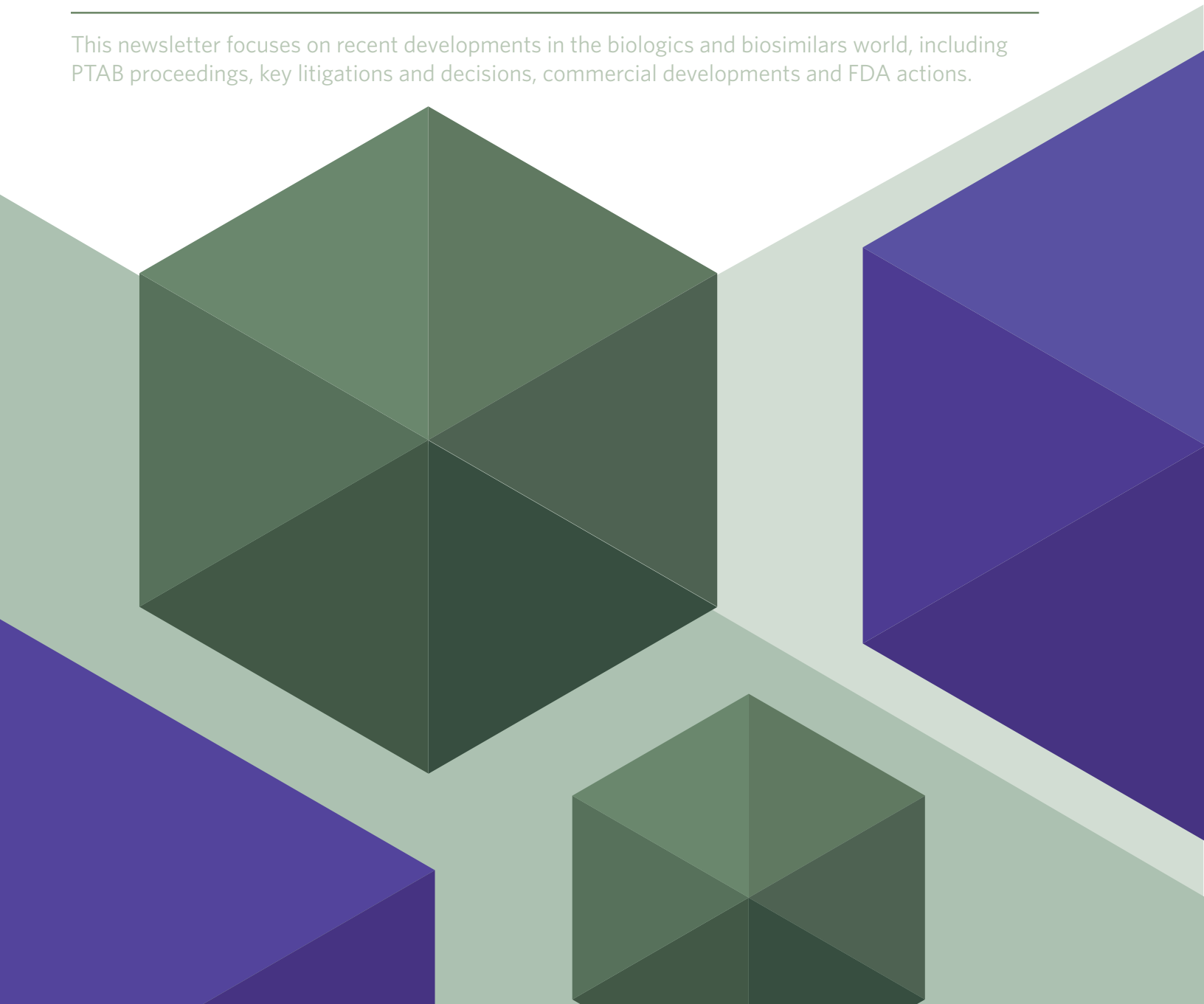
THE BIO-QUARTERLY:
WILLKIE'S BIOLOGICS AND BIOSIMILARS NEWSLETTER

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



Contents

Key developments at the Patent Trial and Appeal Board ("PTAB") regarding biologics and biosimilars

PTAB Quarterly Update

Final Written Decisions

The PTAB issued several Final Written Decisions relating to biologics during the past quarter.

Trastuzumab (HERCEPTIN®):

On November 29, 2018, the PTAB issued Final Written Decisions in favor of petitioners Celltrion, Pfizer, and Samsung Bioepis, finding claims 1, 2, 4, 25, 29, 30, 31, 33, 62–64, 66, 67, 69, 72, 78, 80, and 81 of Genentech's patent, U.S. Patent No. 6,407,213, anticipated and/or obvious over the prior art. (Case Nos. IPR2017-01374, -01488, and -01239.) However, the PTAB also found that the petitioners had not demonstrated by a preponderance of evidence the obviousness of claims 12, 42, 60, 65, 71, 73–77, and 79. The '213 patent is directed towards a humanized antibody variable domain comprising non-human CDR amino acid substitutions.

In one representative ground, Petitioners had argued that these additional claims were not entitled to an earlier priority date because the full scope of the claims was broader than the exemplified huMAb4D5 embodiments in the earlier patent specification. The PTAB disagreed, based on teachings directed to a "generalized scheme for humanizing any non-human antibody." With the earlier priority date, and Genentech's demonstration of reduction to practice, certain asserted publications were not prior art to those claims under 102(a) or (b). The PTAB also found that the prior art did not invalidate claims 75-77, which require substitution of more than one framework region amino acid. For the remaining asserted claims, the PTAB held that the Petitioners had demonstrated that such claims were anticipated and/or obvious over the prior art.

Insulin Glargine (LANTUS®):

On December 12, 2018, the PTAB issued Final Written Decisions in favor of petitioner Mylan, finding that all claims of Sanofi's patents, U.S. Patent Nos. 7,476,652 and 7,713,930, are invalid as obvious over the prior art. (Case Nos. IPR2017-01526, -01528.) Both patents are directed towards a formulation of insulin glargine. Claim 1 of the '652 patent recites a formulation comprising polysorbate 20 or polysorbate 80, at least one preservative, water, and a pH ranging from 1 to 6.8. Claim 1 of the '930 patent recites the same formulation, except it comprises esters and ethers of polyhydric alcohols instead of polysorbate.

In one representative ground, Mylan alleged that the prior Lantus® label taught every limitation of claim 1 for both patents, except the polysorbate and ester limitations, and that other prior art fills that gap. In

response, Sanofi argued that Mylan did not provide prior art evidence that insulin glargine had a tendency to aggregate, which the recited excipients would address, or that adding such excipients would be routine. The PTAB disagreed, finding that the prior art does not need to expressly articulate or suggest that insulin glargine had a tendency to aggregate. Because Mylan established that a POSA would understand that aggregation was generally a concern in developing insulin formulations and that a surfactant predictably would have been added to the formulations to address that concern, all claims of the '652 and '930 patents would have been obvious over the prior art.

Other Biologic-Related Patents:

On November 28, 2018, the PTAB issued Final Written Decisions in favor of Chugai Pharmaceutical, finding that petitioner Pfizer did not show by a preponderance of evidence that claims 1-8, and 13 of U.S. Patent No. 7,332,289 and claims 1-7, 12, and 14 of U.S. Patent No. 7,927,815 are invalid. (Case Nos. IPR2017-01357, -01258.) Both patents are directed towards a method of removing contaminant DNA from a protein/antibody-containing sample, and the methods claimed in both patents include a step wherein the eluate had a molarity of 100 mM or less.

Pfizer asserted two grounds for each IPR, arguing that the asserted claims were anticipated and would have been obvious over a prior art publication that discloses each of the methods recited in the asserted claims. The PTAB disagreed, finding that the prior art did not expressly or inherently disclose that the total concentration of solute present in the initial eluate is necessarily 100 mM or less, as required by the asserted claims. Thus, it did not anticipate the asserted claims. With regards to obviousness, the PTAB found that the Petitioner addressed obviousness "with only perfunctory assertions," and did not "further elaborate on its assertion that [the prior art] teaches or suggests these claim requirements."

Other Developments

Rituximab (RITUXAN®):

On October 30, 2018, the PTAB instituted Celltrion's petition for IPR against Genentech's patent, U.S. Patent No. 7,976,838, directed towards a method of treating rheumatoid arthritis. (Case No. IPR2018-01019.) In addition, the PTAB joined the proceeding with Pfizer's IPR, Case No. IPR2017-01923, which was instituted on April 4, 2018. Celltrion argued that its current petition was substantially identical to Pfizer's petition, which Genentech did not dispute. The PTAB thus determined that Celltrion had demonstrated a reasonable likelihood that it would prevail in showing the challenged claims are invalid based upon the same grounds and for the same reasons stated in the institution decision in Pfizer's IPR. Genentech argued that Celltrion's petition should be denied based on the *General Plastics* factors. The PTAB disagreed, holding that the Patent Owner's analysis of the factors was not persuasive for establishing abuse for the situation where a different petitioner files a "me-too" or "copycat" petition in conjunction with a timely motion to join.

On November 8, 2018, the PTAB granted Pfizer's and Genentech's joint motion to terminate, due to settlement, Pfizer's IPR petition regarding Genentech's patent, U.S. Patent No. 9,296,821. (Case No. IPR2018-00186.) The '821 patent is directed towards a method for treating low-grade or follicular non-Hodgkin's lymphoma.

Trastuzumab (HERCEPTIN®):

On December 7, 2018, Pfizer and Genentech filed a joint motion to terminate, pursuant to a settlement, Pfizer's IPR petitions regarding Genentech's patents, U.S. Patent Nos. 6,339,142 and 9,249,218. (Case Nos. IPR2017-02019, -02020.) Both patents are directed towards compositions comprising a mixture of an anti-HER2 antibody with one or more acidic variants.

Insulin Glargine (LANTUS®):

On October 29, 2018, Mylan filed an IPR petition against Sanofi's patent, U.S. Patent No. 8,992,486, directed towards a pen-type injector for self-administering drugs such as insulin. (Case No. IPR2019-00122.) Mylan asserted one ground, challenging claims 1-6, 12-18, 20, 23, 26-30, 32-33, 36, and 38-40 as obvious over one prior art reference. Mylan contends that the prior art reference describes all features of the asserted claims, except that the "dose dial sleeve" includes a helical rib rather than a helical groove on its outer surface to engage threading on the main housing. According to Mylan, a POSA would have viewed helical ribs and helical grooves as interchangeable.

Other Biologic-Related Patents:

On October 1, 2018, Adello and Apotex filed a petition for Post-Grant Review ("PGR") against Amgen's patent, U.S. Patent No. 9,856,287, directed towards a method of refolding proteins expressed in non-mammalian expression systems. (Case No. PGR2019-00001.) The petitioners asserted eight grounds of invalidity, including lack of written description, lack of enablement, anticipation, and obviousness.

For questions, or for copies of any of the decisions, please contact us here.

Key appellate and district court decisions, new suits, settlements, and other notable events

Litigation Quarterly Update

Key District Court Decisions

Immunex v. Sandoz. As reported last quarter, a bench trial in this action regarding Sandoz's proposed biosimilar to Immunex's ENBREL® (etanercept) was held before Judge Cecchi in the District Court for the District of New Jersey from September 11 to September 25, 2018. On December 10, 2018, Judge Cecchi ordered the parties to attend a post-trial mediation conference, which is scheduled for January 8, 2019.

Texas v. Azar. On December 14, Judge Reed O'Connor of the Northern District of Texas ruled that the Affordable Care Act was unconstitutional, though no injunction has yet been issued. Notably, the BPCIA pathway was enacted through the ACA. If Judge O'Connor's decision is upheld, the biosimilar approval process may need to be reenacted.

New Litigation

Genentech v. JHL. Although there have not been any new BPCIA litigations filed in the past quarter, a newly revealed trade secrets dispute between Genentech and JHL Biotech, Inc., a Taiwanese biopharmaceutical company, may affect the biologics and biosimilars industry. On October 25, 2018, the U.S. Attorney for the Northern District of California filed a criminal indictment charging four JHL employees, including three former Genentech employees, with theft of trade secrets, computer fraud, and other crimes. On October 29, 2018, Genentech filed a civil complaint against JHL, several of its executives and the four defendants named in the criminal indictment in the District Court for the Northern District of California pursuant to the Defend Trade Secrets Act of 2016, the Computer Fraud and Abuse Act, and various provisions of California state law. In its complaint, Genentech alleges that the former employees misappropriated trade secrets relating to, among other products, Genentech's HERCEPTIN® (trastuzumab), AVASTIN® (bevacizumab), and RITUXAN® (rituximab).

Settlements and Stipulations

This quarter saw a wave of settlements and licensing agreements that have terminated a number of ongoing BPCIA infringement litigations, and in some cases prevented them from ever being filed.

AbbVie v. Sandoz. On October 11, 2018, AbbVie and Sandoz announced that they had reached a global settlement resolving all litigation between the two parties relating to HYRIMOZ™, Sandoz's proposed biosimilar to AbbVie's HUMIRA® (adalimumab). A

stipulation dismissing the BPCIA action in the District Court for the District of New Jersey in August 2018 was filed the next day and was entered on October 16, 2018. According to the companies' press releases, under the terms of the confidential settlement agreement, AbbVie will grant Sandoz a non-exclusive license to its adalimumab-related patents. The license period began on October 16, 2018 in most European countries, and will begin on September 30, 2023 in the United States, a date that will not be altered by market entry of any other companies that have taken an adalimumab license from AbbVie.

Genentech v. Celltrion. On November 1, 2018, Genentech, Celltrion, and Teva announced that they had agreed to a settlement resolving the dispute regarding TRUXIMA®, Celltrion and Teva's jointly marketed biosimilar to Genentech's RITUXAN® (rituximab). Pursuant to that agreement, a stipulation dismissing all claims was filed in the District Court for the District of New Jersey.

Additionally, on December 20, 2018, the same parties filed a joint stipulation of dismissal, terminating their litigation in the District Court for the District of Delaware regarding HERZUMA®, Celltrion and Teva's proposed biosimilar to Genentech's HERCEPTIN® (trastuzumab). In addition to terminating the BPCIA suits, the parties also agreed that Celltrion would voluntarily dismiss its appeals to the Federal Circuit, seeking to overturn the PTAB's final written decisions finding that Celltrion had not established that claims of certain patents related to rituximab and trastuzumab were invalid.

AbbVie v. Momenta. On November 6, 2018, AbbVie and Momenta announced that Momenta had taken a global, royalty-bearing, non-exclusive license to all of AbbVie's intellectual property regarding HUMIRA® (adalimumab). Under the terms of the agreement, Momenta will be able to launch M923, its proposed adalimumab biosimilar, in the United States on November 20, 2023, and in Europe upon receipt of regulatory approval from the European Medicines Agency. At the time of the agreement, Momenta had not yet filed an aBLA for M923.

AbbVie v. Pfizer. On November 30, 2018, AbbVie and Pfizer announced a global settlement of all ongoing disputes regarding Pfizer's proposed biosimilar to AbbVie's HUMIRA® (adalimumab). Under the terms of the settlement, Pfizer will take a non-exclusive, royalty-bearing license to all of AbbVie's intellectual property related to adalimumab. In the United States, the license will take effect on November 20, 2023 and this effective date will not be accelerated by market entry of any of the other companies that have taken a similar license from AbbVie. In Europe, the license will become effective as soon as Pfizer receives regulatory approval for its biosimilar from the European Medicines Agency.

Genentech v. Pfizer. On December 4, 2018, Genentech and Pfizer filed a joint stipulation of dismissal terminating their BPCIA litigation relating to PF-05280014, Pfizer's proposed biosimilar to Genentech's HERCEPTIN® (trastuzumab). The stipulation, approved by Judge Connolly of the District Court for the District of Delaware, terminates that suit, but to date neither party has publicly revealed any details regarding the terms of the settlement agreement. Willkie Farr & Gallagher represented Pfizer in this action.

Genentech v. Sandoz. On December 6, 2018, Genentech and Sandoz filed a joint stipulation dismissing the BPCIA suit relating to Sandoz's now-abandoned biosimilar to Genentech's RITUXAN® (rituximab). Sandoz received a Complete Response Letter from the FDA earlier in the year and announced in November that it was abandoning its application. Sandoz then unilaterally moved to dismiss as moot Genentech's BPCIA litigation against it in the District Court for the District of New Jersey. Judge Marie Bumb denied that motion and instructed the parties to agree to a joint dismissal by the end of the month, or else continue with the suit. After that deadline passed with no agreement, Judge Bumb ordered Sandoz to show cause on December 5, 2018. The joint stipulation of dismissal was filed the following day, along with an apology to Judge Bumb for the delay from Sandoz. To date, neither party has publicly revealed any details regarding the terms of any settlement agreement that may have led to the joint stipulation of dismissal.

New biologic and biosimilar launches, and other marketplace developments

Market Quarterly Update

Pricing and Reimbursement Updates

On October 25, 2018, the Trump administration unveiled a plan that would allow the Centers for Medicare and Medicaid Services ("CMS"), to set pricing for drugs based on prices paid in other nations. Under the proposal, CMS would use an "International Pricing Index" to price Medicare Part B drugs, which the administration said could generate a 30% savings in total spending. The current model is based on average U.S. sales prices, plus a 4.3% add-on.

New Biologic and Biosimilar Launches

In early October 2018, Regeneron launched its newly-approved LIBTAYO® (cemiplimab-rwlc) as the first treatment indicated for advanced cutaneous squamous cell carcinoma. According to a press release, Regeneron and Sanofi will jointly market LIBTAYO® in the United States, at a list price of $9,100 per three-week treatment cycle.

On October 23, 2018, Sun Pharma announced its launch of ILUMYA™ (tildrakizumab-asmn), which was approved in March for the treatment of moderate-to-severe plaque psoriasis. Pricing information is not currently available for ILUMYA™.

On November 8, 2018, Coherus announced that it would launch UDENYCA™ (pegfilgrastim-cbqv), a biosimilar to Amgen's NEULASTA®, on January 3, 2019. On its quarterly earnings call, Coherus announced a list price of $4,175 per syringe, a 33% discount over NEULASTA®. That list price is the same as Mylan's pegfilgrastim biosimilar, FULPHILA™, which launched in July 2018.

On November 14, 2018, Pfizer announced its launch of RETACRIT® (epoetin alfa-epbx), biosimilar to Amgen's EPOGEN® and J&J's PROCRIT®.[1] The first epoetin alfa biosimilar, RETACRIT® is approved for all indications of the reference products. According to Fierce Pharma, the wholesale list price for RETACRIT® is $11.03 per 1000 units/mL, a 33.5% discount over EPOGEN® and a 57% discount over PROCRIT®.

Other Market Developments

On December 3, 2018, GlaxoSmithKline announced a $5.1 billion purchase of Waltham, MA-based Tesaro, a company specializing in oncology treatments. Although Tesaro's lead candidate is a small molecule

[1] Under a licensing agreement between Amgen and J&J, PROCRIT® and EPOGEN® are marketed for different uses.

PARP inhibitor, niraparib, its pipeline includes several monoclonal antibodies currently in Phase 1 clinical trials for the treatment of various tumor types.

Also on December 3, 2018, Dutch biopharma company Argenx announced a global collaboration and license agreement with Cilag, a Janssen subsidiary, for cusatuzumab (ARGX-110), a monoclonal antibody currently in Phase 1/2 trials for the treatment of acute myeloid leukemia and high-risk myelodysplastic syndrome. The deal is worth $300 million up front, with a $200 million equity investment in Argenx, and up to $1.3 billion in additional development, regulatory, and sales milestones.

On December 5, 2018, shareholders of Shire and Takeda separately approved the $62 billion merger of the two companies. Notably, Shire obtained approval in August for TAKHZYRO™ (lanadelumab-flyo), for the treatment of hereditary angioedema.

Breaking News:

On January 3, 2019, Bristol-Myers Squibb announced that it would acquire Celgene in a cash and stock transaction worth $74 billion. Celgene's pipeline includes several biologics, including bb2121, a CAR-T therapy currently under evaluation for the treatment of multiple myeloma.

Key developments at the FDA regarding biologics and biosimilars

FDA/Regulatory Quarterly Update

Recent FDA Biosimilar Approvals

On December 14, 2018, the FDA approved Celltrion's HERZUMA® (trastuzumab-pkrb) as a biosimilar to Genentech Inc.'s HERCEPTIN® (trastuzumab). HERZUMA® (trastuzumab) is a HER2/neu receptor antagonist that is approved for fewer than all reference product indications: HERZUMA® is indicated for the treatment of HER2-overexpressing breast cancer, but not for HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

On November 28, 2018, the FDA approved Celltrion's TRUXIMA™ (rituximab-abbs), the first filgrastim biosimilar to Genentech's RITUXAN® (rituximab). TRUXIMA™ is a CD20-directed cytolytic antibody that is approved for fewer than all reference product indications: TRUXIMA™ is indicated for the treatment of non-Hodgkin's lymphoma, but not for chronic lymphocytic leukemia, rheumatoid arthritis, granulomatosis or pemphigus vulgaris.

On November 2, 2018, the FDA approved Coherus BioSciences' UDENYCA™ (pegfilgrastim-cbqv), a biosimilar to Amgen's NEULASTA® (pegfilgrastim). UDENYCA™ (pegfilgrastim-cbqv) is a leukocyte growth factor that is approved for fewer than all reference product indications: UDENYCA™ is indicated to decrease the incidence of infection in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs but is not indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation.

On October 31, 2018, the FDA approved Sandoz's HYRIMOZ™ (adalimumab-adaz), a biosimilar to AbbVie's HUMIRA® (adalimumab). HYRIMOZ™ is approved for fewer than all reference product indications: HYRIMOZ™ is approved for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis in patients four years of age and older, psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, ulcerative colitis and plaque psoriasis but is not approved for hidradenitis suppurativa and uveitis.

Biologics and Biosimilars Under Development

On December 17, 2018, Amgen announced the submission of a BLA for ABP 710, a biosimilar candidate to REMICADE® (infliximab).

On December 17, 2018, NeuClone announced that it is developing a proposed pertuzumab biosimilar to Genentech's PERJETA®. Pertuzumab is an IgG1 humanized monoclonal antibody that targets HER2. It is

intended to be used for the treatment of HER2-positive early or metastatic breast cancer.

On December 10, 2018, Samsung Bioepis announced that a one-year follow-up study comparing event-free survival in patients treated with SB3, a trastuzumab biosimilar, showed that the biosimilar has similar safety and efficacy profiles to Genentech's HERCEPTIN®.

On November 7, 2018, Oncobiologics announced that it has dosed the first patients with wet age-related macular degeneration in a clinical trial of ONS-5010, an ophthalmic bevacizumab candidate. Oncobiologics announced that the ophthalmic formulation of bevacizumab will be administered as an intravitreal injection and, if eventually approved, the drug will be available in a single-use vial for injection.

FDA Proposes Rule to Change the Definition of "Biological Product"

On December 11, 2018, the FDA proposed a rule that would change the definition of "biological product" to incorporate changes made by the BPCIA and to provide its interpretation of the statutory terms "proteins" and "chemically synthesized polypeptides."

The FDA proposed that "protein" be defined as "any alpha amino acid polymer with a specific, defined sequence" with a size that is greater than 40 amino acids. A "chemically synthesized polypeptide" would be defined as "any alpha amino acid polymer that is made entirely by chemical synthesis" with a size that is between 40 and 100 amino acids. According to the FDA, the proposed rule clarifies the statutory framework regulating such products. Comments on the rule will be accepted through February 25, 2019.

FDA Provides Guidance on the "Deemed to be a License" Provision

On December 11, 2018, the FDA released draft and final guidance relating to the FDA's interpretation of the "deemed to be a license" provision in § 7002(e) of the BPCIA. By way of background, although the majority of biological products have been licensed under § 351 of the Public Health Service (PHS) Act, some products historically have been approved under § 505 of the FD&C Act. Under § 7002(e) of the BPCIA, an application for a biological product that previously could have been submitted as an NDA or ANDA under § 505 of the FD&C Act must now be submitted under § 351 of the PHS Act.

This requirement is subject to certain exceptions during a 10-year transition period ending on March 23, 2020. During the transition period, an application for a biological product may be submitted under § 505 of the FD&C Act if the product is in a class that was approved under § 505 of the FD&C Act not later than March 23, 2010. However, such an application may not be submitted under § 505 of the FD&C Act if there is another biological product approved under § 351(a) of the PHS Act that could be a "reference product" if such application were submitted under § 351(k) of the PHS Act.

The BPCIA provides that on March 23, 2020, any approved application for a biological product "shall be deemed" to be a BLA for the product, but the statute is silent regarding the process for accomplishing this transition and the implications of such a transition.

The FDA's final guidance clarifies that on March 23, 2020, any *approved* application for a biological product that was the subject of an approval under § 505 of the FD&C Act will be "deemed to be" a BLA, will be removed from the Orange Book and the FDA will no longer consider any Orange Book patents as relevant for the timing of an ANDA/505(b)(2) application. After

that transition date, the FDA will no longer approve any pending or tentatively approved application submitted under § 505 of the FD&C Act for a biological product.

With respect to exclusivities, a biological product that was first approved in an NDA under § 505 of the FD&C Act and deemed "licensed" under § 351(a) of the PHS Act will not be eligible for the 12 and four-year exclusivity periods under 351(k)(7)(A) and (B), respectively. Moreover, with the exception of orphan drug exclusivity and pediatric exclusivity, any unexpired period of exclusivity associated with the approved NDA (e.g., five-year exclusivity or three-year exclusivity) for a biological product will cease to have any effect. Any unexpired period of orphan drug exclusivity would continue to apply to the biological product for the protected use after the transition date. Similarly, any unexpired period of pediatric exclusivity associated with an approved NDA for a biological product would continue to apply to a deemed 351(a) BLA, provided that the conditions in § 351(m) of the PHS Act are met.

With respect to pending applications, any 505(b)(2) application for a biological product pending on March 20, 2020 that relies on findings of safety or effectiveness of a biologic NDA will receive a complete response letter. In addition, any 505(b)(1) application for a biological product and any 505(b)(2) application that does not rely on findings of safety or effectiveness of a biologic NDA pending on March 23, 2020 will also receive a complete response letter. Such applications may be withdrawn and resubmitted under the PHS Act. The FDA also recommended that applicants consider revising their development programs so that applications for biological products can be submitted via the PHS Act pathway rather than the FD&C Act pathway.

In the draft guidance, the FDA provided a link to a new FDA website with a preliminary list of biological products to be affected by the transition. The draft guidance clarifies how the FDA will handle certain administrative aspects of the transition, such as how the FDA will contact NDA holders, and how the FDA will number transitioned BLAs. The draft guidance also explains how PDUFA and BsUFA fees will be assessed. In addition, the draft guidance provides details on how the holders of a deemed BLA will be required to conform to statutory and regulatory requirements for BLAs. Comments on the draft guidance will be accepted through February 11, 2019.

FDA Issues Final and Draft Guidances on Biosimilar Development and the BPCIA

On December 11, 2018, the FDA issued a final guidance document related to the development of biosimilars and interchangeability products entitled "Questions and Answers on Biosimilar Development and the BPCI Act," as well as a draft guidance document on the same topic, entitled "New and Revised Draft Q&As on Biosimilar Development and the BPCI Act (Revision 2)." These are companion guidances. The FDA issues each question and associated answer in the draft guidance document, receives comments on the draft question and answer, and, after reviewing comments and incorporating suggested changes (if any), moves the question and answer to the final guidance document.

The guidances generally address: (1) requirements for biosimilarity and interchangeability; (2) BPCIA provisions related to a "biological product;" and (3) exclusivity. The final guidance presents the FDA's views on a wide variety of topics, including procedures for contacting the FDA regarding a development program; differences between a reference product and a biosimilar; using data from non-U.S. licensed products; pediatric studies for biosimilars; interpretations of certain BPCIA provisions; and determination of exclusivities.

In the draft guidance, two questions (I.12, relating to the "strength" of an interchangeable injectable product and II.1, relating to the definition of a "protein") were moved from the final guidance to the draft guidance. One question relating to the Pediatric Research Equity

Act was updated and retained in the draft guidance. The remaining questions and answers, mainly relating to biosimilarity and interchangeability, were newly presented in the draft guidance. Comments on the draft guidance will be accepted through February 11, 2019.

For copies of any of the above guidance, please contact us here.

The Patient Right to Know Drug Prices Act requires disclosure of biosimilar-related settlements to the FTC and DOJ

FEATURED ARTICLE

New Law Harmonizes Biosimilar Settlement Disclosure Requirements with Hatch-Waxman Litigation

On October 10, 2018, the Patient Right to Know Drug Prices Act (Public Law 115-263, the "Patient Right to Know Act") was enacted, requiring all settlement agreements relating to the "manufacture, marketing, or sale" of biosimilar products to be reported to the FTC and the DOJ.

Under the BPCIA, the submission of a biosimilar application to the FDA can (and often does) trigger patent litigation, delaying a biosimilar product's ability to enter the market. Given the costs of litigation and the potential risks involved for both parties, companies often settle their patent disputes by choosing a specific date on which the biosimilar may enter the market. Where this delay in market entry is paid for by the reference product sponsor ("pay-for-delay settlement"), antitrust concerns may arise.

The courts have previously addressed these antitrust issues in the Hatch-Waxman context. The Supreme Court explained in *FTC v. Actavis* that even if such pay-for-delay settlement agreements might fall within the scope of a patent's exclusionary right, it does not immunize the agreement from a violation of antitrust law. In a pay-for-delay settlement, a party with "no claim for damages (something that is usually true of a paragraph IV litigation defendant) walks away with money simply so it will stay away from the patentee's market." The Supreme Court found that this "is something quite different" from typical settlement agreements. The Court clarified, however, that "avoided litigation costs or fair value for services" do not constitute pay-for-delay, and not all "reverse payment" agreements will incur anticompetitive consequences. After the Supreme Court's decision in *FTC v. Actavis*, the FTC evaluated agreements between brand and generic pharmaceutical manufacturers, and determined that 21 final settlements may have constituted pay-for-delay because they contained "both explicit compensation from a brand manufacturer to a generic manufacturer and a restriction on the generic manufacturer's ability to market its product in competition with the branded product."

The Patient Right to Know Act was intended to harmonize biosimilar litigation with Hatch-Waxman litigation by requiring that biosimilar settlements face similar FTC and DOJ scrutiny.

(*continued*)

Congress Focuses on High Drug Prices and Pay-for-Delay Tactics

The Patient Right to Know Act was introduced in the Senate in March 2018 by Senator Susan Collins (R-Maine), along with Senators Claire McCaskill (D-Missouri), and Debbie Stabenow (D-Michigan), and originally focused on eliminating pharmacy "gag clauses" that prevented pharmacists from notifying patients when they could receive their medication for a lower price by paying out-of-pocket instead of paying through insurance. While in committee, the bill was amended to also require that biosimilar related settlements be submitted to the FTC and the DOJ. The revised bill passed in the Senate on September 17, 2018 with a Yea-Nay vote of 98 to 2. The bill then passed the House on September 25, 2018 and President Trump signed the bill into law on October 10, 2018.

According to the Senate Republican Policy Committee webpage, the Patient Right to Know Act "amends the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 to extend current reporting requirements for generic and brand pharmaceutical companies to submit patent settlement agreements to the Federal Trade Commission and the Justice Department.... The inclusion of biologics and biosimilars will ensure patent settlement agreements between these companies are not anti-competitive in nature, delaying biosimilar drugs from entering the market."[1]

Under the Patient Right to Know Act, a brand company and biosimilar applicant that enter into an agreement must each file the agreement with the FTC and the DOJ if the agreement relates to:

- the manufacture, marketing, or sale of the branded reference product;
- the manufacture, marketing, or sale of the biosimilar product for which an aBLA was submitted; or
- the one-year commercial marketing exclusivity afforded to a first biosimilar product approved as interchangeable for the reference product.

In addition, biosimilar applicants that have entered into an agreement with one another regarding the one-year commercial marketing exclusivity for the same biosimilar must also each file the agreement.

Notably, these reporting provisions are triggered only where the biosimilar applicant provides a statement under section 3(B). As such, it appears that the reach of the Patient Right to Know Act is more limited than its Hatch-Waxman counterpart.

Additional Scrutiny for Biosimilar Settlements?

While the Patient Right to Know Act does not substantively alter antitrust law, it may prompt the FTC to take a closer look at the wave of biosimilar settlements that have occurred in the last year. In a June 22, 2018 letter, Senators Amy Klobuchar (D-Minnesota) and Chuck Grassley (R-Iowa) urged the FTC to examine whether makers of biologic medicines are using strategies like "pay for delay" to hinder or delay biosimilars from entering the market:

> Biologics play an important role in treating many serious illnesses and are among the fastest growing classes of therapeutic products.... Without biosimilar competition, U.S. patients and payers will likely see additional price increases on biologics in the years to come.... In light of the importance of biosimilar competition to drive down prices and improve the quality of life for American patients, we urge the FTC to examine global patent settlements

[1] https://www.rpc.senate.gov/legislative-notices/s-2554_patient-right-to-know-drug-prices-act.

> relating to biosimilars to ensure they are not in violation of antitrust laws.[2]

The letter specifically calls out the global settlements AbbVie entered into with Amgen and Samsung Bioepis for their biosimilars of Humira. The senators complain that:

> Amgen and Samsung will not launch their products in the United States until 2023, but both companies will be able to launch their biosimilars into the European market in October 2018. This means that while European patients will benefit from biosimilar competition later this year, Americans may be without access to Humira biosimilars for almost five more years. While such terms in patent settlement agreements may not always be inappropriate, the incentives for parties to delay biosimilar entry are present, and biologic markets could be susceptible to patent settlement abuse.

In a July 12, 2018 earnings call, AbbVie CEO Richard Gonzalez commented that "[g]iven the breadth of the IP that we have and the overwhelming strength of the patents that we have, the license entry date represents what I would describe as a fairly negotiated license agreements [sic] that expedites biosimilar entry into the United States." Gonzalez further noted that none of the Humira settlements include any sort of payment from AbbVie to the biosimilar.[3]

In addition to Congress, the FDA has also noted concerns regarding pay-for-delay settlements in the biosimilars context. In a March 2018 statement, FDA Commissioner Scott Gottlieb, MD, explained that pay-for-delay settlements can be more than simple reverse payments. He elaborated that "in these biosimilar pacts, the tactics are dressed in the guise of rebates and contracting provisions between manufacturers and [pharmacy benefit managers] that discourage biosimilar market entry."

Effects on Biosimilar Settlements Remain Unclear

To date, it does not appear that the FTC has taken any action with respect to a biosimilar settlement. However, with the recent boom in settlements (please see the Litigation Update for details), it appears the FTC will have a long list of agreements to review. Continued monitoring of FTC/DOJ involvement in biosimilar settlements will be necessary to determine how the FTC will scrutinize and pursue potential antitrust violations.

Willkie continues to monitor developments related to biosimilar settlement antitrust liability. Please click here if you would like to be notified of key developments.

[2] https://www.klobuchar.senate.gov/public/index.cfm/2018/6/klobuchar-grassley-urge-federal-trade-commission-to-examine-whether-pay-for-delay-tactics-are-keeping-cheaper-biosimilar-medicines-off-the-market.

[3] https://seekingalpha.com/article/4191427-abbvie-inc-s-abbv-ceo-rick-gonzalez-q2-2018-results-earnings-call-transcript?part=single.

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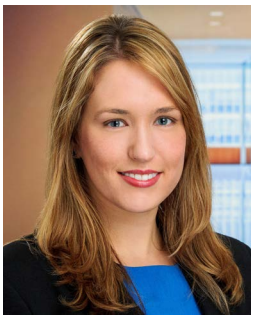

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If you have any questions regarding this newsletter, please contact Michael or Tara.

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