WILLKIE FARR & GALLAGHER LLP

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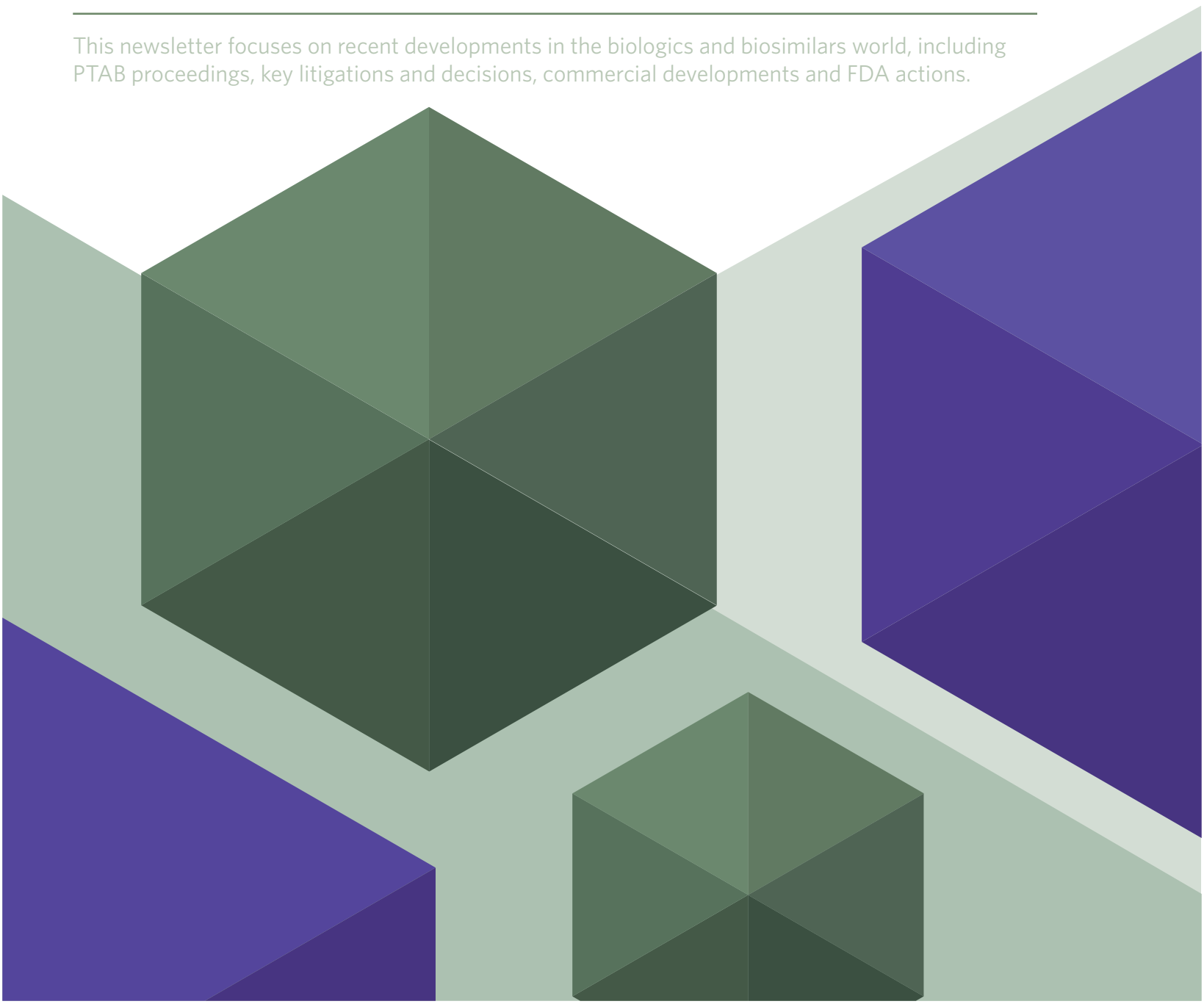
INTELLECTUAL PROPERTY NEWSLETTER

January 2020

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.



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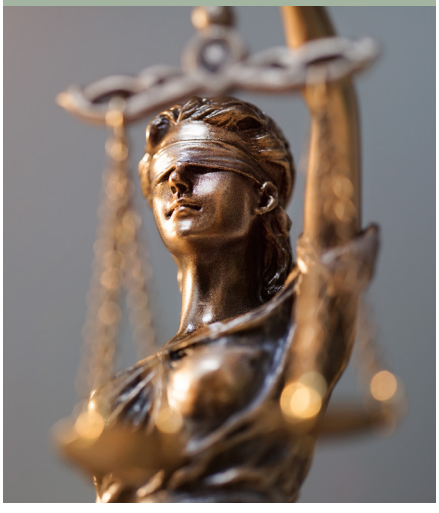

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Key developments at the Patent Trial and Appeal Board ("PTAB") regarding biologics

PTAB Quarterly Update

Filgrastim (NEUPOGEN®)/ Pegfilgrastim (NEULASTA ®):

On October 16, 2019, the PTAB denied institution of Fresenius Kabi USA, LLC's petition for inter partes review of Amgen's U.S. Patent No. 9,856,287 (IPR2019-00971). Adello Biologics LLC, Apotex Inc., and Apotex Corp. had previously filed a petition for post-grant review of the '287 patent that was instituted on April 19, 2019 (PGR2019-00001). In denying institution, the PTAB found that all *General Plastic* factors weighed against institution, specifically pointing to the similarity of the prior art used in instituted post-grant review, the six-month delay in Fresenius's petition as compared to PGR2019-00001, and the ability of Fresenius to file the petition after reviewing Amgen's preliminary response in PGR2019-00001.

On October 4, 2019, the PTAB granted Apotex Inc. and Apotex Corp.'s unopposed motion for adverse judgment in PGR2019-00001, removing both parties from the PGR. On December 6, 2019, the PTAB terminated PGR2019-00001 following a joint request to terminate following settlement by Amgen and Adello.

On December 20, 2019, Fresenius Kabi USA, LLC and Fresenius Kabi SwissBioSim GmbH filed a petition requesting inter partes review of the '287 patent under identical grounds as put forth in IPR2019-00971 (IPR2020-00314). The petition argued that it should be instituted under the *General Plastic* factors because PGR2019-00001 had been terminated following settlement, mooting the reasoning for denying institution in IPR2019-00971. The petition emphasized that Fresenius is unrelated to Adello and Apotex such that denying institution would invite gamesmanship by allowing a patent owner to shield its patent from challenge by settling with the first challenger. Fresenius argued that this new petition has not gained any unfair advantage from delay as it asserted the identical grounds of invalidity as presented in IPR2019-00971, which was filed before an institution decision in PGR2019-00001. Fresenius also emphasized that this new petition does not unduly burden the PTAB because there are now no other petitions challenging the '287 patent.

Amgen's preliminary response may be filed before March 20, 2019.

On December 6, 2019, the PTAB terminated two Kashiv IPR petitions filed against two of Amgen's patents directed to a method of purifying a non-native limited solubility form in a non-mammalian expression system comprising a series of steps including lysing, solubilizing, forming a refold solution, applying the refold solution to a separation matrix, washing, and eluting -- U.S. Patent Nos. 8,940,878 (IPR2019-00791) and 9,643,997

(IPR2019-00797). In requesting the termination, the parties stated that they have settled their dispute and all litigation relating to the patents challenged in these proceedings. The two IPRs were instituted on September 11, 2019.

Four days after granting the termination of the Kashiv IPRs, the PTAB instituted for review Fresenius Kabi's petition, also against the '997 patent (IPR2019-01183). Amgen argued that the PTAB should deny institution because (1) the prior art had already been presented to the PTO during prosecution, (2) the petition is duplicative of Kashiv's petition in IPR2019-00797, and (3) Fresenius does not have a reasonable likelihood of prevailing on its asserted grounds of unpatentability. The PTAB rejected Amgen's first argument because the asserted prior art was not before the examiner. The PTAB rejected Amgen's second argument because the PTAB had already terminated the Kashiv IPR, distinguishing this petition from its decision to deny institution in IPR2019-00971 (discussed above) by stating that "we are of the opinion that the potential for abuse by instituting an arguably follow-on Petition in this case has been ameliorated by the termination of the '797 IPR proceeding."

Finally, the PTAB found that Fresenius had a reasonable likelihood of prevailing on its claims of unpatentability. The petition includes grounds for anticipation by Wang, Reardon, and Dietrich and two obviousness grounds in light of Wang and Cutler or Komath '944 and Komath '056. As a preliminary matter, Amgen argued that Fresenius could not prevail because the petition fails to establish that the references relied upon qualify as prior-art printed publications. The PTAB rejected this argument, based on the publication dates on the face of Wang and Cutler, but encouraged Amgen to develop the record if it wanted to continue to challenge the printed-publication status of the references. Amgen also argued that Fresenius improperly mixed and matched elements from different embodiments disclosed in Wang to put forth its anticipation ground. The PTAB rejected this argument by finding that the petition maps the limitations of the claims to a specific experiment disclosed in Wang. Having determined that Fresenius established a reasonable likelihood of success for its anticipation ground based on Wang, the PTAB offered limited remarks on the remaining grounds.

Amgen's response is currently due on March 3, 2020.

Ixekizumab (TALTZ®):

On October 7, 2019, the PTAB instituted post-grant review of Eli Lilly's petition of Genentech's Patent No. 10,011,654. The '654 patent is directed to a genus of antibodies that are functionally defined by the ability to bind protein IL-17A/F. First, the PTAB found that the patent is eligible for post-grant review even though its parent applications were filed before passage of the AIA because those parent applications did not provide written description support for the claimed invention. The PTAB rejected Genentech's argument that the patent could not be eligible for post-grant review because the specification was identical to the specification used in applications before the passage of the AIA.

The PTAB found that Eli Lilly is more likely than not to demonstrate that at least one claim of the '654 patent lacks written description support. In its petition, Eli Lilly argues that the '654 patent claims a structurally and functionally diverse genus of antibodies defined solely by reference to the antigen they bind rather than any associated structural features. The petition goes on to argue that the specification fails to provide sufficient written description of the claimed genus. The PTAB instituted review based on its findings that the specification fails to disclose the amino acid sequence for the light chains for any claimed antibody and the disclosure of 34 Fab clones in the specification does not allow a person of ordinary skill in the art to identify structural features common to all members of the claimed genus.

The PTAB did not address Eli Lilly's additional grounds based on lack of enablement and anticipation in the

institution decision. Genentech's response is due on January 23, 2020.

Other Biologic-Related Patents:

On October 6, 2019, the PTAB terminated Pfizer's instituted inter partes review against claims in Genentech's Patent No. 8,314,225, which is directed to nucleic acid sequences that encode the C-terminal part of a human immunoglobulin heavy chain and a method for improving the expression of such immunoglobulin by using the claimed sequences. The termination was requested by the parties following settlement. The PTAB also lifted its stay of an ex parte examination of the '225 patent, which was put in place when the PTAB instituted the IPR.

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

Litigation Quarterly Update

Key Appellate Developments

Amgen v. Hospira. On December 16, 2019, the United States Court of Appeals for the Federal Circuit issued an opinion and order affirming the judgment of the United States District Court for the District of Delaware in Amgen's suit regarding RETACRIT™ (epoetin alfa-epbx), Hospira's biosimilar to Amgen's EPOGEN® (epoetin alfa). Addressing Hospira's appeal, the panel upheld Judge Richard G. Andrews's jury instructions regarding the safe harbor provided by 35 U.S.C. § 271(e)(1) and his construction of one asserted claim of U.S. Patent No. 5,856,298 ("the '298 patent"), claiming methods related to erythropoietin isoforms, but did not address a second asserted claim. In addition, the panel found that substantial evidence supported the jury's finding of infringement of the '298 patent, its safe-harbor determinations, and its damages award. On Amgen's cross-appeal, the panel found that substantial evidence supported the jury's verdict that Hospira's product did not infringe U.S. Patent No. 5,756,349, claiming a method of expressing erythropoietin in vertebrate cells. In both appeals, the panel found no error in the district court's denial of the parties' cross motions for JMOL or a new trial.

AbbVie v. United States. On January 7, 2020, the United States Court of Appeals for the Federal Circuit issued a Rule 36 judgment affirming without opinion the Final Written Decisions of the Patent Trial and Appeal Board ("PTAB") in five Inter Partes Review ("IPR") challenges to multiple AbbVie patents claiming methods of administration of adalimumab. Three of the IPRs had been filed by Coherus Biosciences, and challenged claims of U.S. Patents No. 8,889,135 ("the '135 patent"), 9,017,680, and 9,073,987. The remaining two IPRs were filed by Boehringer Ingelheim and both challenged the same claims of the '135 patent over different combinations of prior art. In all five IPRs, the PTAB found all of the challenged claims invalid as obvious over the cited prior art. The United States Patent and Trademark Office intervened in the appeals to defend the PTAB's decisions after Coherus and Boehringer Ingelheim withdrew pursuant to settlements with AbbVie.

Key District Court Developments

Genentech v. Amgen. Genentech and Amgen filed a joint stipulation on October 21, 2019 in their ongoing litigation regarding MVASI™ (bevacizumab-awws), Amgen's biosimilar to Genentech's AVASTIN® (bevacizumab). In the stipulation, which was approved by Judge Colm F. Connolly of the United States District Court for the District of Delaware on October 29, 2019, the parties agreed to entry of judgment of non-infringement of all

claims and dismissal of all counterclaims related to U.S. Patent No. 8,512,983 ("the '983 patent"), which claims a method of production in a glutamine-free production culture medium. The parties stipulated that the court's June 17, 2019 opinion rejecting Genentech's proposed construction of the term "a glutamine-free production culture medium" "materially affects Genentech's infringement analysis for the asserted claims of the '983 patent" and that "[b]ased on the evidence produced by Amgen in discovery, Genentech cannot sustain its burden of proof to establish infringement of the asserted claims of the '983 patent." Genentech's appeal of Judge Connolly's denial of its motion for a preliminary injunction barring marketing of MVASI is still pending before the Federal Circuit, and discovery remains ongoing in this district court action as to the remaining patents-in-suit.

New Litigation

Chugai v. Alexion. Chugai Pharmaceutical brought a new litigation against Alexion Pharmaceuticals on November 12, 2019 in the District of Delaware, alleging that Alexion's ULTOMIRIS® (ravulizumab-cwvz) infringes Chugai's U.S. Patent No. 10,472,623, which, according to the complaint, claims a technology that "extends the half-life of an antibody in blood plasma, thereby improving the duration of time in which the antibody binds and neutralizes target antigens." The complaint also alleged that Alexion sought to license Chugai's technology in 2012 and 2013, and hired an attorney to file a third-party submission seeking to prevent the patent-in-suit from issuing. This is the second suit filed by Chugai against Alexion—on November 15, 2018, Chugai sued Alexion, alleging that ULTOMIRIS® infringed Chugai's U.S. Patent No. 9,890,377, directed to a similar multiple-binding antibody technology. Notably, neither case is brought pursuant to the BPCIA, as ULTOMIRIS® is not a biosimilar.

Settlements and Stipulations

Amgen v. Accord. On November 15, 2019, the United States District Court for the Southern District of Florida approved the stipulation of dismissal filed by the parties in this action concerning Accord's proposed biosimilar to Amgen's NEULASTA® (pegfilgrastim). This litigation, which was originally filed as a follow-on suit against Apotex before Accord was substituted by stipulation in August 2019, asserted that Accord's product would infringe U.S. Patent No. 9,856,287, which claims a method of refolding proteins. In their stipulation, the parties agreed to dismiss all remaining claims and counterclaims without prejudice.

Amgen v. Kashiv. On November 22, 2019, Amgen and Kashiv filed a stipulation agreeing to dismiss without prejudice all claims and counterclaims in their litigation in the United States District Court for the District of New Jersey concerning Kashiv and Amneal's proposed biosimilar to Amgen's NEUPOGEN® (filgrastim). This litigation, involving 17 patents related to the production of filgrastim, was originally filed against Adello Biologics, before Amneal was added as a defendant in an amended complaint on October 3, 2018. Kashiv was then substituted for Adello by stipulation on June 10, 2019 after it acquired all interest in Adello's biosimilar filgrastim aBLA. Judge Claire C. Cecchi approved the stipulation and ordered dismissal on November 25, 2019.

Coherus v. Amgen. On November 25, 2019, Coherus and Amgen filed a stipulation dismissing all claims, counterclaims, and affirmative defenses in this suit concerning AMGEVITA™ (biosimilar adalimumab). In this suit, Coherus asserted that Amgen's manufacture of AMGEVITA™ in the United States for sale in Europe infringed four Coherus patents claiming stable aqueous formulations of adalimumab. Judge Richard G. Andrews of the United States District Court for the District of Delaware approved the stipulation and dismissed the suit on November 26, 2019.

Amgen v. Tanvex. On December 19, 2019, Amgen and Tanvex Biopharma filed a joint stipulation, approved by Judge Marilyn L. Huff of the United States District Court for the Southern District of California on the same day, dismissing all claims and counterclaims in the suit concerning Tanvex's proposed biosimilar to Amgen's NEUPOGEN® (filgrastim). Amgen's complaint, filed in July 2019, asserted that Tanvex's biosimilar filgrastim product would infringe U.S. Patent No. 9,856,287, which claims a method of refolding proteins. With the approval of this stipulation of dismissal and the others discussed above, Amgen has terminated all ongoing district court biosimilars actions concerning its filgrastim and pegfilgrastim patents except for its suit against Hospira in the District of Delaware.

For questions, or copies of any of the decisions or documents discussed herein, please click here.

New biologic and biosimilar launches, and other marketplace developments

Market Quarterly Update

Pricing and Reimbursement Updates

On October 8, California enacted legislation aimed at ending so-called "pay for delay" in drug infringement settlements. The law, AB 824, is the first state-level action to make agreements presumptively anticompetitive if an applicant receives anything of value from the drug sponsor, according to a statement by Gov. Newsom. In order to overcome the presumption, applicants must demonstrate that the value exchanged "is a fair and reasonable compensation" or that the agreement has "directly generated procompetitive benefits that outweigh the anticompetitive effects of the agreement." Under AB 824, each person "that violates or assists in [a] violation" must pay the greater of the value received or $20 million. The law has already been challenged in federal court as unconstitutional under the Dormant Commerce Clause, Eighth Amendment, and Due Process Clause, as well as preempted by federal law, though a preliminary injunction seeking to halt enforcement was denied in December.[1]

On December 12, the House of Representatives approved H.R. 3, the Lower Drug Costs Now Act, a bill aiming at reducing drug prices by empowering the federal government to negotiate with pharmaceutical manufacturers. Among other provisions, the legislation would allow the Secretary of Health and Human Services to negotiate the cost for between 50 and 250 drugs per year, with prices capped at 120% of the average cost in six other countries. Pharmaceutical companies refusing to negotiate on the price of a given drug would be taxed up to 95% of gross sales of that drug, a cost which will not be deductible from income tax. The bill is not expected to pass the Senate, according to news reports.

On December 19, the United States-Mexico-Canada Agreement passed the House of Representatives. In the weeks leading up to that vote, a provision that would have guaranteed 10 years of market exclusivity for biologic drugs in all three countries was stripped from the deal. With that amendment, the status quo for market exclusivity will be preserved, guaranteeing biologic manufacturers 12 years without biosimilar competition in the United States, eight years in Canada, and five years in Mexico.

Biologic and Biosimilar Launches

On October 8, Novartis launched BEOVU® (brolucizumab-dbll), which was approved that month for wet age-related macular degeneration. The list

1 *See Ass'n for Accessible Meds. v. Becerra*, No. 2:19-cv-02281-TLN-DB (E.D. Cal.)

price of BEOVU® is $1,850 per dose, with an injection schedule of every 12 weeks.

On November 7, Teva and Celltrion announced their launch of TRUXIMA® (rituximab-abbs), the first marketed biosimilar to Genentech's RITUXAN®. According to a press release, TRUXIMA® will be priced at a 10% discount to the reference product; the wholesale acquisition cost for a 100 mg vial is $845.55, and the wholesale acquisition cost for a 500 mg vial is $4,222.75. According to the manufacturers, further rebates and discounts will be available.

On November 15, Novartis and Sandoz confirmed their launch of ZIEXTENZO® (pegfilgrastim-bmez), a biosimilar to Amgen's NEULASTA®. The wholesale acquisition cost for ZIEXTENZO® is $3,925 per unit, a 37% discount to the reference biologic drug. ZIEXTENZO® became the third pegfilgrastim biosimilar on the market, after Coherus' UDENYA® and Mylan and Biocon's FULPHILA®, which launched in January 2019 and July 2018, respectively. ZIEXTENZO® is priced below the other pegfilgrastim biosimilars, which both have a wholesale acquisition cost of $4,175 per unit, according to the Center for Biosimilars.

Also in November, Celgene and Acceleron launched REBLOZYL® (luspatercept-aamt), which was approved earlier that month. REBLOZYL® is the first and only FDA-approved erythroid maturation agent, and is indicated for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell transfusions. According to news reports, REBLOZYL® is priced at $3,441 per 25 mg vial.

On December 2, Mylan and Biocon announced their launch of OGIVRI™ (trastuzumab-dkst), a biosimilar to Genentech's HERCEPTIN®. OGIVRI™ is the second trastuzumab biosimilar on the market, joining Amgen and Allergan's KANJINTI™, launched July 2019. Mylan did not release the list price for OGIVRI™, but stated in a press release that it will have a "competitive discount" to its reference drug.

On January 6, Pfizer announced the launch of ZIRABEV® (bevacizumab-bvzr), which was approved in June 2019. ZIRABEV® became the second marketed biosimilar to Genentech's AVASTIN®, joining Amgen's MVASI™, which was launched in July. The WAC for ZIRABEV® is $61.34 per 10 mg, a 23% discount compared to the reference biologic – and approximately a 10% discount compared to MVASI™.

Other Market Developments

On October 10, UCB Pharma announced its acquisition of Cambridge, MA-based Ra Pharmaceuticals in a deal worth $2.5 billion. Ra's lead candidate is zilucoplan, a subcutaneous peptide inhibitor of C5 currently in a Phase III clinical study for the treatment of generalized myasthenia gravis. According to a press release, additional potential indications for zilucoplan include immune-mediated necrotizing myopaths, amyotrophic lateral sclerosis, and other tissue-based complement-mediated disorders. UCB will also gain access to Ra's proprietary technology platform, ExtremeDiversity™, to produce synthetic macrocylic peptides.

On December 3, Astellas Pharma announced that it had entered into a definitive agreement to acquire San Francisco-based Audentes Therapeutics, in a deal worth approximately $3 billion. Audentes' lead candidate, AT132, is a gene therapy for the treatment of X-linked myotubular myopathy, which will be filed for approval next year, according to news reports. Astellas also acquires Audentes' remaining pipeline, which focuses on gene therapies for rare neuromuscular diseases.

On December 9, Sanofi announced its acquisition of San Diego-based Synthorx, Inc., in a deal worth approximately $2.5 billion. Synthorx's portfolio focuses on immune-oncology drugs; its lead candidate, THOR-707, is a variant of interleukin-2 (IL-2), and is in clinical development for multiple solid tumor types, according to a press release.

On December 19, New York-based Turnstone Biologics announced that it had entered into a global collaboration and license agreement with Takeda to advance Turnstone's lead program, RIVAL-01, and to identify additional product candidates based on Turnstone's proprietary vaccinia virus platform. According to a press release, Turnstone will receive $120 million in upfront cash, with an additional $900 million in potential milestone payments.

Key developments at the FDA regarding biologics and biosimilars

FDA/Regulatory Quarterly Update

FDA News

On December 17, 2019, Dr. Stephen M. Hahn was sworn in as the 24th Commissioner of the FDA. Dr. Hahn is a physician, scientist and health care leader with a background in patient care, academic research and executive leadership.

Also on this day, the FDA announced that it has removed the exclusion of "chemically synthesized polypeptides" from the new drug application (NDA) to biologic license application (BLA) transition that is set to take place in March 2020. According to the FDA, removing "this exclusion will help patients because it provides the potential for chemically synthesized follow-on insulins and other protein products to come to market through more efficient abbreviated pathways, regardless of how they are manufactured." Additionally, "removing this exclusion will help to promote potential innovation in manufacturing methods, which could lead to future efficiencies in manufacturing processes." The FDA reasoned that unless the exclusion were removed, chemically synthesized polypeptides would not be able to come to market through the generic drug pathway because the sponsor product would be classified as a biologic.

Recent FDA Biologics and Biosimilar Approvals

FDA Approves ENHERTU® (fam-trastuzumab deruxtecan-nxki)

On December 20, 2019, the FDA approved Daiichi Sankyo's ENHERTU® (fam-trastuzumab deruxtecan-nxki) for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor and a platinum-containing chemotherapy. The FDA granted the application Accelerated Approval, Priority Review and Breakthrough Therapy designations.

FDA Approves PADCEV™ (enfortumab vedotin-ejfv)

On December 18, 2019, the FDA approved Sarepta Therapeutics' PADCEV™ (enfortumab vedotin-ejfv) for the treatment of adults with unresectable or HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. The FDA granted the application Accelerated Approval, Breakthrough Therapy and Fast Track designations.

FDA Approves VYONDYS 53™ (golodirsen)

On December 12, 2019, the FDA approved Astellas Pharma US Inc.'s VYONDYS 53™ (golodirsen) injection for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. The FDA granted the application Priority Review, Orphan Drug and Fast Track designations. In addition, Astellas received a Rare Pediatric Disease Priority Review Voucher.

FDA Approves AVSOLA™ (infliximab-axxq)

On December 6, 2019, the FDA approved Amgen's AVSOLA™ (infliximab-axxq), the 4th biosimilar to REMICADE®, for the treatment of adult and pediatric Crohn's disease, adult and pediatric ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis.

FDA Approves TECENTRIQ® (atezolizumab)

On December 18, 2019, the FDA approved Genentech's TECENTRIQ® (atezolizumab) in combination with chemotherapy (ABRAXANE® and carboplatin) for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer with no EGFR or ALK genomic tumor aberrations. The FDA granted the application Accelerated Approval, Breakthrough Therapy and Fast Track designations. TECENTRIQ® was previously approved as a stand-alone product in 2016 for the treatment of locally advanced or metastatic urothelial carcinoma and metastatic non-small cell lung cancer in those who have disease progression during or following platinum-containing chemotherapy.

FDA Approves ABRILADA™ (adalimumab-afzb)

On November 18, 2019, the FDA approved Pfizer's ABRILADA™ (adalimumab-afzb), the 5th biosimilar to HUMIRA® (adalimumab), for the treatment for the treatment of certain patients with rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, ulcerative colitis and plaque psoriasis.

FDA Approves ADAKVEO® (crizanlizumab-tmca)

On November 15, 2019, the FDA approved Novartis's ADAKVEO® (crizanlizumab-tmca) to reduce the frequency of vaso-occlusive crisis, a common and painful complication of sickle cell disease that occurs when blood circulation is obstructed by sickled red blood cells, in patients 16 years and older. The FDA granted the application Priority Review, Breakthrough Therapy and Orphan Drug designations.

FDA Approves REBLOZYL® (luspatercept-aamt)

On November 15, 2019, the FDA approved Celgene's REBLOZYL® (luspatercept-aamt) for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell transfusions. The FDA granted the application Fast Track and Orphan Drug designations.

FDA Approves ZIEXTENZO™ (pegfilgrastim-bmez)

On November 5, 2019, the FDA approved Sandoz's ZIEXTENZO™ (pegfilgrastim-bmez), a biosimilar to NEULASTA® (pegfilgrastim), to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

An updated analysis of BPCIA complaints, and how the patent dance has continued to evolve since Amgen v. Sandoz

The Patent Dance Revisited: Updated Analysis of Pre-Complaint Exchanges

In the April 2018 issue of this newsletter, we analyzed more than 20 complaints filed under the Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") and discussed how aBLA applicants, and sponsors of biologic drugs had engaged in the pre-suit exchanges contemplated by the BPCIA.

In that issue, we found that parties typically engaged in the "patent dance" provided for by the BPCIA, but often failed to fully complete that process. We also noted that the two-phase litigation contemplated by the BPCIA appeared to be giving way to a single, streamlined action, and that future areas of interest include the sufficiency of an applicant's production.

In this article, we provide an update, incorporating the past two years of BPCIA complaints to our data set. We also analyze whether any trends can be discerned in the wake of the 2017 *Sandoz v. Amgen* decision from the Supreme Court, and the Federal Circuit's subsequent holding on remand limiting sponsors from challenging an applicant's compliance with BPCIA provisions.[1]

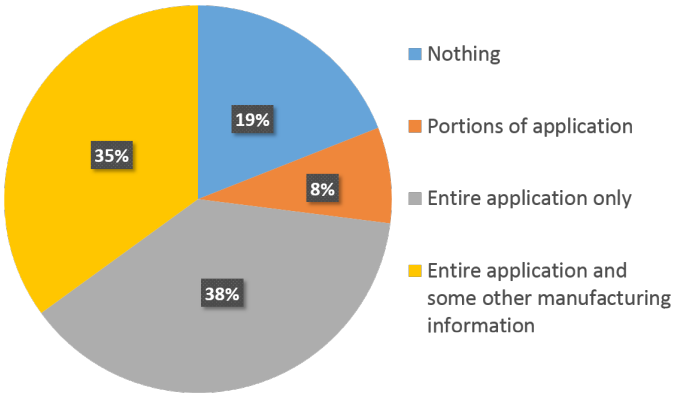
Production

After filing an aBLA, an applicant must decide what, and how much, to produce to the reference product sponsor; the choice often centers around providing a full application, or only portions relevant to potential patents, and whether or not to provide additional manufacturing information, some details of which may contain or reflect confidential third-party information.

Despite the lack of any private right of action to enforce the provisions of the BPCIA, most complaints still allege that the applicant's production has been in some way deficient. Nevertheless, most applicants have produced at least portions of their aBLA to kick off the patent dance. However, applicants have often been less willing to produce additional manufacturing information requested by the sponsor.

[1] *Amgen v. Sandoz* was decided by the Supreme Court in June 2017. In this article, we use October 2017 as the post-*Amgen* cutoff, to reflect that complaints filed in the months following the Supreme Court's decision involved production and exchanges under the BPCIA within a pre-*Amgen* framework.

What did the Applicant produce?



There has been an increasing trend in nonproduction of aBLA filings since the Supreme Court's *Amgen* decision. Specifically, in the 11 complaints filed prior to that decision, only one alleged that the applicant had failed to produce its aBLA. In the 15 complaints filed since, four sponsors have alleged nonproduction of aBLA filings, with two additional complaints alleging that the applicant produced only an incomplete aBLA.

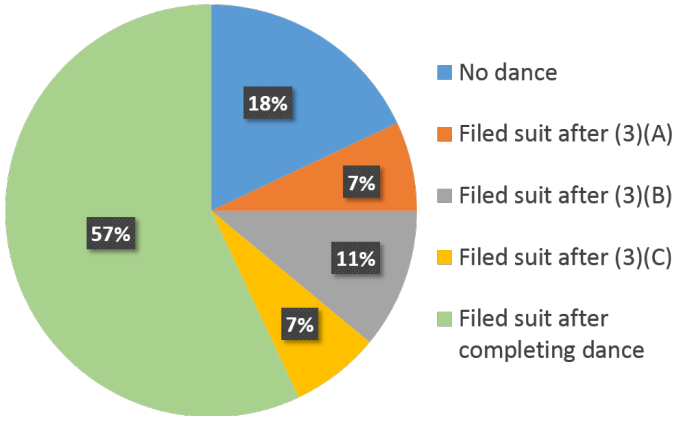
However, the data suggests no difference in the proportion of applicants willing to provide additional manufacturing information post-*Amgen*. Specifically, among the 10 pre-*Amgen* complaints in which the applicant had provided its aBLA, four applicants (40%) provided such information. And of the 11 post-*Amgen* applicants who provided at least some of their aBLA, a similar proportion, five (45%) produced additional manufacturing information.

When to Sue?

After an applicant makes the decision whether to engage in the dance, and how much information to produce, the sponsor bears the burden of deciding when to file suit. Where an applicant refuses to make any production, of course, there is no incentive to engage in the exchanges contemplated by the patent dance. But under the BPCIA, a sponsor can still surrender its right to initiate a two-phase litigation by breaking off the patent dance early and bringing suit. Moreover, after being notified of the patents that could be reasonably asserted against them, some applicants sought to file complaints for declaratory judgment in a preferred forum.

In our April 2018 issue, we noted that suits had been filed at every stage of the contemplated BPCIA exchanges. In the intervening years, however, the patent dance has become an increasingly binary proposition. Not only does the Supreme Court's decision in *Amgen* deny sponsors any private right of action to enforce BPCIA provisions, but district courts have clearly refused applicants' attempts to break off the patent dance and file declaratory judgment acts in the venue of their choosing.[2] Thus, within a framework in which applicants and sponsors both clearly have the option as to whether or not to engage in the patent dance, those choosing to do so may be more committed to completing the BPCIA exchanges.

How far into the dance was suit filed?



In the instances in which applicants refused to provide their aBLA or any manufacturing information, sponsors, understandably, sued without submitting a (3)(A) statement. But post-*Amgen*, in each instance where the applicants decided to engage in the BPCIA exchanges, they were fully completed, albeit occasionally with reservations as to the sufficiency of production.

[2] *See, e.g.*, *Amgen, Inc. v. Genentech, Inc.*, No. CV 17-7349-GW(AGRX), 2018 WL 910198, at *3 (C.D. Cal. Jan. 11, 2018); *Celltrion, Inc. v. Genentech, Inc.*, No. 18-CV-00274-JSW, 2018 WL 2448254, at *5 (N.D. Cal. May 9, 2018), appeal dismissed, No. 2018-2160, 2018 WL 7046651 (Fed. Cir. Nov. 30, 2018).

Notably, in several cases where the patent dance was completed, the parties could not come to an agreement as to the patents to litigate in a first-wave litigation. However, two fairly recent contrasting and inapposite cases demonstrate the broad set of potential outcomes under these circumstances. In *AbbVie v. Sandoz*,[3] the sponsor maintained in its 3(C) statement that it could reasonably assert infringement as to 84 patents against the aBLA product. The parties, however, were unable to agree as to which of those 84 patents should be litigated in an initial infringement action. With negotiations having failed, Sandoz was entitled to select a number of patents each party could identify to litigate under § 262(*l*)(5)(B)(i) – and selected just one. Thus, after completing the dance, Sandoz was able to whittle down AbbVie's list of 84 patents to two for the first-phase litigation. In its complaint, AbbVie cast this action as Sandoz delaying the inevitable, with the remaining 82 patents available to be litigated upon receipt of a notice of commercial marketing.

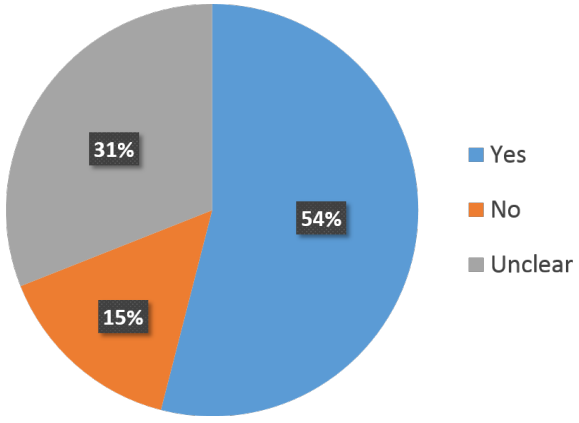
While *AbbVie v. Sandoz* illustrates an aBLA applicant's ability to limit the first-phase litigation to as few as two patents, *Genentech v. Pfizer*[4] demonstrates the inverse proposition. There, after participating in the initial exchanges, Genentech listed 17 patents in its 3(C) statement of which it could allege infringement. Rather than engage in any further negotiations, Pfizer sent a letter responding that it "accepted" the 17 patents for litigation and that negotiations were concluded. Unlike Sandoz, which used failed negotiations as a sword to limit the scope of a first-wave action, Pfizer attempted to use the exchanges to shield itself from a potential second-wave action linked to its notice of commercial marketing.

Notice of Commercial Marketing:

As noted above, the BPCIA contemplates a two-wave litigation: first, sponsors and applicants agree on a list of patents to immediately litigate upon acceptance of an aBLA; second, after an applicant provides its notice of commercial marketing, a patentee can bring suit on any remaining unlitigated or newly issued patents.

As we noted in our April 2018 issue, and as remains the case today, this two-wave litigation remains theoretical, as no such second-phase action has yet been filed. Moreover, under the Supreme Court's decision in *Amgen*, applicants may provide their notice of commercial marketing at any time – including prior to FDA approval.

Notice given before Complaint filed?



Although the appropriate timing of a notice of commercial marketing was at issue in *Amgen*, most biosimilar applicants before that decision did provide such notice during the exchanges. In fact, in only one pre-*Amgen* complaint did the sponsor explicitly note that such notice had not been given.

Interestingly, even though the Supreme Court clarified that early notice of commercial marketing was permitted under the BPCIA, more applicants have elected *not* to provide notice prior to the filing of a complaint, opting instead to maintain the two-phase litigation contemplated by the BPCIA. Indeed, three of 15 (20%) post-*Amgen* complaints note that notice had not been given. Perhaps the *AbbVie v. Sandoz* action best illustrates how declining to provide early notice may benefit an applicant. By withholding a sponsor's ability to immediately bring suit on all patents at its disposal,

[3] *AbbVie, Inc. et al. v. Sandoz, Inc. et al.*, No. 3:18-cv-12668 (D. N.J.).
[4] *Genentech Inc., et al. v. Pfizer Inc.*, No. 1:19-cv-00638 (D. Del.)

an applicant can control the pace and scope of a first-wave action, either choosing to litigate a limited set of issues – as Sandoz did – or a more comprehensive set of patents.

Takeaways Several factors have affected the pre-complaint exchanges contemplated by the BPCIA, including the Supreme Court's decision in *Amgen* and several lower-court decisions rejecting declaratory judgment actions brought by applicants. Taken together, these rulings suggest that while the patent dance remains expressly optional, there is no incentive for applicants to break off the exchanges prior to the filing of a complaint.

Interestingly, despite clear guidance that there is no mandate to produce an aBLA, applicants continue to do so – and, in some cases, to provide additional manufacturing information. Under the *Amgen* framework, applicants may view these exchanges as an opportunity to narrow the scope of a subsequent infringement litigation, especially as BPCIA practice trends towards a single-phase action.

Alternatively, with most BPCIA litigation heading towards settlement and no second-phase action yet commenced, applicants may be inclined to follow the approach taken by Sandoz discussed above – completing the patent dance, but agreeing only to an extremely limited set of patents. By forcing Amgen to allege infringement of just two patents, and delaying litigation as to the other 82 patents it identified, Sandoz was able to limit the scope and cost of a first-wave action, which it could reasonably expect would result in a global settlement as to all patents on the reference biologic.

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