

Biosimilars

2019 Year in Review

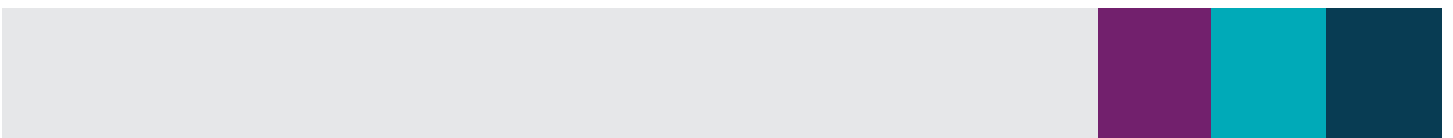
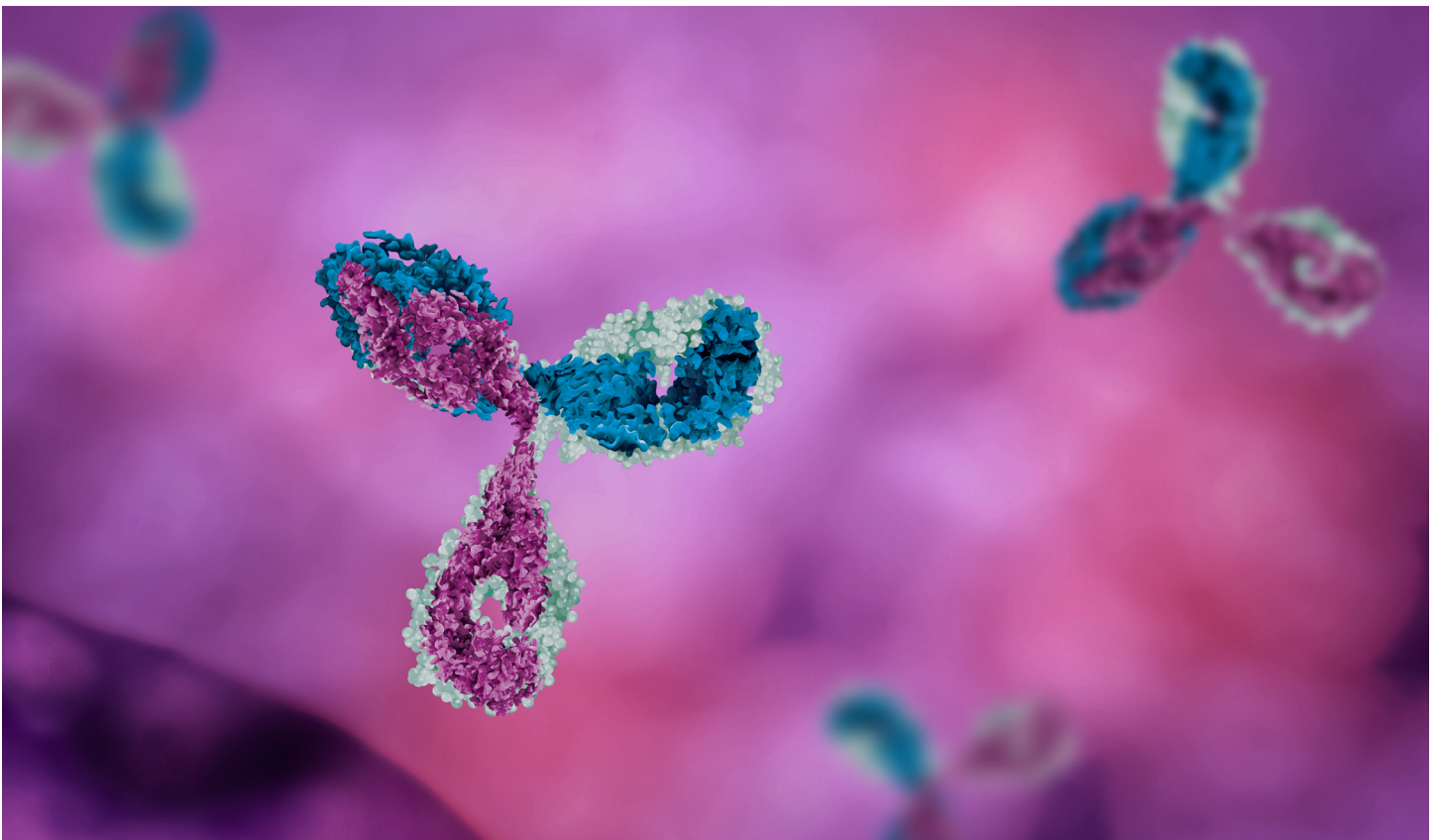




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Introduction

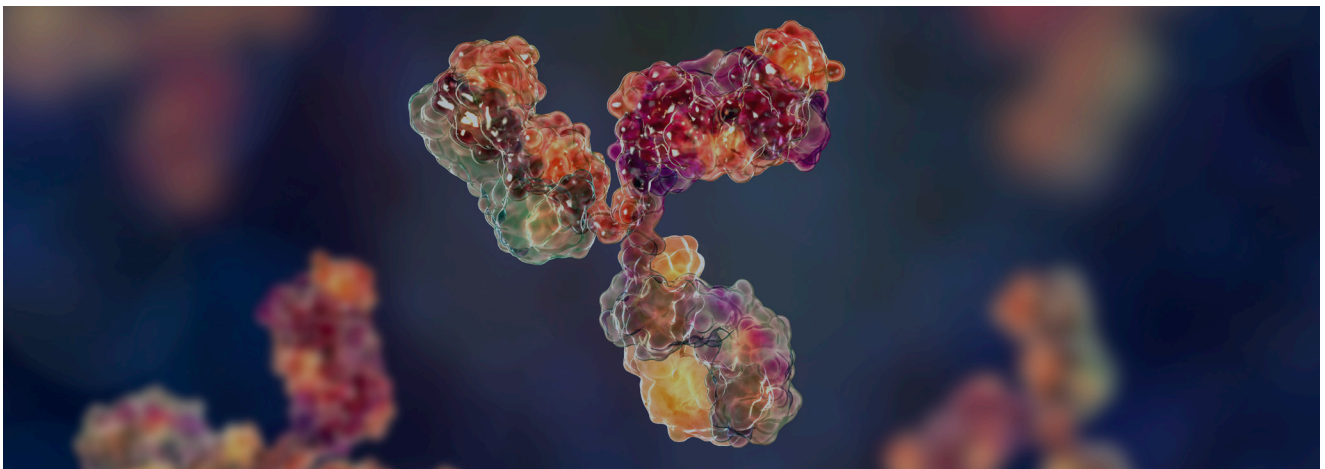
In many ways, 2019 was a notable year for biosimilars in the U.S. FDA approved the 26th biosimilar product and the 13th biosimilar product was launched in the U.S. market. These developments were accompanied by a flurry of activity at FDA, new proposed and enacted legislation, and new developments in court and in post-grant proceedings. Below, we review the developments in the field in terms of biosimilar approvals and launches, FDA guidance on biosimilars, pending biosimilar legislation, litigation under the Biosimilars Price Competition and Innovation Act (BPCIA), litigation related to alleged anticompetitive behavior on the part of reference product sponsors, and biologic-related post-grant challenges.

I. Biosimilar Approvals and Launches in 2019

In 2019, there was a notable uptick in both FDA approvals and biosimilar launches. FDA topped its previous record from 2018, approving ten new Biologics License Applications (BLAs). Below is a list of biosimilar approvals from 2019, including the manufacturer of each product:

- Ontruzant® (trastuzumab), Samsung Bioepis
- Trazimera™ (trastuzumab), Pfizer
- Eticovo™ (etanercept), Samsung Bioepis
- Kanjinti™ (trastuzumab), Amgen
- Zirabev™ (bevacizumab), Pfizer
- Ruxience™ (rituximab), Pfizer
- Hadlima™ (adalimumab), Samsung Bioepis
- Ziextenzo® (pegfilgrastim), Sandoz
- Abrilada™ (adalimumab), Pfizer
- Avsola™ (infliximab), Amgen

This increase in the number of biosimilar approvals in 2019 is consistent with FDA's trend over the last five years, as illustrated in Figure 1 below. Unsurprisingly, the increase in biosimilar approvals has correlated with an increase in the number of U.S. product launches, with seven new launches in 2019, and more biosimilars launched in early 2020.



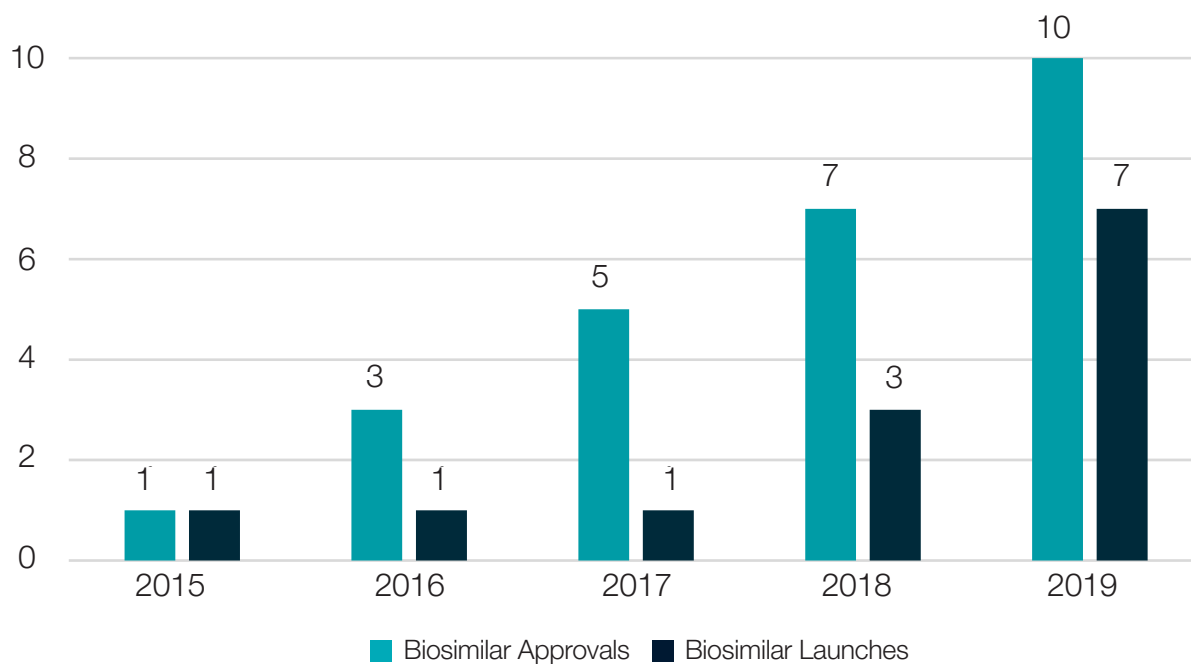


Figure 1. Biosimilar Approvals and Launches by Year

The following tables summarize publicly available information regarding approved and select pending BLAs, and illustrate additional trends in the biosimilars industry.

Table 1 summarizes information related to biosimilars approved as of 2019. As can be seen below, Pfizer has been one of the most active players in the biosimilars space, with four product launches as of 2019, two launches in early 2020, and having developed biosimilars of eight different reference products (Remicade®, Epogen®/Procrit®, Neupogen®, Avastin®, Herceptin®, Rituxan®, Neulasta®, and Humira®).

Table 2 shows some select pending BLAs for which information is publicly available. Dr. Sarah Yim, Acting Director of FDA’s Office of Therapeutic Biologics and Biosimilars, stated in November of 2019 that there are 74 programs for 38 different reference products currently enrolled in its Biosimilar Product Development Program.

Table 1. Biosimilars Approved as of 2019

Biosimilar Drug	Biologic Drug	Biosimilar Code Name	FDA Approval Date	Time from BLA Acceptance to Approval ¹	Commercial Launch Date	Reported Price Discount at Launch
Avsola™ (Amgen)	Remicade® (Johnson & Johnson)	infliximab-axxq	December 6, 2019	12 months		
Abrilada™ (Pfizer)	Humira® (AbbVie)	adalimumab-afzb	November 15, 2019	12 months	No earlier than November 20, 2023 per settlement	

¹ Approval time is calculated from the first BLA submission date, not any resubmission date.

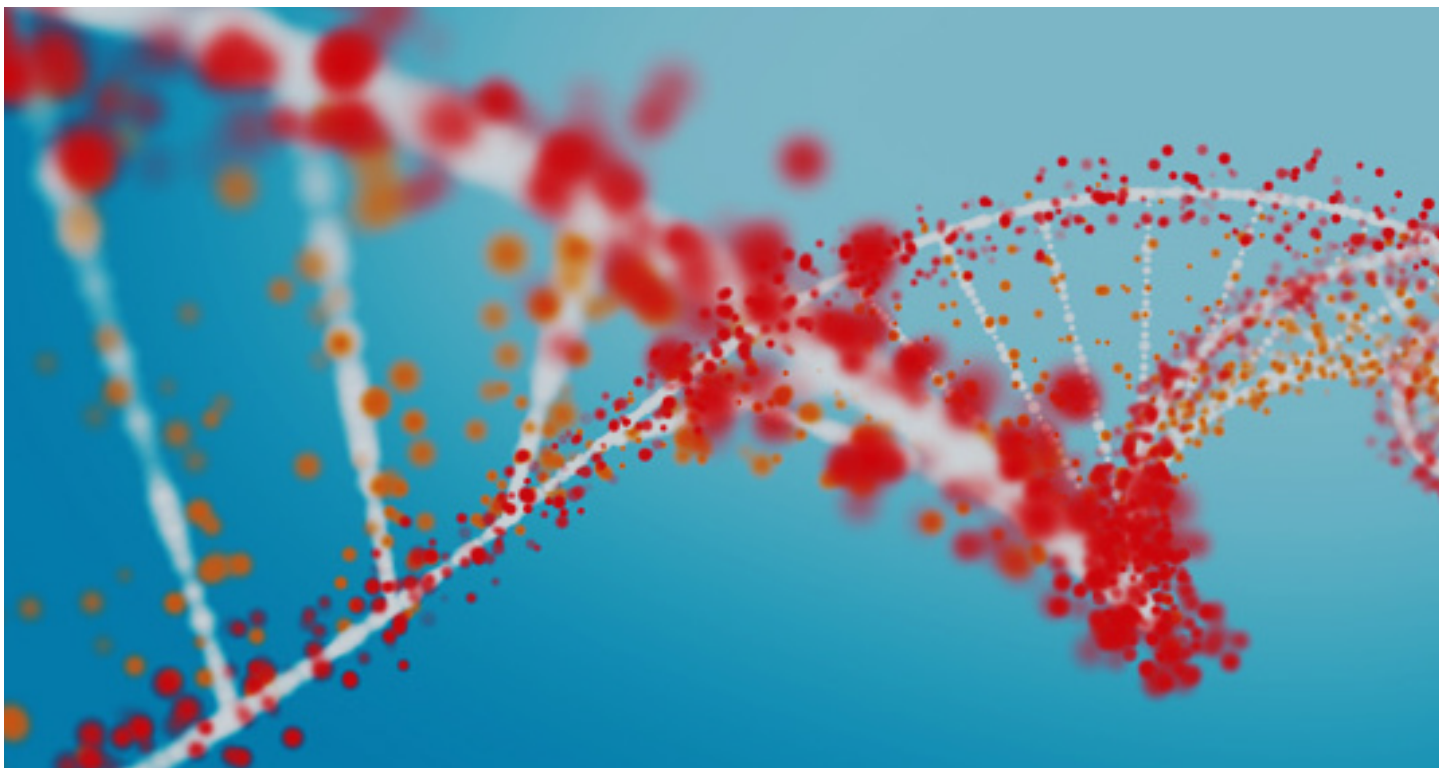
Ziextenzo™ (Sandoz)	Neulasta® (Amgen)	pegflgrastim- bmez	November 4, 2019	50 months (first submission Aug. 2015; resubmitted Feb. 2019)	November 15, 2019	37% off WAC for Neulasta®
Hadlima™ (Samsung Bioepis)	Humira® (AbbVie)	adalimumab- bwwd	July 23, 2019	12 months	No earlier than June 30, 2023 per settlement	
Ruxience™ (Pfizer)	Rituxan® (Roche/ Genentech)	rituximab-pvr	July 23, 2019	12 months	January 23, 2020	24% off WAC for Rituxan®
Kanjinti™ (Amgen)	Herceptin® (Genetech)	trastuzumab- anns	June 13, 2019	22.5 months (first submission July 2017; resubmitted Dec. 2018)	July 18, 2019	13% off ASP; 15% off WAC for Herceptin®
Zirabev™ (Pfizer)	Avastin® (Roche)	bevacizumab- bvzr	June 27, 2019	12 months	December 31, 2019	23% off WAC for Avastin®
Eticovo™ (Samsung Bioepis)	Enbrel® (Amgen)	etanercept-ykro	April 25, 2019	23 months (first submission May 2017; resubmitted Oct. 2018)		
Trazimera™ (Pfizer)	Herceptin® (Genetech)	trastuzumab- qyyp	March 11, 2019	20.5 months (first submission June 22, 2017; resubmitted Sept. 28, 2018)	Anticipated February 15, 2020	Anticipated 22% off WAC for Herceptin®
Ontruzant® (Samsung Bioepis)	Herceptin® (Genetech)	trastuzumab-dttb	January 18, 2019	15 months		
Herzuma® (Celltrion/ Teva)	Herceptin® (Genetech)	trastuzumab- pkrb	December 14, 2018	18.5 months (first submission May 2017; resubmitted June 2018)		
Truxima® (Celltrion/ Teva)	Rituxan® (Roche/ Genentech)	rituximab-abbs	November 28, 2018	19 months (first submission April 2017; resubmitted May 2018)	November 11, 2019	10% off Truxima® list price
Udenyca® (Coherus)	Neulasta® (Amgen)	pegfilgrastim- cbqv	November 2, 2018	27 months (first submission Aug. 2016; resubmitted May 2018)	January 3, 2019	33% off Neulasta®
Hyrimoz™ (Sandoz)	Humira® (AbbVie)	adalimumab- adaz	October 30, 2018	12 months	No earlier than September 30, 2023 per settlement	
Nivestym™ (Pfizer/ Hospira)	Neupogen® (Amgen)	filgrastim-aafi	July 20, 2018	10 months	October 1, 2018	30.3% off Neupogen®; 20.3% off Zarxio®; and 14.1% off Granix®
Fulphila™ (Mylan/ Biocon)	Neulasta® (Amgen)	pegfilgrastim- jmdb	June 4, 2018	18 months (first submission Dec. 2016; resubmitted Dec. 2017)	July 26, 2018	33% off Neulasta®
Retacrit® (Pfizer/ Hospira)	Epogen®/ Procrit® (Amgen/ J&J)	epoetin alfa-epbx	May 15, 2018	41 months (first submission Dec. 2014; resubmitted Dec. 2016 and Nov. 2017)	November 12, 2018	33.5% off Epogen®; 57% off Procrit®
Ixifi® (Pfizer)	Remicade® (Johnson & Johnson)	infliximab-qbtx	December 13, 2017	10 months	No U.S. launch intended	

Ogivri® (Mylan)	Herceptin® (Genentech/ Roche)	trastuzumab-dkst	December 1, 2017	13 months	December 2, 2019	
Mvasi® (Amgen/ Allergan)	Avastin® (Roche)	bevacizumab-awwb	September 14, 2017	10 months	July 18, 2019	12% off ASP and 15% of WAC of Avastin®
Cyltezo® (Boehringer Ingelheim)	Humira® (AbbVie)	adalimumab-adbm	August 25, 2017	10 months	No earlier than July 1, 2023 per settlement	
Renflexis® (Samsung Bioepis/ Merck)	Remicade® (Johnson & Johnson)	infliximab-abda	April 21, 2017	13 months	July 2017	35% off Remicade®
Amjevita® (Amgen)	Humira® (AbbVie)	adalimumab-atto	September 23, 2016	10 months	No earlier than January 31, 2023 per settlement	
Erelzi® (Sandoz)	Enbrel® (Amgen)	etanercept-szsz	August 30, 2016	13 months		
Infectra® (Pfizer/ Celltrion)	Remicade® (Johnson & Johnson)	infliximab-dyyb	April 5, 2016	20 months (first submission Aug. 2014; resubmitted Oct. 2015)	November 2016	15% off Remicade®
Zarxio® (Sandoz)	Neupogen® (Amgen)	filgrastim-sndz	March 6, 2015	10 months	September 2015	15% off Neupogen®

Table 2. Select Pending BLAs as of December 2019

Biosimilar Drug	Biologic Drug	Biosimilar Code Name	FDA Status
ABP 798 (Amgen / Allergan)	Rituxan® (Roche / Genentech)	rituximab	Submitted: December 2019
TX-01 (Tanvex Biopharma)	Neupogen® (Amgen)	filgrastim	Submitted: October 2018 Complete Response Letter: September 2019
Lapelga™ (Apotex)	Neulasta® (Amgen)	pegfilgrastim	Submitted: December 2014
Grastofil® (Apotex)	Neupogen® (Amgen)	filgrastim	Submitted: February 2015
ABP 710 (Amgen / Allergan)	Remicade® (Johnson & Johnson)	infliximab	Submitted: December 2018
SB8 (Samsung Bioepis)	Avastin® (Roche)	bevacizumab	Submitted: November 2019


II. FDA Guidance



Consistent with its announcements in 2018, including the Biosimilars Action Plan, FDA continued its efforts in 2019 to improve the efficiency of the biosimilar approval process to promote growth of the United States biosimilars market.

For example, in March 2019, FDA issued a draft guidance, “Nonproprietary Naming of Biological Products: Update,” describing FDA’s current thinking on nonproprietary names of biological products licensed under Section 351 of Public Health Service Act (PHS Act). Among other things, FDA proposes to remove transition biological products from the scope of the naming convention described in FDA’s January 2017 Naming Guidance. The draft guidance also states that FDA no longer intends to retroactively modify the names of approved biologics to include 4-letter suffixes devoid of meaning, though it will continue to assign suffixes to newly approved biologics, biosimilars, or interchangeable biosimilars.

On May 9, 2019, FDA published its final Guidance for Industry titled “Considerations in Demonstrating Interchangeability With a Reference Product.” The Guidance is an update to the draft Guidance released in January 2017 for notice and comment, and like the draft Guidance, focuses on the evidence required to establish interchangeability with a reference biologic product. FDA explains that in evaluating an application for



interchangeability, it will consider the totality of the evidence provided by the sponsor. FDA also notes that the information necessary to meet the statutory requirements “may vary depending on the nature of the proposed interchangeable product,” and that an interchangeable designation will typically require a switching study. Further, the Guidance suggests that the evaluation process is somewhat flexible, stating that, where applicable, an applicant may provide a “scientific justification” explaining the differences between the reference product and the proposed interchangeable.

Later in May, FDA issued a second guidance document, titled “Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations.” There, FDA sets forth its considerations and recommendations on the design and evaluation of comparative analytical studies that aim to demonstrate that a proposed therapeutic protein product is biosimilar to a reference product licensed under the PHS Act. The Guidance also provides recommendations to sponsors on the scientific and technical information for the chemistry, manufacturing, and controls portion of a section 351(k) marketing application.

In September, FDA issued its final Guidance for Industry on “Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act,” which seeks to lessen the impact of certain citizen petitions on pending approval actions involving an ANDA, repurposed drug application under 505(b)(2), or a BLA. The Guidance discusses FDA’s current thinking on what constitutes a 505(q) petition and the various factors that FDA will consider in determining whether a petition is submitted with the primary purposes of delaying the approval of a drug application.

In November, FDA published a draft guidance titled “Clinical Immunogenicity Considerations for Biosimilar and Interchangeable Insulin Products.” According to then-acting FDA Commissioner Brett P. Giroir, M.D., the guidance is intended to “help facilitate the development of, and improve patient access to, life-saving insulin products.” The guidance incorporates, *inter alia*, the public comments received by FDA in response to a May 2019 public meeting concerning development of insulin biosimilars and explains that, in general, comparative clinical immunogenicity studies are not necessary to support a demonstration of biosimilarity or interchangeability to obtain approval for proposed biosimilar or interchangeable insulin products. The guidance and public meeting are part of FDA’s efforts to facilitate the upcoming March 23, 2020 transition of approved marketing applications for biological products regulated under the Federal Food, Drug, and Cosmetic Act to be approved biologic license applications under the PHS Act.

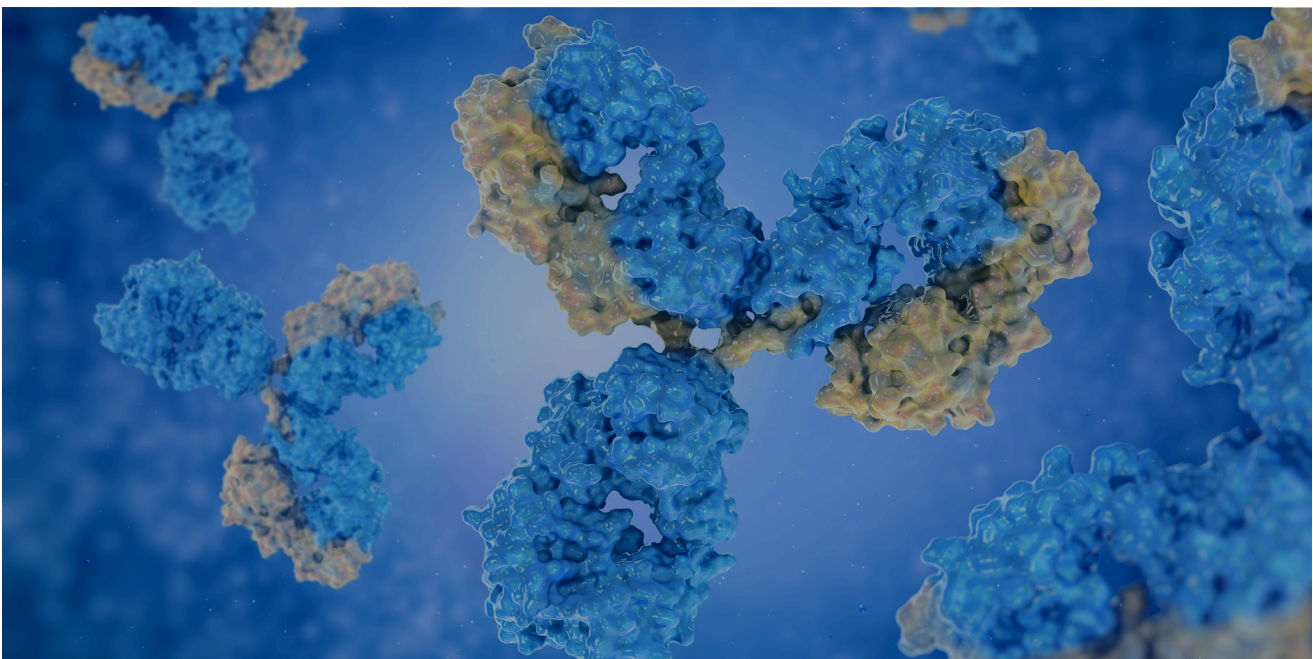
III. Pending Legislation Relating to Biologics


In 2019, state and federal legislators once again put the spotlight on the biopharmaceutical industry. At the federal level, bipartisan lawmakers proposed a variety of new legislation concerning biologic drug pricing and access that could have important implications for the biosimilars market in the U.S. At the state level, legislators continued to enact laws permitting or requiring biosimilar substitution by pharmacists.

A. Federal Legislation

Federal legislators focused their energies on improving biosimilar uptake and reducing drug prices in the U.S. market. Their proposed legislation targets everything from anticompetitive tactics by reference product sponsors to improved resources for doctors, patients, and biosimilar manufacturers. Below, we identify many of the pending bills, which are in various stages of the legislative process.

The Purple Book Continuity Act of 2019 (H.R. 1520) and the Biologic Patent Transparency Act (BPTA) (S. 659) are two exemplary pieces of legislation seeking to reduce uncertainty for potential biosimilar manufacturers by making patent information for biologic drugs more readily available in the “Purple Book,” analogous to the information available in the “Orange Book” for small molecule drugs.





Several proposals focus on curbing anticompetitive conduct by biologic drug manufacturers, such as “product hopping,” “pay-for-delay” agreements, abusive or sham citizen petitions, and patent “evergreening.” Such proposed legislation includes the Affordable Prescriptions for Patients Act of 2019 (S. 1416), the Protecting Consumer Access to Generics Act of 2019 (H.R. 1499), the Preserve Access to Affordable Generics and Biosimilars Act (H.R. 2375), the Stop Significant and Time-wasting Abuse Limiting Legitimate Innovation of New Generics (STALLING) Act (S. 1224/H.R. 2374), the Stop the Overuse of Petitions and Get Affordable Medicines to Enter Soon (STOP GAMES) Act of 2019 (H.R. 2387), the Terminating the Extension of Rights Misappropriated (TERM) Act (H.R. 3199) and the Second Look at Drug Patents Act of 2019 (S. 1617).

A number of bills seek to lower barriers to entry for biosimilars by ensuring that potential biosimilar competitors have sufficient quantities of reference product for testing. These bills include, for example, the Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2019 (H.R. 965/S. 340), the Fair Care Act of 2019 (H.R. 1332), and the Fair Access for Safe and Timely (FAST) Generics Act of 2019 (H.R. 985).

Other pending biosimilar-related legislation includes:


- Lower Health Care Costs Act (S. 1895)
- Protecting Access to Biosimilars Act of 2019 (S. 1140/H.R. 2011)
- Prescription Drug Price Relief Act of 2019 (S. 102)
- Lowering Prescription Drug Costs and Extending Community Health Centers and Other Public Health Priorities Act (H.R. 2700)
- Lower Drug Costs Now Act of 2019 (H.R. 3)
- Bolstering Innovative Options to Save Immediately on Medicines (BIOSIM) Act (H.R. 4455)
- Affordable Insulin Act of 2019 (H.R. 1478)
- Hatch-Waxman Integrity Act of 2019 (S. 344/H.R. 990)
- Affordable and Safe Prescription Drug Importation Act (H.R. 447)
- Star Ratings for Biosimilars Act (H.R. 4629)
- Advancing Education on Biosimilars Act of 2019 (S. 1681)

B. State Biosimilar Substitution Laws

Although FDA controls the approval of interchangeable biosimilars, state legislatures regulate biosimilar substitution at the pharmacy. FDA has yet to approve any interchangeable products, but state lawmakers nationwide, beginning in 2013, have pushed to enact interchangeable biosimilar substitution laws. In 2019, four more states—Alabama, Arkansas, Maine, and Mississippi—followed this trend. Now, at least 49 U.S. states and Puerto Rico have biosimilar substitution laws on the books permitting or requiring pharmacists to dispense an interchangeable biological product under certain circumstances.

The particular approaches taken by the states vary, but there are several features and requirements that are frequently included in state substitution laws:

1. FDA approval as “interchangeable.” Any biological product under consideration for substitution must satisfy federal standards of interchangeability, as set forth in 42 U.S.C. § 262(k)(4) (*i.e.*, the product must be approved as an interchangeable by FDA).

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2. Prescriber does not indicate that substitution is prohibited. The prescriber can prevent substitution by stating, for example, “dispense as written” or “brand medically necessary” or “do not substitute.”
 3. “Notification” vs “Communication.” Some states require that the patient and prescriber “must be notified” of any allowable substitution made at a pharmacy, while other states require that the pharmacy must “communicate” such information to the patient and prescriber.
 4. Permissive vs. mandatory. States generally either permit or mandate that the pharmacist substitute a prescribed biologic, although the specific conditions for permitting or mandating substitution vary.
 5. Cost savings required. Many states require that the substituted biologic dispensed be less or no more expensive than the prescribed biologic and that some of the cost savings be passed on to the purchaser.
 6. Patient Notification and Consent. Some states require that the individual patient be notified that a substitute or switch has been made. In some cases, patient consent is also required before any switch is made.
 7. Recordkeeping. Many states with biosimilar substitution laws require that the pharmacist and the physician retain records of, for example, substituted biologic medications for a certain period of time. The specific types of information and length of time for which records must be maintained vary.
 8. Immunity. Some states provide legal immunity for pharmacists who make a substitution in compliance with state biologics laws.
 9. Publication of FDA-approved interchangeable products. Some states are required to maintain a public or web-based list of FDA-approved interchangeable biosimilars.
 10. Disclosure. Some states require pharmacists to explain the cost or price of the biologic and the interchangeable biosimilar.

IV. BPCIA Litigation

BPCIA litigants and district courts grappled with new issues in 2019. The Federal Circuit was also busy, with numerous BPCIA issues pending at the Federal Circuit and a handful of new Federal Circuit decisions issued. Below, we briefly summarize overall statistics regarding BPCIA district court litigation and, in the subsequent sections, we review ongoing BPCIA district court cases, BPCIA district court cases that settled in 2019, and pending and newly decided BPCIA appeals.

Since the BPCIA's enactment in 2010, over 40 BPCIA cases have been filed in district courts. (See Figure 2.) Amgen (with 15 cases) and Genentech (with 13 cases) are the most active plaintiffs and together account for the plaintiff side in more than half of all BPCIA litigation to date. Amgen is also the most common BPCIA defendant (with 8 cases), while Celltrion (defendant in 7 cases) and Sandoz (defendant in 6 cases) are not far behind. BPCIA litigation has involved biosimilars of nine different reference products: Remicade®, Neulasta®, Neupogen®, Avastin®, Herceptin®, Rituxan®, Humira®, Enbrel®, and Epogen®. Unsurprisingly, these mirror the nine reference products for which there are FDA-approved biosimilars (see Section I, above). The District of Delaware, the District of New Jersey, and the Northern District of California have emerged as the most common venues for BPCIA litigation.

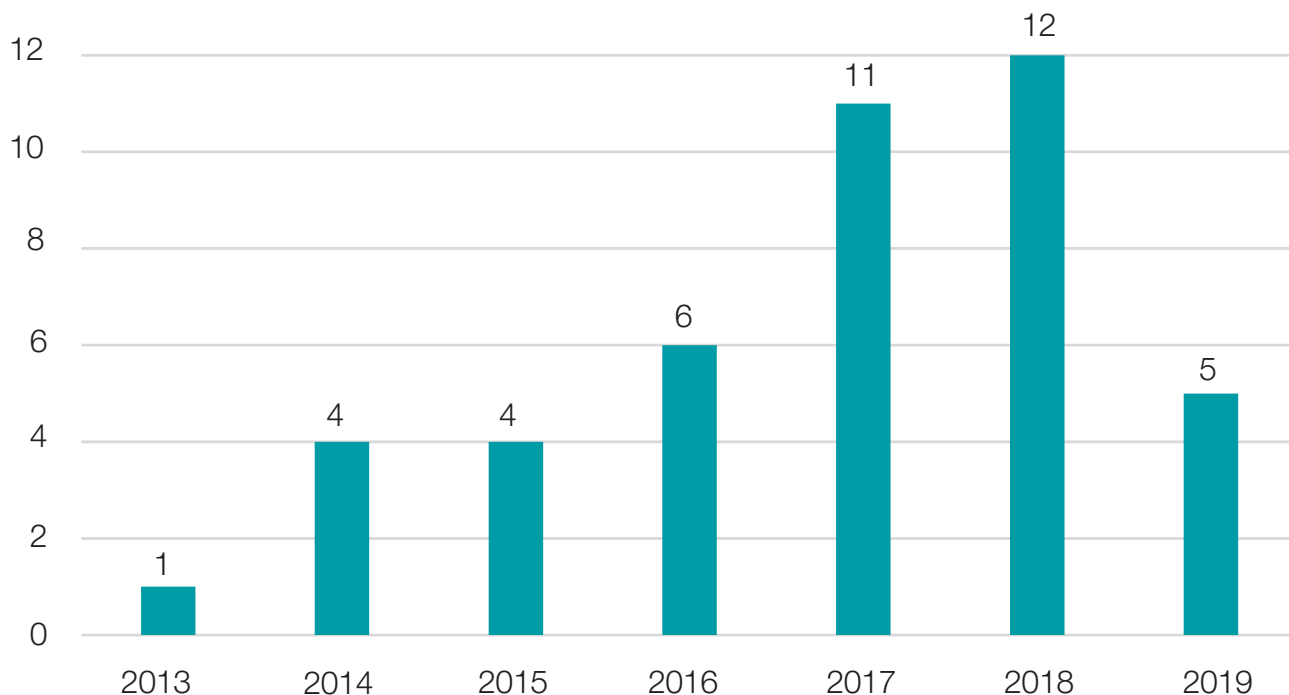


Figure 2. BPCIA Cases Filed by Year since BPCIA Enactment

2019 saw a decrease in new BPCIA district court filings in comparison to the last three years (see Figure 2). Further, several of the 2019 cases were follow-on cases to add new patents, as opposed to new disputes involving new parties and/or biosimilars. Of the five new BPCIA district court cases filed in 2019, only *Genentech v. Immunex* and *Immunex v. Samsung Bioepis* are still ongoing; the remainder have been dismissed. The newly filed BPCIA cases are summarized in Table 3, and discussed individually below in the sections addressing ongoing litigation and litigation resolved in 2019.

Table 3. BPCIA Cases Filed in 2019

Case Name	Court	Filing Date	Drug at Issue	Type of Complaint	Number of Initially Asserted Patents
<i>Sandoz v. Amgen</i> (3:19-cv-00977)	N.D. Cal.	2/21/2019	Neulasta® (pegfilgrastim)	Declaratory judgment	1
<i>Genentech v. Immunex</i> (1:19-cv-00602)	D. Del.	3/29/2019	Avastin® (bevacizumab)	Patent infringement	14
<i>Genentech v. Pfizer</i> (1:19-cv-00638)	D. Del.	4/5/2019	Avastin® (bevacizumab)	Patent infringement	22
<i>Immunex v. Samsung Bioepis</i> (2:19-cv-11755)	D.N.J.	4/30/2019	Enbrel® (etanercept)	Patent infringement	5
<i>Amgen v. Tanvex</i> (3:19-cv-01374)	S.D. Cal.	7/23/2019	Neupogen® (filgrastim)	Patent infringement	1

A. Ongoing BPCIA District Court Litigation

As discussed above, the BPCIA cases filed in 2019 that are currently ongoing include:

- *Genentech v. Immunex* (19-cv-00602 D. Del.); Avastin®/Mvasi™
- *Immunex v. Samsung Bioepis* (19-cv-11755 D.N.J.); Enbrel®/Eticovo™

In addition, several cases filed prior to 2019 remain ongoing:


- *Genentech v. Amgen* (17-cv-01407 D. Del.); Avastin®/Mvasi™
- *Genentech v. Amgen* (18-cv-00924 D. Del.); Herceptin®/Kanjinti™
- *Amgen v. Hospira* (18-cv-01064 D. Del.); Neupogen®/Nivestym™
- *Amgen v. Coherus* (17-cv-00546 D. Del.); Neulasta®/Udenyca®

We discuss each ongoing BPCIA district court case briefly below.

Genentech v. Immunex (19-cv-00602 D. Del.)

This case concerns Mvasi™, Amgen’s biosimilar to Genentech’s Avastin® (bevacizumab). The case relates to two prior cases between the parties consolidated into Case No. 17-1407 (D. Del.), discussed in further detail below.

Genentech filed this new suit in response to a supplement to Amgen’s BLA for Mvasi™ filed in August 2018 and



produced during litigation in the previous cases. Genentech contended that a supplement to the BLA was an “application” within the meaning of § 262(l)(2), thus triggering the contention-exchange process and other aspects of the BPCIA “patent dance.” (Dkt. 24 at 5.) In a heavily redacted complaint, Genentech asserted fourteen patents, including twelve that it had asserted previously in Case No. 17-1407, and two new patents directed to manufacturing processes, U.S. Patent Nos. 9,493,744 and 9,714,293. (Dkt. 12.)

On May 13, 2019, Amgen moved to dismiss the complaint for failure to state a claim. Amgen argued that plaintiffs “missed the deadline to request leave to add these [two new] patents to the 1407 Case (because they did not have good cause to do so) and now hope to sidestep the Court’s good cause requirement.” (Dkt. 20 at 1.) Among other allegations, Amgen alleged that Genentech was engaging in “claim-splitting” based on the “groundless premise that a new round of the BPCIA exchange process automatically begins, and a follow-on complaint may be filed, whenever a biosimilar applicant submits a supplemental BLA for approval of an [redacted] for an already-approved product.” (*Id.* at 2.) Genentech opposed dismissal. (Dkt. 24.) No decision on this motion is available on the public docket.

In July 2019, when Amgen announced it was preparing to immediately launch Mvasi™, Genentech filed two emergency motions seeking to enforce the BPCIA’s 180-day notice of commercial marketing requirement in connection with the new supplements and a temporary restraining order (TRO) to prevent potential marketing of Mvasi™. (Dkt. 29; Dkt. 31.) Although Amgen had provided notice of commercial marketing back in October 2017, Genentech argued that new notice was required because “Mvasi is a new product ... accompanied by a new label, and the subject of several applications, FDA reviews, and FDA approvals.” (Dkt. 50 at 10.) The Court denied both motions (Dkt. 47), which Genentech immediately appealed on July 19, 2019. (Dkt. 43.) The appeal, CAFC 19-2155, is discussed below. That same day, the district court also denied Genentech’s motion for an injunction pending appeal. Amgen launched Mvasi™ in the United States in July 2019.

Immunex v. Samsung Bioepis (19-cv-11755 D.N.J.)

This case involves the reference product Enbrel® (etanercept) and Samsung Bioepis’ biosimilar, Eticovo™. On April 30, 2019—only five days after FDA approved Eticovo™—Immunex asserted five patents against Samsung Bioepis, three of which were owned by Immunex and two that Immunex had exclusively licensed from Roche. (Dkt. 1 at 3.) Samsung Bioepis answered the complaint on August 5, 2019. (Dkt. 70.)

Early in the litigation, on May 29, 2019, Sandoz moved to intervene in this case with a heavily redacted brief in support of the motion. (Dkt. 37.) In a separate lawsuit with Immunex, *Immunex v. Sandoz* (16-cv-01118 D.N.J.), Sandoz had challenged validity of the Roche-owned patents, U.S. Patent Nos. 8,063,182 and 8,163,522. (*Id.* at 10.) In its brief, Sandoz claimed it had a “substantial and central interest in the property that is the subject of the litigation” that may be impaired, and that its interests were not adequately represented by the parties. (*Id.* at 6, 8-9.) The court has not ruled on Sandoz’s motion.

On December 10, 2019, a scheduling order issued, setting the close of fact discovery for December 21, 2020 and the close of expert discovery for April 13, 2021. (Dkt. 101 at 3-4.) On January 15, 2020, the court ordered that this matter be administratively stayed consistent with a confidential stipulation previously entered by the Court. (Dkt. 116.)

Genentech v. Amgen (17-cv-01407, 17-cv-01471 D. Del)

This litigation involves Amgen's biosimilar version of Genentech's reference product Avastin® (bevacizumab). This case saw significant activity in 2019 as the parties engaged in fact discovery.

One notable dispute arose over waiver of attorney-client privilege in both this case and Civil Action No. 18-cv-00924 related to Herceptin®. Genentech had asserted claims of willful infringement, to which Amgen responded with an advice-of-counsel defense. In an order dated June 20, 2019, the court found that "Amgen's production of its opinion letters ... has effected a subject matter waiver of Amgen's attorney-client privilege concerning infringement and validity of those patents," and the waiver "extends to communications pre-dating the opinion letters and extends to Amgen's in-house counsel" but not "outside trial counsel." (Dkt. 407 at 1.) Amgen filed a motion for reargument (Dkt. 423), which the court denied. (Dkt. 488.)

The court also granted-in-part a motion by Amgen to compel Genentech to produce "licensing and/or settlement agreements" with other biosimilar developers, including Pfizer and Celltrion. (Dkt. 387.) The court required Genentech to produce "any other terms ... that have any relevance to the value placed upon any of the patents implicated therein, including but not limited to royalties, lump sum payments, or any other consideration identified in the agreements." (*Id.*)

A jury trial is set for November 30, 2020.

Genentech v. Amgen (18-cv-00924 D. Del.) (TRO/PI Appeal: CAFC 19-2156)

This case, filed in June 2018, relates to Genentech's Herceptin® (trastuzumab) and Amgen's biosimilar, ABP 980, marketed under the trade name Kanjinti™.

On July 10, 2019, Genentech filed a motion for a TRO and preliminary injunction to prevent Amgen from commercially launching Kanjinti™ until the court rendered a decision on the merits following a full trial. (Dkt. 308.) The court denied the motion, finding that Genentech waited too long to file ("fourteen months after receiving the Notice of Commercial Marketing, three months after receiving a fairly specific launch date, and almost one month after Amgen had FDA approval to launch Kanjinti"). (Dkt. 315 at 5.) The court determined that Genentech's undue delay was sufficient to deny its motion and that Genentech would not suffer irreparable harm due to its previous licensing of certain asserted patents. (*Id.* at 6.) Genentech appealed on July 19, 2019. (CAFC 19-2156, discussed below.) Genentech launched Kanjinti™ in July 2019.

A jury trial is scheduled to start on April 20, 2020.

Amgen v. Hospira (18-cv-01064 D. Del.)

This case involves Nivestym™, Hospira and Pfizer's biosimilar of Amgen's Neupogen® (filgrastim). On July 18, 2018, Amgen asserted one patent in its initial complaint: U.S. Patent No. 9,643,997, directed to protein purification. (Dkt. 1 at 3.)

The parties are currently engaged in expert discovery. A jury trial is set for June 15, 2020. (Dkt. 26.)

Amgen v. Coherus (17-cv-00546 D. Del.)

This case involves Amgen's Neulasta® (pegfilgrastim) and Coherus' biosimilar Udenyca® / CHS-1701. The District of Delaware granted Coherus' motion to dismiss, finding that Amgen was barred by both prosecution history estoppel and the disclosure-dedication doctrine from asserting infringement under the doctrine of equivalents. The Federal Circuit affirmed on July 29, 2019, as discussed below.

In October 2019, Coherus filed a motion seeking to recover its attorneys' fees. (Dkt. 92.) Coherus argued that this case was exceptional for a number of reasons, including the weakness of Amgen's infringement case and Amgen's insistence on litigating all the way through appeal. (Dkt. 92, at 6–11; Dkt. 97.) Amgen opposed. (Dkt. 95.) The motion is still pending before the court.

B. BPCIA Litigation Settled or Dismissed in 2019

A number of BPCIA cases settled or were otherwise dismissed in 2019. In particular, many of Amgen's cases involving Neupogen® or Neulasta® were among those resolved, including cases against Sandoz, Apotex, Kashiv, Mylan, and recently, Tanvex (Amgen's suit against Hospira regarding Neupogen®, however, remains ongoing).

As discussed above, *Sandoz v. Amgen* (No. 19-cv-00977 N.D. Cal.), *Genentech v. Pfizer* (No. 19-cv-00638 D. Del.), and *Amgen v. Tanvex* (No. 19-cv-01374 S.D. Cal.) were filed and resolved in 2019. Additional cases settled or dismissed in 2019 include:

- *AbbVie v. Boehringer Ingelheim*, (No. 17-cv-01065 D. Del.); Humira®/Cyltezo®
- *Amgen v. Mylan* (No. 17-cv-01235 W.D. Pa.); Neulasta®/MYL140H
- *Amgen v. Kashiv* (Adello) (No. 18-cv-03347 D.N.J.); Neupogen®/TPI-G-CSF
- *Amgen v. Apotex* (No. 18-cv-61828 S.D. Fla.); Neupogen®/Grastofil®, Neulasta®/Lapelga
- *Genentech v. Samsung Bioepis* (No. 18-cv-01363 D. Del.); Herceptin®/Ontruzant®


In addition, the first biosimilar versus biosimilar case, *Coherus v. Amgen*, was filed and dismissed in 2019.

We discuss each of these resolved cases briefly below.

Sandoz v. Amgen (19-cv-00977 N.D. Cal.)

This case, filed in 2019, was a follow-on to Sandoz and Amgen's years-long dispute over Sandoz's biosimilar versions of Amgen's Neupogen® (filgrastim) and Neulasta® (pegfilgrastim). Sandoz's biosimilar filgrastim product, Zarxio®, has been on the market since 2015, while its biosimilar pegfilgrastim product, Ziextenzo™, was neither approved nor launched at the time this lawsuit was filed (but was subsequently approved by FDA in November 2019 and launched shortly thereafter).

In previous cases, which were on appeal at the time that Sandoz filed this suit, Amgen had accused Sandoz of infringing a purification patent, U.S. Patent No. 8,940,878. During that previous litigation, a continuation of the '878 patent issued, U.S. Patent No. 9,643,997 (issued May 9, 2017). Sandoz claimed that the '997 patent and the previously litigated '878 patent "are in the same patent family and are similar or identical in several key respects." (Dkt. 1.) Sandoz also claimed that it "invited Amgen to include the '997 patent as part of those cases



and resolve all proceeding in the prior action,” but “Amgen did not amend to add those claims in the then-pending litigation.” (*Id.*) In December 2017, the Northern District of California granted summary judgment of non-infringement with respect to the '878 patent. While that ruling was on appeal, in February of 2019, Sandoz provided Amgen notice of commercial marketing for Sandoz’s pegfilgrastim biosimilar and filed this declaratory judgment action with respect to the '997 patent. Sandoz sought to “ensure that any issues with respect to the '997 patent, including any preliminary injunction motion, are resolved promptly, efficiently, and well in advance of the launch of Sandoz’s pegfilgrastim product.” (*Id.*)

On April 24, 2019, Amgen moved to dismiss for failure to state a claim, arguing that § 262(l)(9) of the BPCIA barred Sandoz from bringing this type of declaratory judgment action. (Dkt. 22.) Amgen argued for dismissal for two reasons: (1) Sandoz was barred from bringing a declaratory judgment action under § 262(l)(9)(B) because it failed to provide a (3)(B) statement for its pegfilgrastim product after Amgen identified the newly issued '997 patent; and (2) Sandoz was barred from bringing a declaratory judgment under § 262(l)(9)(C) because it opted not to dance and did not provide information under (2)(A) for its filgrastim product. (*Id.*)

On May 13, 2019, before Sandoz responded to Amgen’s motion, Sandoz voluntarily dismissed the case soon after the Federal Circuit issued its opinion in the appeal from the related cases (Case Nos. 14-cv-04741 and 16-cv-02581), where the Federal Circuit affirmed the grant of summary judgment of non-infringement of the '878 patent. See *Amgen Inc. v. Sandoz Inc.*, 923 F.3d 1023, 1025 (Fed. Cir.), *reh’g granted, opinion modified*, 776 F. App’x 707 (Fed. Cir. 2019).

Note that Amgen has also asserted the '997 patent against Adello Biologics, Hospira, and Mylan in its other lawsuits involving filgrastim and pegfilgrastim.

Genentech v. Pfizer (19-cv-00638 D. Del.)

This case, filed in 2019, involved Genentech’s reference biologic product Avastin® (bevacizumab) and Pfizer’s biosimilar version, Zirabev™. Pfizer provided notice of commercial marketing for Zirabev™ on January 18, 2019, and a few months later, on April 5, 2019, Genentech asserted twenty-two patents in its complaint. Pfizer answered Genentech’s complaint on April 29, 2019, asserting affirmative defenses and counterclaims for declaratory judgment of non-infringement and invalidity of the asserted patents. (Dkt. 14.)

Genentech moved to dismiss Pfizer’s counterclaims and some of its affirmative defenses, arguing that (1) the declaratory judgment counterclaims were actions barred by the BPCIA because Pfizer had failed to fully comply with the BPCIA’s information disclosure requirements; (2) Pfizer’s validity challenges were “facially deficient” because they alleged grounds broader than those disclosed during the patent dance, and (3) Pfizer’s counterclaim that “Genentech committed inequitable conduct during prosecution of one of the patents-in-suit by allegedly misrepresenting the content of the prior art” was also facially deficient. (Dkt. 21 at 2-3.) Pfizer opposed dismissal, contending that even if it had not fully complied with the information disclosure requirements in subsection (2)(A) of the BPCIA, “[t]he remedy of precluding counterclaims in defense of the action brought by Plaintiffs is inconsistent with the language and the purpose behind the BPCIA.” (Dkt. 22 at 2-3.) Pfizer also argued that the BPCIA did not “limit Pfizer to only the legal theories in its detailed statements pursuant to [its (3)



(B) Statement]).” (*Id.* at 3.)

The court did not have the opportunity to address these issues, as the parties jointly stipulated to dismissal in September 2019 as a result of settlement. (Dkt. 36.)

Amgen v. Tanvex (19-cv-01374 S.D. Cal.)

This case, filed in 2019, involved TX-01, Tanvex’s biosimilar version of Amgen’s reference product Neupogen® (filgrastim). After engaging in the patent dance, Amgen alleged infringement of just one patent, U.S. Patent No. 9,856,287, directed to methods of refolding proteins. Tanvex admitted to providing Amgen with notice of commercial marketing on April 1, 2019 (Dkt. 27 at 12), but TX-01 has not yet been approved by FDA and Tanvex announced that FDA recently issued a Complete Response Letter regarding TX-01. Two other biosimilars of Neupogen®, Pfizer’s Nivestym™ and Sandoz’s Zarxio®, have also already been FDA approved and launched in the U.S.

The parties jointly stipulated to dismissal on December 19, 2019. (Dkt. 43.)

Note that the ’287 patent has been the subject of several disputes, including two other unrelated district court litigations involving Apotex and Kashiv and several PGR and IPR challenges at the PTAB.

AbbVie v. Boehringer Ingelheim (No. 17-cv-01065 D. Del.)


This case concerned Boehringer Ingelheim’s product Cyltezo®, a biosimilar of AbbVie’s Humira® (adalimumab). This was the last pending BPCIA litigation related to Humira®. The case settled in May 2019, after a claim construction hearing, but before the court issued its claim construction order.

Amgen v. Mylan (17-cv-01235 W.D. Pa.)

This case, which settled on September 17, 2019, involved Fulphila™, Mylan’s biosimilar of Amgen’s Neulasta® (pegfilgrastim). Amgen dismissed its infringement claims for the two patents-in-suit following the Federal Circuit’s rulings in other litigation related to those patents, *Amgen v. Coherus*, 923 F.3d 1023 (Fed. Cir. 2019) and *Amgen v. Sandoz*, 923 F.3d 1023 (Fed. Cir. 2019), discussed below. This resolved a contentious litigation, in which the court lamented that “counsel have successfully convinced the Court of their mutual capacity to litigate in this Court wi[th] unnecessary finger pointing and complexity, and at times, passing compliance with the letter of this Court Orders, and their willingness to use email rather than direct human communication to accomplish that.” (Dkt. 278.)

Amgen v. Kashiv (18-cv-03347 D.N.J.)

Amgen filed this suit after Adello (now Kashiv BioSciences) submitted a BLA for a biosimilar of Amgen’s Neupogen® (filgrastim) without engaging in the patent dance. In its amended complaint, Amgen alleged that Adello and Amneal entered into a license and commercialization agreement in which Amneal would market and sell Adello’s filgrastim biosimilar and Adello would develop, obtain regulatory approval, and manufacture the biosimilar product. (Dkt. 84 at 7.) In February 2019, Amneal filed a motion to dismiss on two separate



grounds. First, Amneal contended that Amgen’s amended complaint failed to state a claim upon which relief could be granted because only Adello, the BLA applicant, could commit the artificial act of infringement under the BPCIA. (Dkt. 85-1.) Second, Amneal argued that there is no declaratory judgment jurisdiction because Amgen’s allegations of future marketing and sales—if and when FDA approves the biosimilar—do not give rise to a justiciable controversy. (*Id.*) Alternatively, Amneal requested that the court decline to exercise declaratory judgment jurisdiction so as not to “upend the carefully crafted BPCIA statutory scheme.” (*Id.* at 3.) Although Amneal’s motion was fully briefed, the court did not issue a publicly available order on this matter and Amneal continued as a defendant until the case was resolved.

The parties stipulated to dismissal on November 25, 2019. (Dkt. 161.)

Amgen v. Apotex (18-cv-61828 S.D. Fla.)

This case involved Apotex’s biosimilars to Amgen’s Neupogen® (filgrastim) and Neulasta® (pegfilgrastim). The parties had previously litigated two cases related to these biosimilars, Case Nos. 15-cv-61631 and 15-cv-62081. Here, Amgen asserted a new patent, U.S. Patent No. 9,856,287, which issued after the Federal Circuit affirmed non-infringement of the patent in the prior cases.

Apotex moved to dismiss the complaint, alleging non-infringement on grounds of prosecution history estoppel and collateral estoppel. (Dkt. 9.) On April 5, 2019, the court denied the motion. (Dkt. 65.) As to collateral estoppel, the court distinguished between the ’287 patent and U.S. Patent No. 8,952,138, the great-grandparent patent of the ’287 patent that was asserted in previous disputes. In particular, the court found that there may be differences in claim construction that would make the issues in this case not “identical” to those in the prior case. (*Id.* at 8-11.) On prosecution history estoppel, the court declined to rule at the motion to dismiss stage that “the prosecution statements cited by Apotex ... evince[d] a clear and unmistakable surrender of subject matter as the law requires.” (*Id.* at 13.)

On November 15, 2019, the court entered the parties’ stipulation to the dismissal of this action. (Dkt. 120.)


Genentech v. Samsung Bioepis (18-cv-01363 D. Del.)

This case concerned Genentech’s Herceptin® (trastuzumab) and Samsung Bioepis’ biosimilar Ontruzant®, which FDA approved in January 2019. In a joint stipulation of dismissal, the parties informed the court that they entered into a settlement agreement and had agreed to dismiss all claims and counterclaims. The case was dismissed on July 1, 2019. (Dkt. 160.)

Other District Court Litigation – Coherus v. Amgen (19-cv-00139 D. Del.)

In another newly filed (and recently dismissed) biosimilar-related district court case, Coherus sued Amgen in the District of Delaware in the first biosimilar versus biosimilar litigation. This suit concerned two biosimilar versions of AbbVie’s Humira® (adalimumab) reference product—Coherus’ CHS-1420 and Amgen’s Amjevita™.

In its amended complaint, Coherus alleged infringement of four formulation patents based on Amgen’s “actively offering for sale and selling Amjevita™ throughout Europe” and “actively manufacturing Amjevita™ in the United



States for sale in Europe.” (Dkt. 7 at 4-5.) Amgen had launched Amjevita™ in Europe in October of 2018, while CHS-1420 awaits FDA approval. Both Coherus and Amgen have settled with AbbVie with launch dates no earlier than 2023.

The parties stipulated and agreed to dismissal of this case on November 25, 2019. (Dkt. 52.)

On December 9, 2019, Amgen filed a motion to declare this case exceptional under § 285 and award Amgen attorneys’ fees. (Dkt. 55.) The redacted accompanying memorandum alleges that the motion is based on “Coherus’ wrongful, continued maintenance of this action between June 5, 2019—by which time Coherus knew or reasonably should have known that its infringement claims were baseless—and October 17, 2019, when Coherus first informed Amgen that Coherus intended to dismiss its claims.” (Dkt. 59 at 1.)

C. BPCIA Appeals Pending at the Federal Circuit

The following appeals, discussed below, are currently pending at the Federal Circuit:

- *Genentech v. Immunex* (CAFC 19-2155); Avastin®/Mvasi™
- *Genentech v. Amgen* (CAFC 19-2156); Herceptin®/Kanjinti™
- *Janssen v. Celltrion* (CAFC 18-2321; 18-2350); Remicade®/Inflectra®
- *Immunex v. Sandoz* (CAFC 20-1037); Enbrel®/Erelzi®

***Genentech v. Immunex* (CAFC 19-2155)**


This is the appeal from Case No. 19-cv-00602 (D. Del.), discussed above, which involves Genentech’s Avastin® (bevacizumab) and Amgen’s biosimilar Mvasi™. The district court denied Genentech’s emergency motions to prevent the launch of Mvasi™. The court did not agree that Amgen needed to provide new notice of commercial marketing after filing new supplemental BLAs.

On appeal, Genentech initially sought an emergency motion for an injunction pending appeal (shortly after the district court denied a similar motion) to prevent Amgen from “flood[ing] the market with its biosimilar immediately.” (Genentech Emergency Motion at 4.) The Federal Circuit denied the motion, stating that “[w]ithout prejudicing the ultimate disposition of this case, we conclude Genentech has not established that an injunction pending appeal is warranted....” (Order dated August 16, 2019.)

Briefing on the merits is complete. Oral argument has not yet been scheduled.

***Genentech v. Amgen* (CAFC 19-2156)**

This is the appeal from Case No. 18-cv-00924 (D. Del.), discussed above, involving Amgen’s biosimilar, ABP 980/Kanjinti™, referencing Genentech’s Herceptin® (trastuzumab). The district court denied Genentech’s emergency motions to prevent the launch of Kanjinti™, finding that Genentech waited too long to file its motion and would not suffer irreparable harm due to its previous licensing activities.



On appeal, Genentech filed a motion for an injunction pending appeal and a request to expedite proceedings. The Federal Circuit denied both, holding that “[w]ithout prejudicing the ultimate disposition of this case, we conclude that Genentech has not established that an injunction pending appeal is warranted . . .” and “while Genentech has and can continue to self-expedite its own filings, it has not shown that Amgen’s time should be shortened.” (Order dated August 7, 2019.)

On the merits of its interlocutory appeal, Genentech has asked the Federal Circuit to find that the district court erred in two ways: both in “inferring that Genentech will not suffer irreparable harm because it waited to seek preliminary injunctive relief until Amgen affirmatively decided to launch” and in “adopting a categorical rule that licensing of *future* activity negates irreparable harm from *present* infringement.” (Genentech Opening Br. at 25-31, 35-38.) Genentech further argued that the other factors for a preliminary injunction “overwhelmingly” favor Genentech, including because the merits of Amgen’s validity defense “merely recycled art and arguments already rejected by the PTAB under a lower standard of proof.” (*Id.* at 52.)

Briefing is complete. Oral argument has not yet been scheduled.

***Janssen v. Celltrion* (CAFC 18-2321, 18-2350)**

This is an appeal from Case No. 17-cv-11008 (D. Mass.) relating to Celltrion’s infliximab biosimilar Inflectra®, referencing Janssen’s Remicade®. Only one patent is at issue, U.S. Patent No. 7,598,083, which covers a cell culture medium used to grow antibody-producing cells.

Janssen argued patent infringement under the doctrine of equivalents, since it was undisputed that Celltrion’s media was outside the claimed concentrations of several of the claimed ingredients. In July 2018, Judge Wolf of the District of Massachusetts granted Celltrion’s motion for summary judgment of non-infringement. The court held that the range of equivalents necessary to cover the accused product would impermissibly ensnare the prior art.

In August 2018, Janssen appealed the non-infringement ruling to the Federal Circuit (CAFC 18-2321). Janssen filed its opening brief on December 10, 2018, arguing the district court erred by (1) impermissibly using hindsight to find that a hypothetical claim covering Celltrion’s cell culture medium would have been obvious; (2) failing to find Celltrion’s arguments regarding ensnarement legally baseless where Celltrion failed to offer any motivation to choose and modify the prior art references; and (3) failing to draw reasonable inferences in Janssen’s favor (e.g., teaching away and evidence of copying) in its summary judgment analysis. (Janssen Opening Br.)

Celltrion cross-appealed on an unrelated issue: lack of standing (CAFC-2350). Celltrion argued that Janssen lacked standing because all co-owners of ’083 patent had not been properly joined as plaintiffs. (Celltrion Opening and Response Br. at 57-73.) Specifically, the patent rights were assigned to “the COMPANY,” a term that, according to Celltrion, was unambiguous and included more companies than just Janssen. (*Id.* at 29-30.) Thus, according to defendants, the case should have been dismissed. (*Id.* at 30.) Janssen disagreed, stating that “[t]he [assignment] agreements are ambiguous, but their most sensible reading is that they assign the ’083 patent to only one entity: Centocor, Inc., Janssen’s predecessor,” and that “Janssen, as Centocor’s successor, has standing to bring this action.” (Janssen Response and Reply Br. at 35.)

Briefing is complete. Oral argument has been scheduled for March 4, 2020.

Note that *Janssen v. HyClone Labs* (16-cv-00071 D. Utah), which involves the same patent and factual scenario, has been administratively closed pending resolution of this appeal, with no other important updates in 2019.

***Immunex v. Sandoz* (CAFC 20-1037)**

This dispute centers on Erelzi[®], Sandoz's biosimilar of Immunex's Enbrel[®] (etanercept). On August 9, 2019, Judge Cecchi of the District of New Jersey held U.S. Patent No. 8,063,182, directed to etanercept, the active ingredient in Enbrel[®], and U.S. Patent No. 8,163,522, directed to Enbrel[®]'s manufacturing process, not invalid. *Immunex Corp. v. Sandoz Inc.*, 395 F. Supp. 3d 366 (D.N.J. 2019). Sandoz appealed.

The appeal, as framed by appellant Sandoz, concerns three main issues: (1) whether the patents-in-suit are invalid for obviousness-type double patenting; (2) whether the asserted claims are invalid for lack of written description; and (3) whether the district court erred in its ruling on obviousness. (Sandoz Opening Br. at 4.)

The parties' briefing is complete. Oral argument has been scheduled for March 4, 2020.

D. BPCIA Federal Circuit Appeals Decided in 2019

In 2019, the Federal Circuit issued decisions in *Amgen v. Coherus*, *Amgen v. Sandoz*, and *Amgen v. Hospira*, in addition to ruling on Genentech's motions for an injunction pending appeal in its cases against Immunex/Amgen (discussed above). We discuss the *Coherus*, *Sandoz*, and *Hospira* decisions below.

***Amgen v. Coherus*, 931 F.3d 1154 (Fed. Cir. 2019) (CAFC 18-1993)**

This decision concerns CHS-170, Coherus' biosimilar of Amgen's Neulasta[®] (pegfilgrastim) and follows from the district court's order dismissing Amgen's complaint for failure to state a claim. *Amgen v. Coherus*, No. 17-cv-546, 2018 WL 1517689 (D. Del. Mar. 26, 2018). In the district court, Amgen alleged infringement of its protein purification patent, U.S. Patent No. 8,273,707, under the doctrine of equivalents based on Coherus' BLA. The district court found that Coherus' biosimilar could not infringe in light of Amgen's "clear and unmistakable surrender" of claim scope during prosecution. *Id.* at *2. As a separate ground for dismissal, the court further found that by disclosing but not claiming other salt combinations, Amgen had dedicated them to the public under the dedication-disclosure doctrine. *Id.* at *3.

On appeal, the Federal Circuit affirmed, explaining that "prosecution history estoppel bars Amgen from succeeding on its claim of infringement under the doctrine of equivalents." *Amgen v. Coherus*, 931 F.3d 1154, 1156 (Fed. Cir. 2019). According to the Court, Amgen had "clearly and unmistakably surrendered unclaimed salt combinations during prosecution" when it successfully distinguished a prior art reference raised by the Examiner by arguing that the reference did not disclose or suggest the "*particular* combinations" of salts recited in the claims. *Id.* at 1160. Amgen was therefore estopped from asserting that other salt combinations infringed its patent, including Coherus' salt combinations. The Federal Circuit did not reach the other independent basis for dismissal under the disclosure-dedication doctrine. *Id.* at 1161.



***Amgen v. Sandoz*, 923 F.3d 1023 (Fed. Cir. 2019) (CAFC 18-1551, 18-1552)**

This appeal involved Sandoz’s biosimilars of Amgen’s Neupogen® (filgrastim) and Neulasta® (pegfilgrastim). In 2017, the Northern District of California granted summary judgment of non-infringement as to U.S. Patent No. 8,940,878, which was directed to methods of protein purification. *Amgen Inc. v. Sandoz Inc.*, 295 F. Supp. 3d 1062 (N.D. Cal. 2017).

On May 8, 2019, the Federal Circuit affirmed the lower court’s ruling. *Amgen Inc. v. Sandoz Inc.*, 923 F.3d 1023 (Fed. Cir. 2019). The district court had construed claim 7 of the ’878 patent to cover a purification method that required *separate* steps of washing and eluting, with the eluting step occurring after the washing step. *Id.* at 1027. Sandoz’s purification process undisputedly involved only a *single* step, with no separate washing or eluting steps, which defeated Amgen’s literal infringement theory. *Id.* at 1029.


Turning to Amgen’s doctrine of equivalents argument, the Federal Circuit concluded that the district court correctly held that Sandoz’s one-step, one-solution process did not function in the same way as the claimed process, further stating that “[t]he doctrine of equivalents applies only in exceptional cases and is not ‘simply the second prong of every infringement charge, regularly available to extend protection beyond the scope of the claims.’” *Id.* at 1029.

Amgen also asserted that the district court improperly denied its Rule 56(d) motion for a continuance in light of Sandoz’s upcoming manufacturing changes. *Id.* But the Federal Circuit disagreed, in part because the proposed pegfilgrastim biosimilar would likely follow the same one-step washing and eluting process, and would therefore not infringe under the affirmed claim construction. However, the Federal Circuit clarified that Amgen would not be without a remedy for possible future infringement should Sandoz change its process: Amgen “may in a future action plead infringement of claim 7 by Zarxio® or, if approved, Sandoz’s pegfilgrastim biosimilar to the extent permitted by the Patent Act and the principles of *res judicata* and collateral estoppel.” *Id.* at 1031.

Amgen petitioned for rehearing *en banc* on June 7, 2019, to argue that a part of the Court’s holding—that the doctrine of equivalents only applies in “exceptional” cases—was contrary to Supreme Court and Federal Circuit precedent, and that under correct standard, the district court’s grant of summary judgment should be reversed. Amgen highlighted the fact that the panel did not define “exceptional.” But on September 3, 2019, the Federal Circuit granted Amgen’s petition for rehearing *en banc* only to remove the statement that the doctrine of equivalents only applies in exceptional cases. *Amgen Inc. v. Sandoz Inc.*, 776 F. App’x 707 (Fed. Cir. 2019). Amgen’s petition was otherwise denied. *Id.*

***Amgen v. Hospira*, 944 F.3d 1327, 2019 WL 6834390 (CAFC 19-1067, 19-1102)**

In September 2017, a jury in the District of Delaware awarded Amgen \$70 million in reasonable royalty damages based on Hospira’s infringement of U.S. Patent No. 5,856,298 in relation to a biosimilar of Amgen’s Epogen® (epoetin alfa). Although Hospira’s biosimilar had not launched before patent expiration, the jury found that certain of Hospira’s biosimilar batches were not “solely for uses reasonably related” to obtaining biosimilar approval and thus did not qualify for safe harbor protection under 35 U.S.C. § 271(e)(1). The jury also found that Hospira did not infringe U.S. Patent No. 5,756,349. In ruling on post-trial motions, Judge Andrews upheld the jury verdict. The court clarified that evidence of intent can be a relevant factor in determining whether an activity is reasonably related to obtaining



FDA approval and therefore subject to the safe harbor. Judge Andrews also upheld the jury's damages award and additionally awarded Amgen prejudgment interest of about \$10 million and post-judgment interest. This case is the first BPCIA case in which damages were awarded.

Hospira appealed the district court's judgment of infringement and validity of the '298 patent and the court's award of approximately \$80 million. Amgen cross-appealed the non-infringement finding for the '349 patent.

On December 16, 2019, the Federal Circuit affirmed the district court's judgment on each issue. *Amgen Inc. v. Hospira, Inc.*, 944 F.3d 1327, 2019 WL 6834390, at *1 (Fed. Cir. 2019). In particular, as to the safe harbor defense, the Federal Circuit held that the jury instructions were not legally erroneous and that substantial evidence supported the jury's finding that certain batches were not protected. *Id.* at *7-8. The jury instructions stated that "[i]f Hospira has proved that the manufacture of a particular batch was reasonably related to developing and submitting information to FDA in order to obtain FDA approval, Hospira's additional underlying purposes for the manufacture and use of that batch do not remove that batch from the Safe Harbor defense." *Id.* at *6. Hospira claimed this was erroneous for focusing on "why each batch ... was manufactured, not how each batch was used or whether that use was reasonably related to the development and submission of information to support Hospira's BLA." *Id.* The Federal Circuit disagreed because "the patented inventions are Amgen's claimed methods of manufacture" and the "accused activity is Hospira's use of Amgen's claimed methods of manufacture," so "[t]he relevant inquiry, therefore, is not how Hospira used each batch it manufactured, but whether each act of manufacture was for uses reasonable related to submitting information to FDA." *Id.* at *7 (emphasis in original).

Further, although Hospira argued that each of its accused 21 batches "were used for the development and submission of information" to FDA, the Federal Circuit found that substantial evidence supported the jury's finding that 14 of those batches were not protected by the safe harbor. *Id.* at *8. For example, evidence was submitted that Hospira was not required by FDA to manufacture additional batches after 2012. *Id.* Relevant, but not dispositive, was evidence that Hospira planned for some of the batches to "serve as commercial inventory," even though Hospira later changed the designation of some of its batches after it received a Complete Response Letter from FDA. *Id.* at *9.

V. Litigation Related to Anticompetitive Conduct

Although 26 biosimilars have been approved by FDA, they have not all entered the U.S. market and many of those that have launched have failed to gain significant market share. Several factors may account for this, but some parties have alleged that the root cause is anticompetitive behavior on the part of reference product sponsors, as exemplified below.

Humira® (adalimumab)

AbbVie’s Humira® (adalimumab) is a top-selling therapeutic and, despite five approved Humira® biosimilars, none are available yet in the U.S. To date, AbbVie has entered into nine settlement agreements with various manufacturers of Humira® biosimilars all sharing a common feature: delaying the Humira® biosimilar launch in the U.S. until 2023.

Table 4. Humira® Biosimilar Settlements

Manufacturer	Date of Settlement	Date of US Entry	Date of EU Entry
Amgen (Amjevita™)	September 2017	01/31/2023	10/16/2018
Samsung Bioepis (Imraldi™)	April 2018	06/30/2023	10/16/2018
Mylan (Hulio™)	July 2018	07/31/2023	N/A
Sandoz (Hyrimoz™)	October 2018	09/30/2023	10/16/2018
Fresenius Kabi (MSB11022)	October 2018	09/30/2023	Date of approval from EMA
Momenta (M923)	November 2018	11/20/2023	Date of approval from EMA
Pfizer (Abrilada™)	November 2018	11/20/2023	Date of approval from EMA
Coherus (CHS-1420)	January 2019	12/15/2023	N/A
Boehringer Ingelheim (Cyltezo®)	May 2019	07/01/2023	N/A

Over the past year, AbbVie has been the target of several class action lawsuits. The first of these suits was filed on March 18, 2019 by UFCW Local 1500 Welfare Fund, a New York-based grocery union, in the Northern District of Illinois against AbbVie and a number of adalimumab biosimilar manufacturers. The complaint alleged that AbbVie violated state and federal antitrust laws by creating an exclusionary “patent thicket” consisting of over 100 patents “designed solely to insulate Humira from any biosimilar competition in the U.S.,” even though the “primary patent” on Humira® expired in 2016. The complaint also accused AbbVie of entering into “illegal market division agreements” with biosimilar manufacturers “in a concerted effort to delay biosimilar entry in the U.S. until at least 2023,” while permitting earlier entry of biosimilars in the European market.

Several other suits against AbbVie containing similar allegations followed, and Judge Manish Shah consolidated the proposed class actions. (*In re: Humira (Adalimumab) Antitrust Litig.*, 19-cv-01873 (N.D. Ill.)) On October 15, 2019,

AbbVie moved to dismiss the consolidated class action complaint. The court has not yet ruled on this motion.

Remicade® (infliximab)

Another series of antitrust litigations involves Johnson & Johnson (J&J) and its subsidiary Janssen related to its Remicade® (infliximab) biologic. In 2017 and 2018, Pfizer (whose infliximab biosimilar is marketed as Inflectra®), retailers Walgreens and Kroger Co., and direct and indirect purchasers of Remicade® filed antitrust suits against J&J and Janssen in the Eastern District of Pennsylvania. The cases involve allegations that J&J and Janssen maintained their market share and pricing for Remicade® through exclusionary contracts, anticompetitive bundling, and coercive rebate schemes.

The various cases are progressing separately. Pfizer's case (17-cv-4180, E.D. Pa.) and the indirect purchasers' case (17-cv-04326, E.D. Pa.) are in fact discovery, and the court has recently addressed several discovery disputes. Walgreens and Kroger's case was dismissed by the district court in March 2019 for lack of standing to assert federal antitrust claims based on the plaintiffs' assignment agreements; Walgreens and Kroger appealed to the Third Circuit and oral argument was held in November 2019. (3d Cir. 19-1730.) The direct purchasers' case (2-18-cv-00303, E.D. Pa.) will now be referred to arbitration. On September 13, 2019, the Third Circuit overturned the district court's denial of J&J's motion to compel arbitration, holding instead that the direct purchasers' antitrust claims must be arbitrated pursuant to the terms of a 2015 distribution contract. *In re Remicade (Direct Purchaser) Antitrust Litig.*, 938 F.3d 515 (3d Cir. 2019).

Additionally, in July of this year, Janssen's 10-Q filing with the Securities and Exchange Commission revealed that "[i]n June 2019, the United States Federal Trade Commission ('FTC') issued a Civil Investigative Demand to Johnson & Johnson in connection with its investigation of whether Janssen's REMICADE® contracting practices violate federal antitrust laws."

Other Allegations of Anticompetitive Behavior

Allegations of anticompetitive behavior have also emerged in other biosimilar-related litigations in 2019.

For example, as discussed above, in *Amgen v. Coherus*, No. 17-cv-00546 (D. Del.), Coherus has requested attorneys' fees following its successful motion to dismiss Amgen's suit, claiming that Amgen brought and maintained a "meritless and anticompetitive suit." (See, e.g., *id.* at Dkt. 97.) Coherus has claimed that Amgen engaged in a "fundamentally anticompetitive litigation strategy" to "cripp[er] a nascent competitor like Coherus." (*Id.*)

Chugai has alleged a different type of anticompetitive behavior—product hopping—in *Chugai Pharm. Co. v. Alexion Pharms., Inc.*, No. 19-cv-02120 (D. Del.). In its complaint, Chugai alleged that Alexion's Ultomiris® (ravulizumab) infringes on Chugai's patent relating to methods of extending the half-lives of antibodies in blood plasma.

Although most allegations in the complaint relate to claims of patent infringement, Chugai also hinted at potentially anticompetitive product hopping by Alexion, including Alexion's warnings to investors about biosimilar competition and its "principal business objective[]" to "facilitate the conversion" of patients from Soliris® (eculizumab) to Ultomiris® prior to the expiration of patents covering eculizumab in 2021. (*Id.* at Dkt. 1.)

VI. Post-Grant Challenges at the PTAB

The number of IPR petitions against patents covering biologic drugs in 2019 was comparable to 2018. In contrast to the record-high year in 2017 with over 80 biologics-related IPRs filed, in 2019, only 14 biologics-related IPRs concerning 12 patents were filed:

- Three petitions were filed by Amgen concerning method of treatment claims covering Alexion Pharmaceuticals' Soliris® (eculizumab). On August 30, 2019, the PTAB instituted IPR on all three of Amgen's petitions.
- Also in August, two petitions were filed by UCB concerning composition and method of treatment claims covering Novimmune's Cosentyx® (secukinumab). No institution decision has yet been reached.
- Three petitions were filed against Amgen over patents relating to methods of protein purification, two by Kashiv Biosciences and one by Fresenius Kabi. The PTAB instituted IPR of Kashiv's petitions in September 2019, but both matters were terminated due to settlement. In December 2019, the PTAB instituted IPR as to Fresenius's petition.
- Adello and Apotex used post-grant review (PGR) to challenge another of Amgen's patents related to methods for folding proteins. Fresenius then challenged that same patent through an IPR petition. The PTAB instituted Adello's PGR and denied Fresenius's IPR using its discretion under 314(a). After institution, Adello and Amgen settled, and the PGR was dismissed. Fresenius has recently filed a new IPR petition challenging that patent on similar grounds.
- Finally, four petitions were filed by Regeneron Pharmaceuticals in 2019 against Kymab concerning patents that relate to transgenic mice engineered to produce antibodies. The PTAB has not yet issued an institution decision as to Regeneron's petitions.

In addition to IPR filings, there were a number of IPR appeals progressing in 2019 involving biologic products, some of which are noted below.

Avastin® (bevacizumab)

The Federal Circuit in *Celgene Corp. v. Peter*, 931 F.3d 1342 (Fed. Cir. 2019), affirmed the PTAB's final written decision invalidating claims of Celgene's patents (directed to methods for safely distributing teratogenic agents to patients while avoiding exposure to a fetus) and held that the use of IPR proceedings for patents issued prior to the enactment of the America Invents Act (AIA) was not an unconstitutional taking under the Fifth Amendment. This decision has already had ripple effects in the biosimilars space. For example, only a day after *Celgene*, a three-judge panel in

Genentech, Inc. v. Hospira, Inc., 774 Fed. Appx. 677 (Fed. Cir. July 31, 2019), affirmed without opinion a PTAB decision invalidating a patent relating to Avastin® (IPR2016-01771), implicitly rejecting Genentech's Fifth Amendment challenge to the use of IPR proceedings for pre-AIA patents.

Humira® (adalimumab)

In 2017, the PTAB issued five final written decisions in IPR2016-00172, -188, -189, -408, and -409, finding claims of AbbVie's U.S. Patent Nos. 8,889,135; 9,017,680; and 9,073,987—generally directed to methods of treating rheumatoid arthritis with adalimumab—unpatentable as obvious in view of the prior art. AbbVie appealed all five decisions, and the Federal Circuit consolidated the cases (CAFC No. 17-2304).

Coherus and Boehringer Ingelheim originally filed the IPRs, but after settling with AbbVie, withdrew from the appeals. The PTO intervened to defend the PTAB's final written decisions in the IPRs. The United States also intervened to respond to AbbVie's constitutional arguments regarding the applicability of IPRs to pre-AIA patents. On January 7, 2020, the Federal Circuit issued a Rule 36 affirmance of the PTAB's decisions, with no discussion of AbbVie's constitutionality arguments.

Rituxan® (rituximab)

Pfizer, in IPR2017-01168, successfully challenged all claims of Biogen's U.S. Patent No. 8,821,873, which generally relates to methods of treating lymphoma with an anti-CD20 antibody (e.g., rituximab). Biogen appealed the PTAB's final written decision of unpatentability (CAFC No. 19-1364). Pfizer declined to participate in the appeal, and the PTO intervened in April 2019 to defend the PTAB's ruling. The Federal Circuit heard oral argument on December 6, 2019.

Neulasta® (pegfilgrastim) / Neupogen® (filgrastim)

In Apotex's IPR challenge to Amgen's U.S. Patent No. 8,952,138, directed to processes for refolding proteins, IPR2016-01542, the PTAB found in favor of Apotex, invalidating 23 of 24 claims of the Amgen's patent in a final written decision in 2018. Following a panel change, the PTAB then *sua sponte* modified its final written decision in May 2019 to invalidate the final claim. Amgen appealed the PTAB's ruling in July 2019 (CAFC No. 19-2171). The PTO intervened to step in for Apotex, which declined to participate in the appeal.

Amgen filed its opening brief on November 4, 2019. In addition to asserting that the PTAB erred in its claim construction and validity determinations, Amgen sought to overturn the PTAB's ruling based on the Federal Circuit's recent decision in *Arthrex, Inc. v. Smith & Nephew, Inc.* (Fed. Cir. Oct. 31, 2019), asking the Federal Circuit to decide whether the "Administrative Patent Judges who served on the Board in this case [were] principal officers of the United States appointed in violation of the Appointments Clause." Amgen filed its reply brief on January 21, 2020.

VII. Conclusion

2019 set a record for the greatest number of BLAs approved and the greatest number of biosimilar products entering the U.S. market. FDA also issued new guidance under its July 2018 Biosimilars Action Plan, taking steps towards growing the biosimilars market in the United States. While FDA was active in approving biosimilars this year, there was a significant drop in the number of new BPCIA district court cases filed in 2019, with only five filed in 2019 as compared to the twelve and thirteen in 2018 and 2017, respectively.

Participants in the U.S. biosimilars market have several things to look forward to in 2020. FDA is expected to continue rolling out further guidance and taking more measures to encourage continued growth of the U.S. biosimilars market. Also, FDA will likely take steps to stop the makers of biologic reference products from filing citizen petitions as a tactic to delay biosimilar market entry, consistent with the final guidance issued late in 2019. In addition, participants in the field are preparing for the March 23, 2020 transition date, when insulin and other biologics previously approved under section 505 of the Federal FD&C Act as drug products will be deemed to be licensed biologics under the PHS Act.

Resolution regarding a number of BPCIA disputes, including several Federal Circuit appeals, and trials in *Genentech v. Amgen* (17-cv-01471), *Genentech v. Amgen* (18-cv-00924), and *Amgen v. Hospira* (18-cv-01064) are also expected in 2020.

Authors



Jenny Shmuel, Ph.D., is a Principal that has helped build Fish's biologics and biosimilar litigation practice. She also represents pharmaceutical clients in competitor litigation and Hatch-Waxman litigation. Dr. Shmuel has extensive experience in all phases of litigation, and, over the last several years, has helped successfully defend a large pharmaceutical franchise and secure a significant damages award for a medical device manufacturer.

Reach Jenny at
shmuel@fr.com.



Tasha Francis, Ph.D., was previously an Associate at Fish & Richardson.



Philip Chen is an Associate in Fish & Richardson's Boston office where he works on various patent litigation matters including pharmaceutical and biosimilar litigation.

Reach Philip at
pchen@fr.com.



Felix Eyzaguirre is an Associate in Fish & Richardson's Silicon Valley office. His practice focuses on patent litigation, including Hatch-Waxman litigation.

Reach Felix at
eyzaguirre@fr.com.



fr.com

Atlanta Austin Boston Dallas Delaware Houston Munich New York Shenzhen Silicon Valley Southern California Twin Cities Washington, DC

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