Life Sciences
Webinar Series

Biosimilars: 2020 Mid-Year Update

July 23, 2020

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Today's Topics

- Market Update
- Regulatory Update
- Litigation Update
- IPR Update
- Other Recent Events to Watch

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U.S. Biosimilar Market

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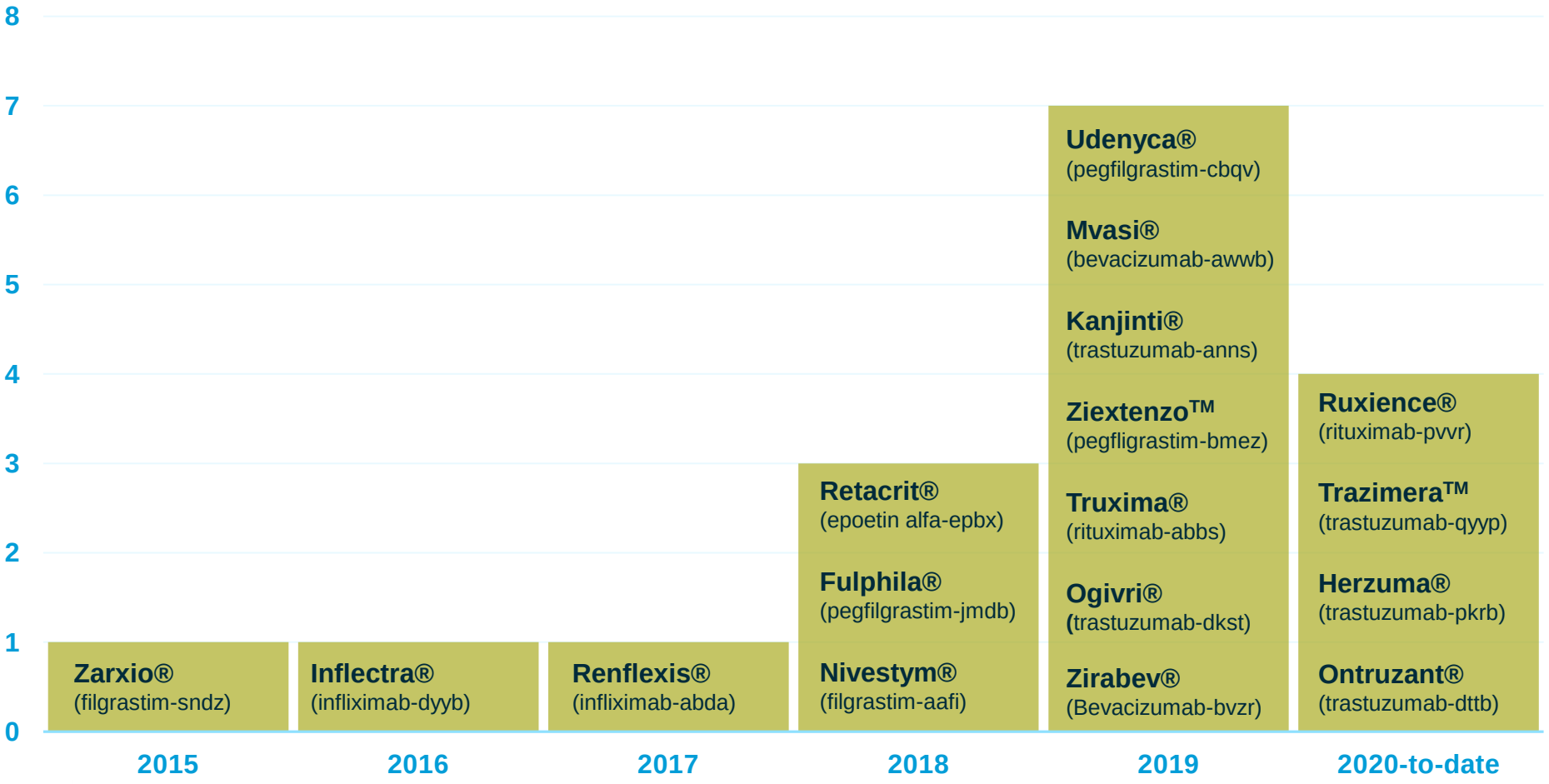
Four Biosimilars Launched in 2020-to-Date

Biosimilars Launched by Year



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Biosimilar Discount at Launch

Biosimilar	Reference Product	Launch Date	% off WAC at Launch
Zarxio®	Neupogen®	Sep 2015	15%
Inflectra®	Remicade®	Nov 2016	15%
Renflexis®	Remicade®	July 2017	35%
Retacrit®	Epogen®	Nov 2018	33.5%
Fulphila®	Neulasta®	Jul 2018	33%
Nivestym®	Neupogen®	Oct 2018	30.3%
Udenyca®	Neulasta®	Jan 2019	33%
Mvasi®	Avastin®	July 2019	15%
Kanjinti®	Herceptin®	July 2019	15%
Ziextenzo™	Neulasta®	Nov 2019	37%
Truxima®	Rituxin®	Nov 2019	10%
Ogivri®	Herceptin®	Dec 2019	10%
Zirabev®	Avastin®	Dec 2019	23%
Ruxience®	Rituxin®	Jan 2020	24%
Trazimera™	Herceptin®	Feb 2020	22%
Herzuma®	Herceptin®	Mar 2020	10%
Ontruzant®	Herceptin®	Apr 2020	15%

Biosimilars with >10% Market Share

Table 1: Biosimilar Companies With Successful Products In The U.S.

Company	Successful Products, Based on > 10% Market Share*
Amgen	Kanjinti
Coherus	Udenyca
Pfizer	Retacrit
Sandoz	Zarxio

*Based on an analysis of Sanford C. Berstein data from January 2020.

Source: https://www.biosimilardevelopment.com/doc/which-biosimilar-companies-will-thrive-in-0001

Biosimilar U.S. Market Share

Biosimilar	U.S. Market Share	Type
Filgrastim	50%	Oncology Support
Pegfilgrastim	20.5%	Oncology Support
Trastuzumab	17%	Oncology
Bevacizumab	15%	Oncology
Infliximab	12%	Immunology

Source: https://www.centerforbiosimilars.com/news/biosimilar-uptake-varies-by-class-of-agent, dated March 20, 2020

Biosimilars of TNF Inhibitors

Biosimilar	Reference Product	FDA Approval Date	Biosimilar Code	Launched?
Inflectra (Pfizer/Celltrion)	Remicade (J&J)	April 2016	Infliximab-dyyb	Yes (2016)
Erelzi (Sandoz)	Enbrel (Amgen)	August 2016	Etanercept-szzs	
Amjevita (Amgen)	Humira (AbbVie)	September 2016	Adalimumab-atto	
Renflexis (Samsung Bioepis/Merck)	Remicade (J&J)	April 2017	Infliximab-abda	Yes (2017)
Cyltezo / BI-695501 (BI)	Humira (AbbVie)	August 2017	Adalimumab-adbm	
Ixifi (Pfizer)	Remicade (J&J)	December 2017	Infliximab-qbtx	
Hyrimoz (Sandoz)	Humira (AbbVie)	November 2018	Adalimumab-adaz	
Eticovo (Samsung Bioepis)	Enbrel (Amgen)	April 2019	Etanercept-ykro	
Hadlima (Samsung Bioepis)	Humira (AbbVie)	July 2019	Adalimumab-bwwd	
Abrilada (Pfizer)	Humira (AbbVie)	December 2019	Adalimumab-afzb	
Avsola (Amgen)	Remicade (J&J)	December 2019	Infliximab-axxq	
Hulio (Mylan)	Humira (AbbVie)	July 2020	Adalimumab-fkjp	

"[B]etween 2016 and 2019, the 2 available infliximab biosimilar drugs made up <1% of tumor necrosis factor inhibitor (TNFi) sales for a large commercial health plan that covers 14 million Americans."

Yazdany, Jinoos, "Failure to Launch: Biosimilar Sales Continue to Fall Flat in the United States," Arthritis & Rheumatology, Vol. 72, No. 6, June 2020, pp. 870-873

Patents Preclude Enbrel® Biosimilar Launch

- **Sandoz and Samsung Bioepis each have FDA-approved Enbrel® biosimilars, but have not launched**
- **Sandoz has stated its patent litigation loss "prevents us from launching an additional treatment option for patients with autoimmune and inflammatory diseases"**
  - Sandoz "reviewing options" including an appeal to the US Supreme Court of the Federal Circuit's recent decision against Sandoz
- **Samsung Bioepis is also involved patent litigation with Amgen**

Humira® Biosimilar Settlements Prevent Launch

Manufacturer	Date of Settlement	Date of U.S. Entry	Associated U.S. BPCIA Litigation
Amgen (Amjevita™)	September 2017	01/31/2023	(16-cv-666, D. Del.)
Samsung Bioepis (Imraldi™)	April 2018	06/30/2023	
Mylan (Hulio™)	July 2018	07/31/2023	
Sandoz (Hyrimoz™)	October 2018	09/30/2023	(18-cv-12668, D.N.J)
Fresenius Kabi (MSB11022)	October 2018	09/30/2023	
Momenta (M923)	November 2018	11/20/2023	
Pfizer (PF-06410293)	November 2018	11/20/2023	
Coherus (CHS-1420)	January 2019	12/15/2023	
BI (Cyltezo™)	May 2019	7/1/2023	(17-cv-1065, D. Del.)

Humira® Antitrust Litigation Dismissed

- ***In re: Humira (Adalimumab) Antitrust Litig.*** **(1:19-cv-1873, N.D. Ill.)**
  - First case filed March 18, 2019, consolidated with >10 class actions
  - Numerous theories:
    - **Patent thickets**
    - **Pay-for-delay settlements (market allocation)**
  - AbbVie's Motion to dismiss GRANTED June 8, 2020
    - **"**AbbVie has exploited advantages conferred on it through lawful practices and to the extent this has kept prices high for Humira, existing antitrust doctrine does not prohibit it."
    - "Here, the vast majority of the alleged scheme is immunized from antitrust scrutiny, and what's left are a few sharp elbows thrown at sophisticated competitors participating in regulated patent and biologic-drug regimes."
  - Plaintiffs requested final judgment so they can pursue appeal
  - Final judgment entered in favor of AbbVie on June 30, 2020

Remicade® Antitrust Litigation Faces Delays

- **Cases filed in 2017-2018 in E.D. Pa alleged J&J/Janssen maintained market share and pricing for Remicade® through exclusionary contracts, anticompetitive bundling, and coercive rebates**
- ***Pfizer v. J&J and Janssen* (No. 17-cv-04180)**
  - Fact discovery ongoing; delays due to COVID-19
- ***In re Remicade (Indirect Purchaser) Antitrust Litig.* (No. 17-cv-04326)**
  - Fact discovery ongoing; delays due to COVID-19
- ***Walgreen Co. and The Kroger Co. v. J&J, et al.* (No. 18-cv-02357)**
  - District Court dismissed for lack of standing to assert federal antitrust claims under assignment agreements
  - Third Circuit reversed and remanded on February 21, 2020
    - "The antitrust claims are a product of federal statute and thus are extrinsic to, and not rights 'under,' a commercial agreement."
  - Janssen/J&J answered the complaint on April 6, 2020
- ***In re Remicade (Direct Purchaser) Antitrust Litig.* (No. 18-cv-00303)**
  - In September 2019, Third Circuit held that these antitrust claims must be arbitrated pursuant to a 2015 distribution contract

Regulatory Update

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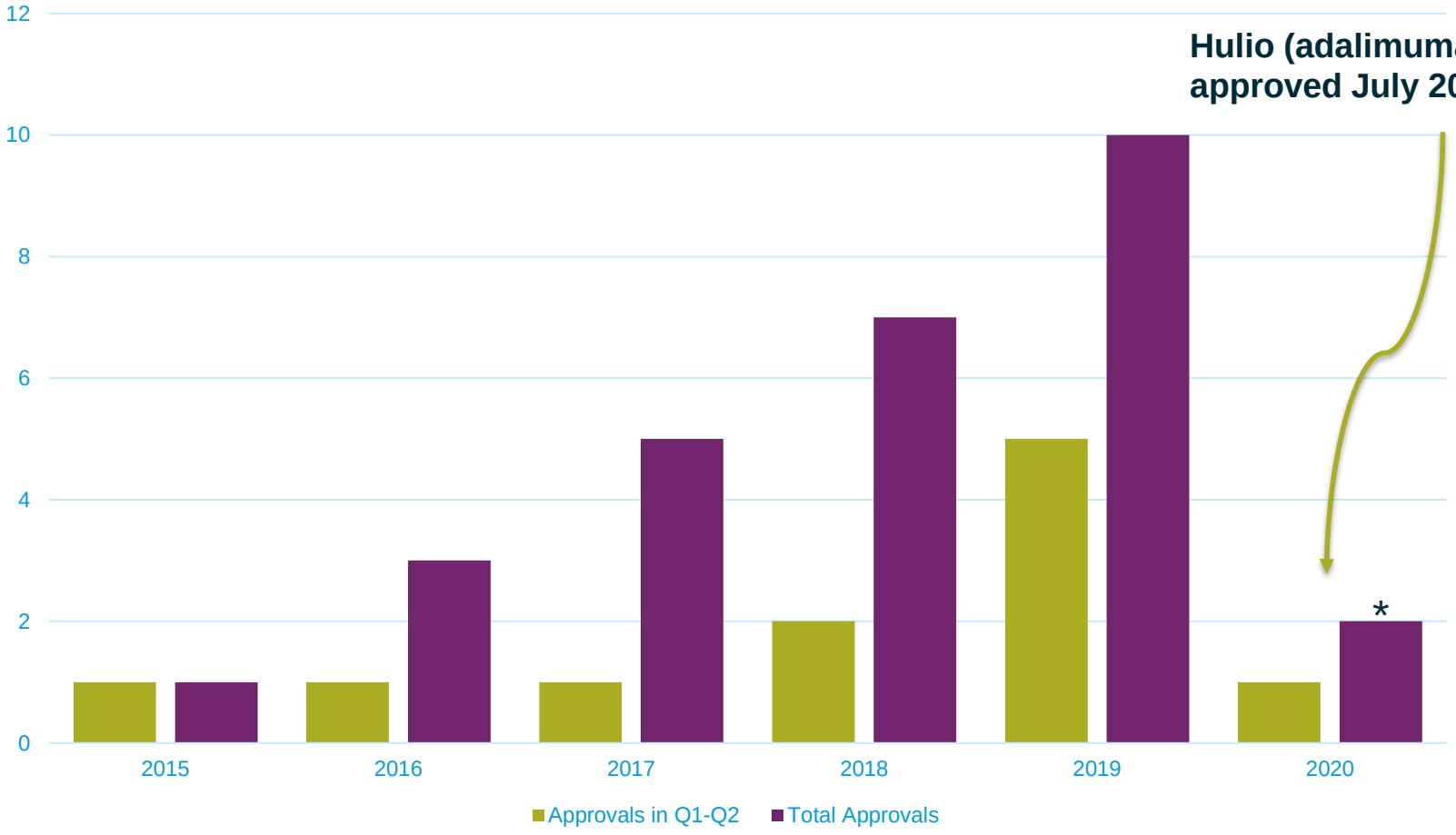
Two New Biosimilars Approved in 2020-to-Date

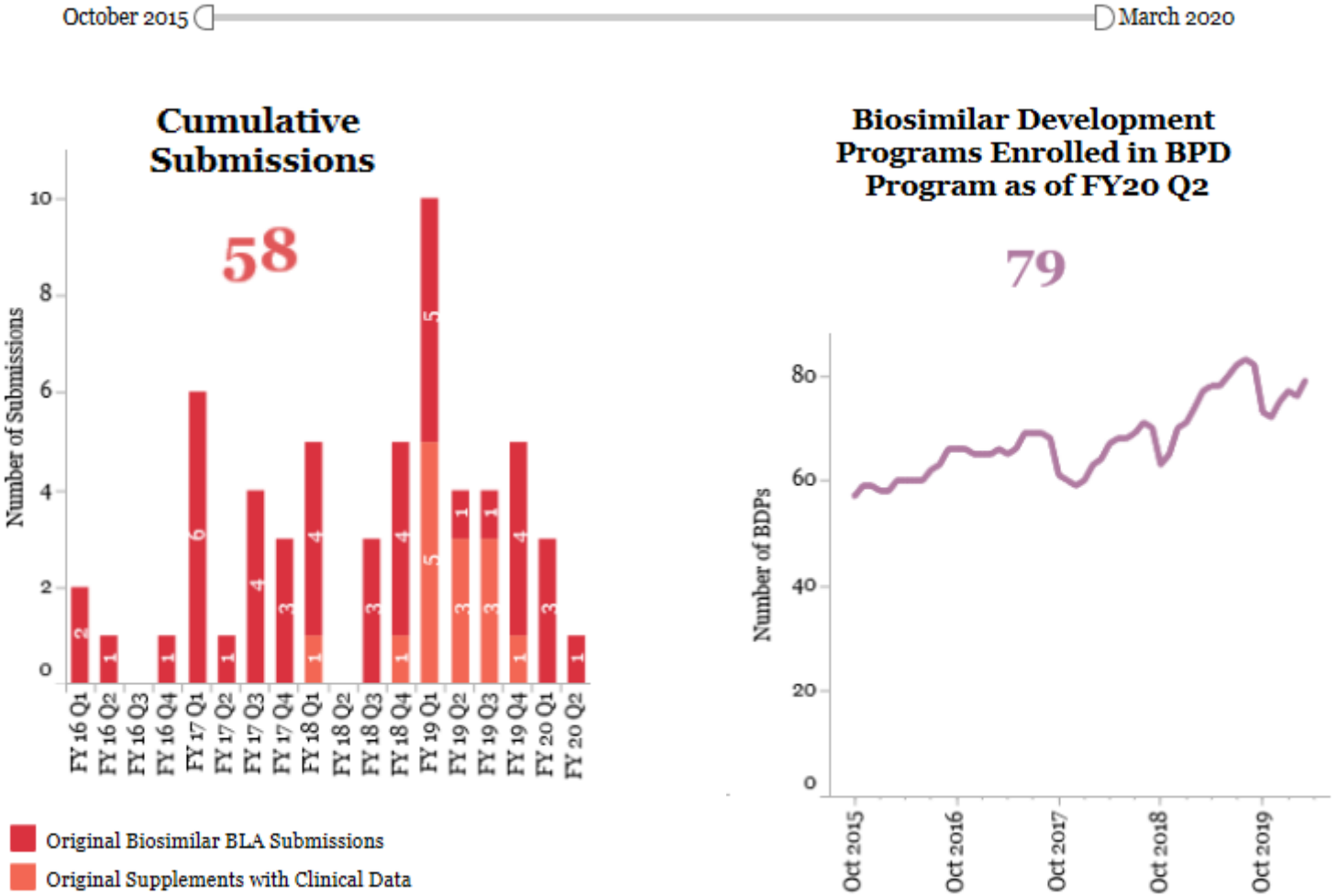
Nyvepria (pegfilgrastim-apgf) approved June 2020

Hulio (adalimumab-fkjp) approved July 2020



* To date

FDA Track – Biosimilars Dashboard



https://www.fda.gov/about-fda/fda-track-agency-wide-program-performance/fda-track-center-drug-evaluation-research-pre-approval-safety-review-biosimilars-dashboard

FDA-FTC Joint Statement on Competition (Feb. 2020)

Joint Statement of the Food & Drug Administration and the Federal Trade Commission Regarding a Collaboration to Advance Competition in the Biologic Marketplace

February 3, 2020

We jointly identified four goals to help in this effort:

1. **FDA and FTC will coordinate to promote greater competition in biologic markets.**
2. **FDA and FTC will work together to deter behavior that impedes access to samples needed for the development of biologics, including biosimilars.**
3. **FDA and FTC intend to take appropriate action against false or misleading communications about biologics, including biosimilars, within their respective authorities.**
4. **FTC will review patent settlement agreements involving biologics, including biosimilars, for antitrust violations.**

New Draft Guidance on Labeling and Ads (Feb. 2020)

- Promotional material may be false or misleading if it represents or suggests
  - that there are clinically meaningful differences between the reference product and its biosimilar in terms of safety, purity, or potency
  - that one is safer or more effective than the other
  - that the two products are not highly similar
- Advised against using individual statements of accurate information to create a misleading representation in a comparative context
- May be misleading to suggest that a biosimilar product is less safe or effective because it is not identical to or interchangeable with the reference product
- Does not address considerations unique to interchangeable biosimilars
- 13 comments have been submitted

Decision re Pfizer's Citizen Petition (Feb. 2020)

We thus grant your Petition in part in that we have issued draft guidance regarding promotional labeling and advertising considerations for biological reference products and biosimilar products. At this time, we deny your petition in part, insofar as it requests that FDA include specific content in guidance, because the specific content of final FDA guidance will be determined after the consideration of the public comments on the draft guidance (and may be periodically updated thereafter, in accordance with the agency's good guidance practices regulation, 21 CFR 10.115).

New Draft Guidance on Indications (Feb. 2020)

- Titled: “Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed”
- “An applicant generally may obtain licensure of a biosimilar or interchangeable for *fewer* than all of the conditions of use for which the reference product is licensed.”
- “However, FDA recommends that an applicant seeking licensure for a proposed interchangeable product seek licensure for all of the reference product’s licensed conditions of use when possible.”
- Recognizes that exclusivities and patents may lead an applicant to seek licensure for fewer indications
- Suggests that applicants wishing to delay licensure to avoid risk of patent infringement request that FDA refrain from acting until a specific date
- 7 comments submitted

“Deemed to be a BLA” – March 23, 2020

- **March 23, 2020: "Deemed to be a BLA" transition date**
  - All “biological product” applications approved under the FD&C Act “transition” to being regulated under the PHS Act
  - Biosimilars and interchangeables of these products now possible
- **FDA issued final guidance on the transition early March 2020**
  - NDA holder for biological product did not need to take any affirmative steps; the transition was automatic
- **Definition of “biological product”**
  - BPCIA (2010): included a “protein (except any chemically synthesized polypeptide)”
  - Dec. 2019: definition amended to remove parenthetical
  - Feb. 2020: FDA issued a final rule to interpret “protein” to mean “any alpha amino acid polymer with a specific defined sequence that is greater than 40 amino acids in size.”

Purple Book Enhancements

- **FDA is transitioning the Purple Book to a "searchable, public-facing online database"**
  - Goal is to "improve transparency and functionality for stakeholders by providing a complete view of biological product options, including biosimilar and interchangeable products, and to advance public awareness about licensed biological products"
- **Feb. 2020 - First phase completed**
  - Transitioned from a table format to a searchable database with a "limited data set"
- **March 2020 – FDA requested comments on Purple Book 1.0**
- **May 2020 – Second phase completed**
  - Release of updated Purple Book with all FDA-licensed, biological products regulated by CDER including transition biological products
  - "Subsequent releases will include information about all FDA-licensed biological products regulated by Center for Biologics Evaluation and Research (CBER), in addition to enhanced functionality."

COVID-19 and Biologics/Biosimilars

- **FDA's CDER suspended "all domestic and foreign routine surveillance facility inspections"**
  - July 10, 2020 – announced resumption of domestic on-site inspections the week of July 20, depending on the local COVID-19 situations
- **FDA has announced it is still "[h]elping to ensure access to cost saving drugs and other needed medications through continued review and approval of generic drugs and biosimilars"**
- **FDA issued numerous guidance documents, e.g.,:**
  - June 2020: guidance re manufacturing controls to prevent contamination of biologics with SARS-CoV-2
  - July 2020: updated guidance on clinical trials in light of COVID-19 and associated closures and quarantines

Litigation Update

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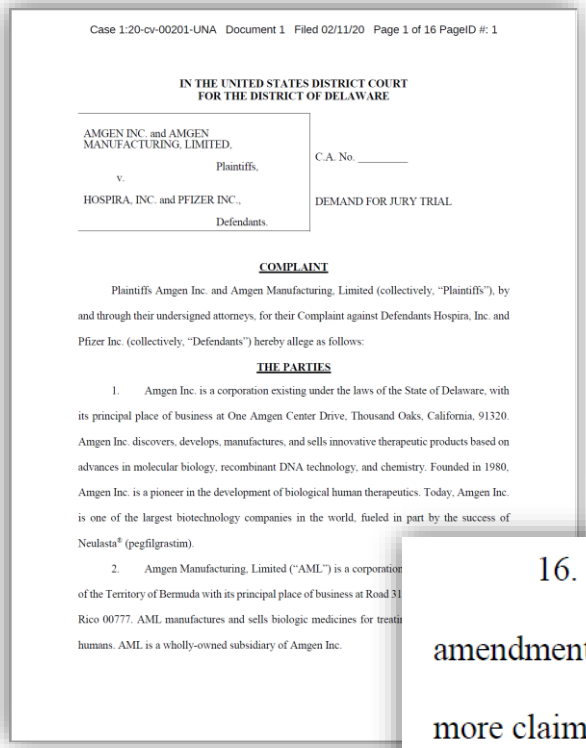
New Biosimilar Cases Filed in 2020

Parties	Case No.	Reference Biologic	Date Filed
Amgen v. Hospira	1:20-cv-00201 (D. Del.)	Neulasta®	Feb. 11, 2020
Amgen v. Hospira	1:20-cv-00561 (D. Del.)	Neupogen®	Apr. 24, 2020
Genentech v. Samsung Bioepis	1-20-cv-00859 (D. Del)	Avastin®	Jun. 28, 2020

Amgen v. Hospira (Neulasta®)



Case 1:20-cv-00201-UNA Document 1 Filed 02/11/20 Page 1 of 16 PageID #: 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC. and AMGEN MANUFACTURING, LIMITED,
Plaintiffs,
v.
HOSPIRA, INC. and PFIZER INC.,
Defendants.

C.A. No. _____

DEMAND FOR JURY TRIAL

COMPLAINT

Plaintiffs Amgen Inc. and Amgen Manufacturing, Limited (collectively, "Plaintiffs"), by and through their undersigned attorneys, for their Complaint against Defendants Hospira, Inc. and Pfizer Inc. (collectively, "Defendants") hereby allege as follows:

THE PARTIES

1. Amgen Inc. is a corporation existing under the laws of the State of Delaware, with its principal place of business at One Amgen Center Drive, Thousand Oaks, California, 91320. Amgen Inc. discovers, develops, manufactures, and sells innovative therapeutic products based on advances in molecular biology, recombinant DNA technology, and chemistry. Founded in 1980, Amgen Inc. is a pioneer in the development of biological human therapeutics. Today, Amgen Inc. is one of the largest biotechnology companies in the world, fueled in part by the success of Neulasta® (pegfilgrastim).

2. Amgen Manufacturing, Limited ("AML") is a corporation
of the Territory of Bermuda with its principal place of business at Road 31
Rico 00777. AML manufactures and sells biologic medicines for treatin
humans. AML is a wholly-owned subsidiary of Amgen Inc.

Case 1:20-cv-00201-UNA Document 1 Filed 02/11/20 Page 1 of 16 PageID #: 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC. and AMGEN MANUFACTURING, LIMITED,
Plaintiffs,
v.
HOSPIRA, INC. and PFIZER INC.,
Defendants.

C.A. No. _____

DEMAND FOR JURY TRIAL

16. The submission of the Hospira aBLA, including on information and belief, any amendments or supplementations thereto, constitutes one or more acts of infringement of one or more claims of the '707 Patent under 35 U.S.C. § 271(e)(2)(C).

17. If FDA approves the Hospira aBLA and Defendants make, offer to sell, sell, use, or import the Proposed Hospira Pegfilgrastim Product within the United States, Defendants will also infringe one or more claims of the '707 Patent under 35 U.S.C. §§ 271(a), (b), (c), and/or (g).

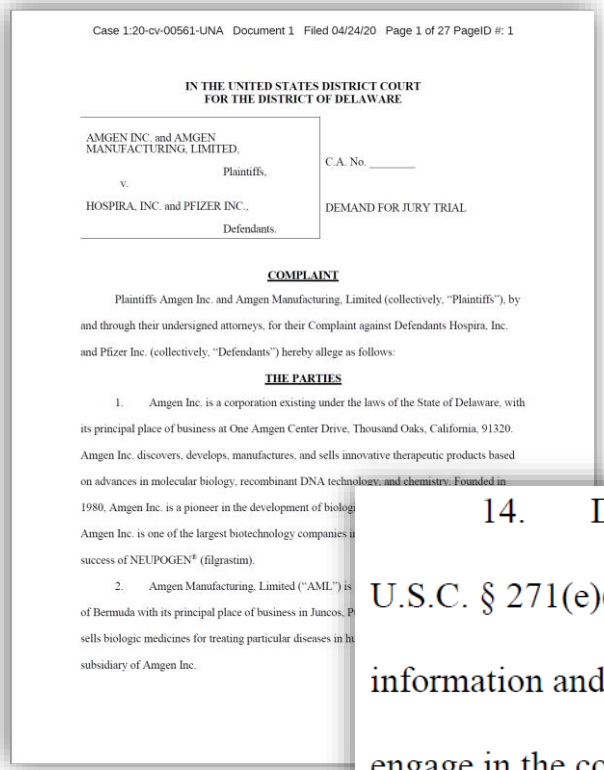
Amgen v. Hospira – Motion to Dismiss

- **Pfizer motion to dismiss under Rule 12(b)(6) (Mar. 4, 2020)**
  - No literal infringement because Pfizer process uses salt concentrations below those claimed
  - Prosecution history estoppel precludes DOE for the same reasons in *Amgen v. Coherus*

- **Amgen opposition (April 1, 2020)**
  - Finding on literal infringement premature because of claim construction and factual issues (e.g., what is "about 0.1 M" and does Pfizer's process meet it?)
  - As to DOE, the *Coherus* decision "was based on the identity of the salts employed, *not* their concentration."
  - *Mylan* decision found that disclaimer did not extend to salt concentrations claimed in the '707 patent

- **Pfizer's reply (April 15, 2020)**
  - Disputes that there are factual or claim construction issues because salt concentration below 0.04 M
  - Distinguishes the *Mylan* case as, in part, "based on legal error"

Amgen v. Hospira (Neupogen®)



Case 1:20-cv-00561-UNA Document 1 Filed 04/24/20 Page 1 of 27 PageID #: 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC. and AMGEN MANUFACTURING, LIMITED,
Plaintiffs,
v.
HOSPIRA, INC. and PFIZER INC.,
Defendants.

C.A. No. _____

DEMAND FOR JURY TRIAL

COMPLAINT

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Amgen Inc. is one of the largest biotechnology companies i
success of NEUPOGEN® (filgrastim).

2. Amgen Manufacturing, Limited ("AML") is
of Bermuda with its principal place of business in Juncos, P
sells biologic medicines for treating particular diseases in hu
subsidiary of Amgen Inc.

Case 1:20-cv-00561-UNA Document 1 Filed 04/24/20 Page 1 of 27 PageID #: 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC. and AMGEN MANUFACTURING, LIMITED,
Plaintiffs,
v.
HOSPIRA, INC. and PFIZER INC.,
Defendants.

C.A. No. _____

DEMAND FOR JURY TRIAL

14. Defendants committed an act of infringement as to the '392 Patent under 35 U.S.C. § 271(e)(2)(C) when they caused Hospira to submit the Hospira aBLA, including on information and belief, any amendments thereto, for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, or sale of the Hospira Filgrastim Biosimilar Product.

17. By Defendants' importation of the Hospira Filgrastim Biosimilar Product into the United States, or offer to sell, sale, or use of that product within the United States, Defendants have infringed at least Claim 22 of the '392 Patent, literally or equivalently, under 35 U.S.C. § 271(g).

Genentech v. Samsung Bioepis

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC.

Plaintiff,

v.

SAMSUNG BIOEPIS CO. LTD.,

Defendant.

C. A. No. _____

JURY TRIAL DEMANDED

3. This action seeks relief under 35 U.S.C. § 271 for patent infringement and the Biologics Price Competition and Innovation Act ("BPCIA") against Bioepis in connection with its manufacture and efforts to commercialize a biosimilar to Avastin®, Genentech's best-selling cancer therapy. Bioepis has infringed or threatens to infringe the following Asserted Patents:

U.S. Patent No.	Issue Date	First Named Inventor
EX A – 6,586,206	Jul. 1, 2003	Dixit
EX B – 7,390,660	Jun. 24, 2008	Behrendt
EX C – 7,485,704	Feb. 3, 2009	Fahrner
EX D – 8,460,895	Jun. 11, 2013	Eisenkraetzer
EX E – 8,512,983	Aug. 20, 2013	Gawlitzek
EX F – 8,574,869	Nov. 5, 2013	Kao
EX G – 9,441,035	Sep. 13, 2016	Carvalhal
EX H – 9,487,809	Nov. 8, 2016	Zhou
EX I – 9,714,293	Jul. 25, 2017	Gawlitzek
EX J – 9,795,672	Oct. 24, 2017	Fyfe
EX K – 10,208,355	Feb. 19, 2019	Bais
EX L – 10,513,697	Dec. 24, 2019	da Silva Ribeiro
EX M – 10,662,237	May 26, 2020	Mehta
EX N – 10,676,710	June 9, 2020	Vijayasankaran

Other District Court Activity in 2020

Parties	Case No.	Reference Drug	Status
Amgen v. Coherus	17-cv-546 (D.Del.)	Neulasta®	Merits resolved by CAFC in 2019; Coherus's attorney fee motion pending
Genentech v. Amgen	17-cv-1407, -1471, 19-cv-602 (D. Del.)	Avastin®	Settled
Genentech v. Amgen	18-cv-924 (D. Del.)	Herceptin®	Settled
Amgen v. Hospira	18-cv-1064 (D. Del.)	Neupogen®	Supplemental fact and expert discovery ongoing
Immunex v. Samsung Bioepis	19-cv-11755 (D.N.J.)	Enbrel®	Administratively stayed
Coherus v. Amgen	19-cv-139 (D.Del.)	Humira®	Stip of Dismissal in 2019; attorney fee motion by Amgen denied
Amgen v. Hospira	20-cv-201 (D. Del.)	Neulasta®	Pfizer and Hospira's motion to dismiss pending
Amgen v. Hospira	20-cv-561 (D. Del.)	Neupogen®	Motion to stay pending
Genentech v. Samsung Bioepis	20-cv-859 (D. Del.)	Avastin®	Complaint filed

BPCIA Disclosures – *Genentech v. Amgen*

- **Genentech sued Amgen for infringement of 26 patents based on Amgen's submission of an aBLA for Avastin® (17-cv-1407, D. Del.)**

- **Genentech filed counterclaims and affirmative defenses that all the patents were invalid and/or unenforceable**

- **Genentech moved to dismiss Amgen's counterclaims and affirmative defenses for alleged failure to comply with the patent dance:**
  - Argued that Amgen's declaratory judgment counterclaims were barred because Amgen did not provide information sufficient to describe its manufacturing process during the patent dance

  - Argued that Amgen's invalidity counterclaims and affirmative defenses were "barred by the BPCIA to the extent they are based on invalidity, unenforceability, and noninfringement contentions that Amgen did not disclose in the patent dance"

BPCIA Disclosures – *Genentech v. Amgen*

- **42 U.S.C. § 262(l)(2)(a) requires applicant to provide a copy of the aBLA and "such other information that describes the process or processes used to manufacture" the biosimilar."**
  - Under § 262(*l*)(9)(C), if an applicant fails to provide this information, "the reference product sponsor, but not the subsection (k) applicant, may bring an action . . . for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product."

- **42 U.S.C. § 262(*l*)(3)(B) requires applicant to provide a detailed statement of the reason why the patents identified by the RPS are invalid, unenforceable, or not infringed**
  - § 262(*l*)(9)(B), if an applicant fails to comply with this step, "the reference product sponsor, but not the subsection (k) applicant, may bring an action . . . for a declaration of infringement, validity, or enforceability" of any patent on the sponsor's § 262(*l*)(3)(A) list of patents.

BPCIA Disclosures – *Genentech v. Amgen*

- **Judge Connolly denied Genentech's motion**

- **Applicant can bring counterclaims of invalidity or non-infringement if does not comply or opts out of the patent dance**
  - "[T]he filing of counterclaims does not constitute 'bringing an action' and, is therefore not barred by § 262(l)(9)(C)."

- **Applicant not precluded from raising defenses not disclosed during the patent dance**
  - Genentech fails to "point to anything in the BPCIA or to case law interpreting the BPCIA that would support barring a biosimilar applicant from making in a BPCIA case contentions not disclosed in the patent dance."
  - Genentech's arguments are also foreclosed by (9)(B) and the Supreme Court's decision in *Sandoz*, holding the remedial provisions of (9)(B) and (9)(C) are the "exclusive remedies"
  - Genentech's "sole remedy" for Amgen's alleged non-compliance in its (3)(B) statements is to "bring a declaratory judgment action for artificial infringement," which Genentech already did

BPCIA Litigation at the Federal Circuit

Case	Status	Reference	Prevailing Party
Janssen v. Celltrion (18-2321, 2350)	Rule 36 **affirmance** (Mar. 5, 2020)	Remicade®	Biosimilar
Amgen v. Hospira (19-1067)	Fed. Cir. **affirmed** (Dec. 16, 2019); denied rehearing *en banc* (Mar. 16, 2020)	Epogen®	RPS
Genentech v. Immunex (19-2155)	Fed. Cir. **affirmed** (July 6, 2020)	Avastin®	Biosimilar
Genentech v. Amgen (19-2156)	Rule 36 **affirmance** (Mar. 6, 2020)	Herceptin®	Biosimilar
Immunex v. Sandoz (20-1037)	Fed. Cir. **affirmed** (July 1, 2020)	Enbrel®	RPS

Janssen v. Celltrion

- **District Court (17-cv-11008, D. Mass.)**
  - Janssen alleged that the cell culture media used by Celltrion to produce its Remicade® biosimilar infringes U.S. Patent No. 7,598,083 (the "'083 Patent") under the doctrine of equivalents
    - DOE theory accounted for "at least twelve differences in concentration" in the claimed cell media component ranges
  - In July 2018, Judge Wolf of the District of Massachusetts granted Celltrion's motion for summary judgment of non-infringement
    - 104-page opinion on ensnarement

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

- **Dec. 2018: Janssen filed its opening brief, 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 from using ferric ammonium citrate and evidence of copying) in its summary judgment analysis.
- **Feb. 2019: Celltrion responded and cross-appealed, arguing:**
  - Janssen does not have standing because not all co-owners of the '083 patent were joined as plaintiffs – assignments for many of the inventors assigned to more than just Janssen.

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

- **March 4, 2020 – Oral Arguments**
  - Panel: Judges Wallach, Taranto, and Stoll
  - Panel's questions focused on selected of particular prior art references as a starting place and interchangeability of specific ingredients
  - Panel expressed skepticism of Celltrion's standing arguments
- **March 5, 2020 – Rule 36 Affirmance**
  - Case concluded in Celltrion's favor
  - No damages for Celltrion's Inflectra® (Infliximab-dyyb) launch-at-risk in 2016

Amgen v. Hospira

- **District Court (15-cv-839, D. Del.)**
  - In September 2017, a jury awarded Amgen $70 million in reasonable royalty damages based on Hospira's infringement of U.S. Patent No. 5,856,298 (the "'298 Patent") in relation to a biosimilar of Amgen's Epogen® (epoetin alfa)
    - **First BPCIA Damages award**
    - **Patent was expired by time of trial**
    - **The biosimilar was neither approved nor launched at time of award**
    - **Damages awarded for "stockpiling" batches not covered by safe harbor of 35 U.S.C. § 271(e)**
  - The jury also found that Hospira did not infringe U.S. Patent No. 5,756,349 (the "'349 Patent")
  - In ruling on post-trial motions, Judge Andrews of the District of Delaware upheld the jury verdict

Amgen v. Hospira (CAFC 19-1067, 1102)

- **Hospira's appeal**
  - Whether the court/jury were correct on claim construction, infringement, and validity of the '298 patent
  - Whether the court incorrectly instructed the jury on Hospira's subjective intent for purposes of the safe harbor rather than objectively reasonable uses of the batches
  - Whether a reasonable jury correctly determined the batches were not covered by the safe harbor
  - Whether the court erred in allowing the jury to consider a damages position from Plaintiffs' damages expert that "goes well beyond what was adequate to compensate for infringement … and was not tied to any damages suffered by Amgen, but sought $170 million in damages for two expired patents, although Hospira made no sales"
- **Amgen's cross-appeal**
  - Whether JMOL of non-infringement of the '349 patent was proper
  - Whether the court properly denied a new trial motion on the '349 patent

Amgen v. Hospira (CAFC 19-1067, 1102)

- **December 16, 2019: Federal Circuit Affirmed on Each Issue**
  - As to the safe harbor defense:
    - **The jury instructions were not legally erroneous**
      - "[T]he 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."
    - **Substantial evidence supported the jury's finding that certain batches were not protected**
      - For example, evidence was submitted that Hospira was not required by FDA to manufacture additional batches after 2012
      - It was relevant (but not dispositive) 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

Amgen v. Hospira (CAFC 19-1067, 1102)

- **January 15, 2020 – Hospira filed a petition for rehearing *en banc***
  - Issue: "[w]hether 35 U.S.C. § 271(e)(1) provides a safe harbor against infringement of patents claiming a method of manufacture, when the product manufactured is used to generate information for submission to [FDA] in order to seek approval of a biosimilar drug"
  - Hospira argued the Federal Circuit's opinion was contrary to precedent
  - Hospira argued the Federal Circuit's opinion rendered "the statutory protection for 'making' a drug …. illusory for a large subset of the patents available to be asserted under the BPCIA"
- **February 27, 2020 – Amgen responded**
  - "The panel did not announce a special Safe Harbor rule for process patents."
  - "[R]ather than use 'how' *or* 'why,' the panel stated the issue in the language of the statute: 'whether each act of manufacture was for uses reasonably related to submitting information to the FDA.'"
- **March 16, 2020: Federal Circuit Denied Rehearing *En Banc***
  - No opinion on the merits

Genentech v. Amgen, Immunex (CAFC 19-2156, 2155)

- Appeals related to the district court's denial of preliminary relief
- Biosimilars in both cases (Mvasi and Kanjinti) launched in July 2019 right after the district court's decisions
- ***Genentech v. Amgen* (CAFC 19-2156)**
  - Related to Amgen's biosimilar of Herceptin®
  - Genentech asserted district court erred by
    - "inferring that Genentech will not suffer irreparable harm because it waited to seek preliminary injunctive relief until Amgen affirmatively decided to launch [Kanjinti]"
    - "adopting a categorical rule that licensing of *future* activity negates irreparable harm from *present* infringement"
  - Rule 36 Affirmance on March 6, 2020
- ***Genentech v. Immunex* (CAFC 19-2155)**
  - Related to Immunex's biosimilar of Avastin®
  - Issue was whether Immunex was required to provide new notice of commercial marketing given its supplemental BLAs for Mvasi

Genentech v. Immunex (CAFC 19-2155)

Federal Circuit Affirmed July 6, 2020

> The statute makes clear that the biosimilar applicant must provide notice to the reference product sponsor prior to commercially marketing *the biological product*.

> Amgen notified Genentech of its intent to commercially market its biological product, Mvasi, on October 6, 2017. Despite its later supplements to its applications adding a manufacturing facility and changing its drug product label, Amgen's biological product, Mvasi, did not change. Genentech, therefore, had notice of Amgen's intent to commercially market Mvasi as required under Section 262(*l*)(8)(A) as early as October 6, 2017.

> A biosimilar applicant that has already provided Section 262(*l*)(8)(A) notice regarding its biological product need not provide another notice for each supplemental application concerning the same biological product.

Immunex v. Sandoz (CAFC 20-1037)

- **District Court (2-16-cv-01118, D.N.J.)**
  - Involved two patents originally prosecuted in 1995, expiring in 2028 and 2029, related to Sandoz's Enbrel® biosimilar
  - Sandoz did not contest infringement
  - Sandoz challenged validity of patents
    - **Written Description**
    - **Enablement**
    - **Obviousness**
    - **Obviousness-type double patenting (ODP)**
  - August 9, 2019: **District court held the patents not invalid**
- **On October 15, 2019, Sandoz appealed**
  - Sandoz challenged the district court's ODP, written description, and obviousness analyses

Immunex v. Sandoz (CAFC 20-1037)

- **Federal Circuit Affirmed July 1, 2020**
  - Patents were not invalid for obviousness-type double patenting
    - **No common ownership with other Immunex patents**
    - **The patents-in-suit were assigned to Roche**
    - **Immunex did not obtain "all substantial rights":**
      - Roche had a secondary right to enforce
      - Roche had "right to veto any assignment of Immunex's interest"
  - Patents were adequately described
  - Patents were non-obvious
    - **The district court did not clearly err by only considering a motivation to combine references for therapeutic uses**
      - It "was a result of the arguments and evidence presented at trial and in the parties' post-trial submissions"
      - Further, therapeutic uses were the stated objective of the invention and pharmaceutical compositions were claimed
    - **No error with objective indicia of non-obviousness analysis**
  - Judge Reyna, in dissent, would have found the patents invalid for obviousness-type double patenting

IPR Update

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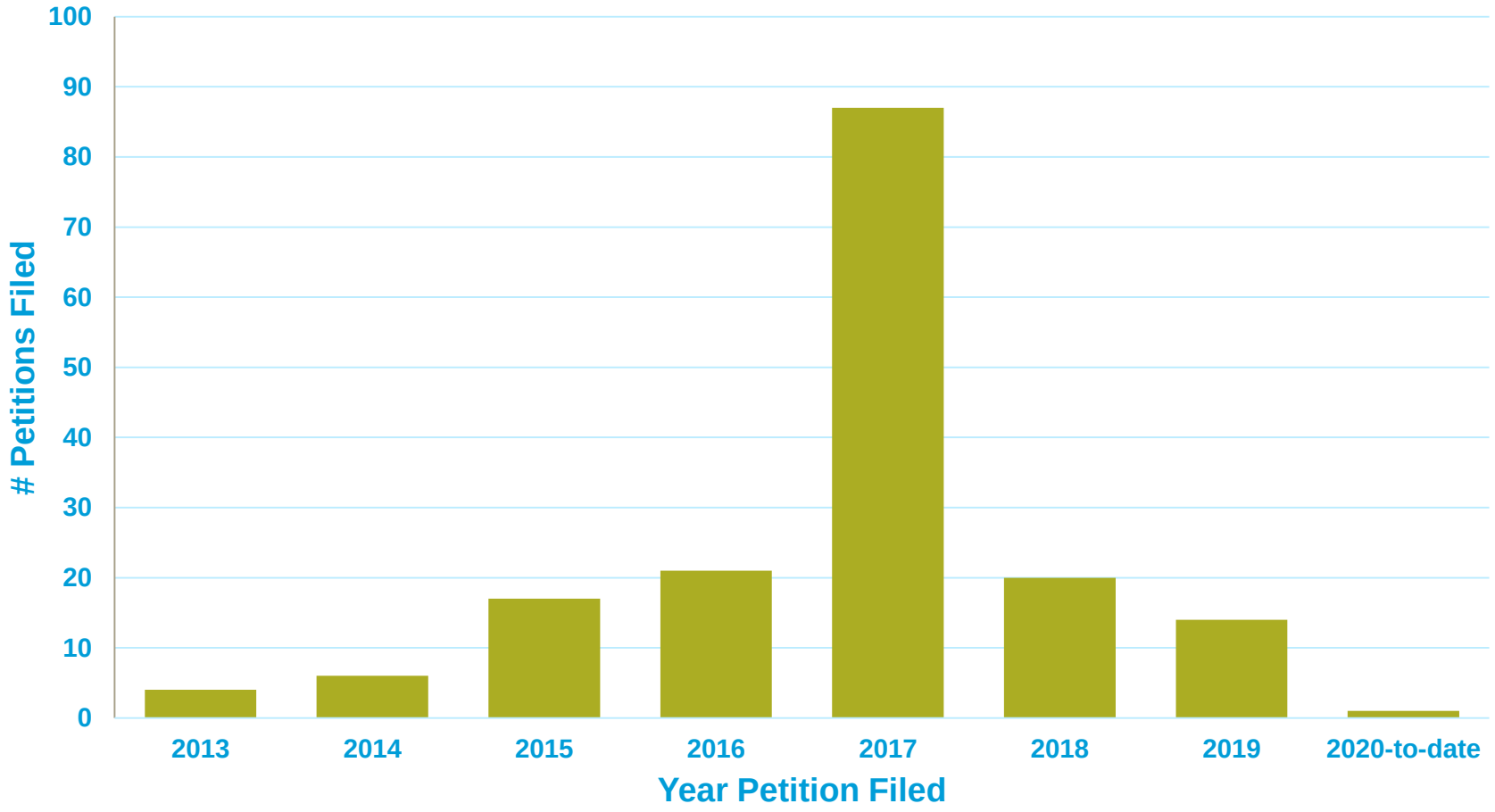
Biologic-Related IPR Filings



Select IPR Resolutions

- **Amgen and Alexion settled three IPRs on Alexion's Soliris® (eculizumab) post-institution**
  - Amgen obtained a non-exclusive, royalty-free license for the U.S.
  - Amgen can bring a biosimilar to market March 1, 2025
- **Novoimmune and UCB settled two IPRs on Novoimmune's Cosentyx® (secukinumab) pre-institution**
- **Amgen and Fresenius settled IPRs to two Amgen manufacturing patents– one pre-institution and one post-institution**
- **PTAB invalidated claims in six patents asserted by Teva against Eli Lilly's Emgality® (galcanezumab); upheld claims in three other patents**

Other Recent Events to Watch

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Constitutionality of ACA (and BPCIA?)

- **The Supreme Court will decide whether the ACA's individual mandate is constitutional and, if not, whether it is severable from the other ACA provisions**
  - The BPCIA was enacted as part of the ACA
  - U.S. Government filed brief in June and took the position that the mandate is not severable

- **Letter to Washington Post by Keith Webber, former acting director of FDA's Office of Biotechnology Products and Office of Generic Drugs (June 28, 2020):**

> The BPCIA is the part of the ACA that allows the Food and Drug Administration to approve biosimilar drugs (often called generic biologics). Should the Supreme Court agree with the Trump administration's brief, the FDA will no longer be allowed to approve new, less expensive biosimilars and, possibly, the FDA's approval of those products now on the market will be retracted.

Biosimilar-Related Legislation

- **Numerous pieces of proposed legislation related to biosimilars are still pending, for example, bills aimed at:**
  - Requiring RPS's to disclose their biologic-related patents
    - **S.659 Biologic Patent Transparency Act**
  - Preventing anti-competitive agreements
    - **S.64: Preserve Access to Affordable Generics and Biosimilars Act**
  - Preventing anti-competitive product hopping
    - **S.1416: Affordable Prescriptions of Patients Act of 2019**
  - Preventing "sham" citizen petitions that interfere with biosimilar approval
    - **S.1224, H.R.2374: Stop STALLING Act**
  - Shortening the exclusivity period for biologics
    - **H.R.3379: Price Relief, Innovation, and Competition for Essential Drug Act**
- **Newest Legislation: S.4134 Increasing Access to Biosimilars Act**
  - Introduced by Senators Cornyn (R-TX) and Bennet (D-CO) on July 1, 2020 to reduce biologics costs for seniors

Biosimilars' Role in COVID-19 Treatment

- **Celltrion's infliximab biosimilar (Remsima, CT-P13) is part of the CATALYST study, assessing the effectiveness of potential therapeutics for the treatment of patients hospitalized with COVID-19.**

- **June 23, 2020 – Korean Herald reported that "Celltrion shares rose 7.58 percent … following news that an Italian COVID-19 patient tested negative for the virus a week after being treated with Celltrion's autoimmune disease treatment Remsima."**

Thank You!

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