Biosimilars 2020 Year-in-Review

January 28, 2021

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Meet the Speakers

John Adkisson
Principal

Geoff Biegler
Principal

Jenny Shmuel
Principal

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Today's Topics

- Market Update
- Regulatory Update
- BPCIA Litigation Update
- IPR Update
- Biosimilar Competition
- Looking forward to 2021

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U.S. Biosimilar Market

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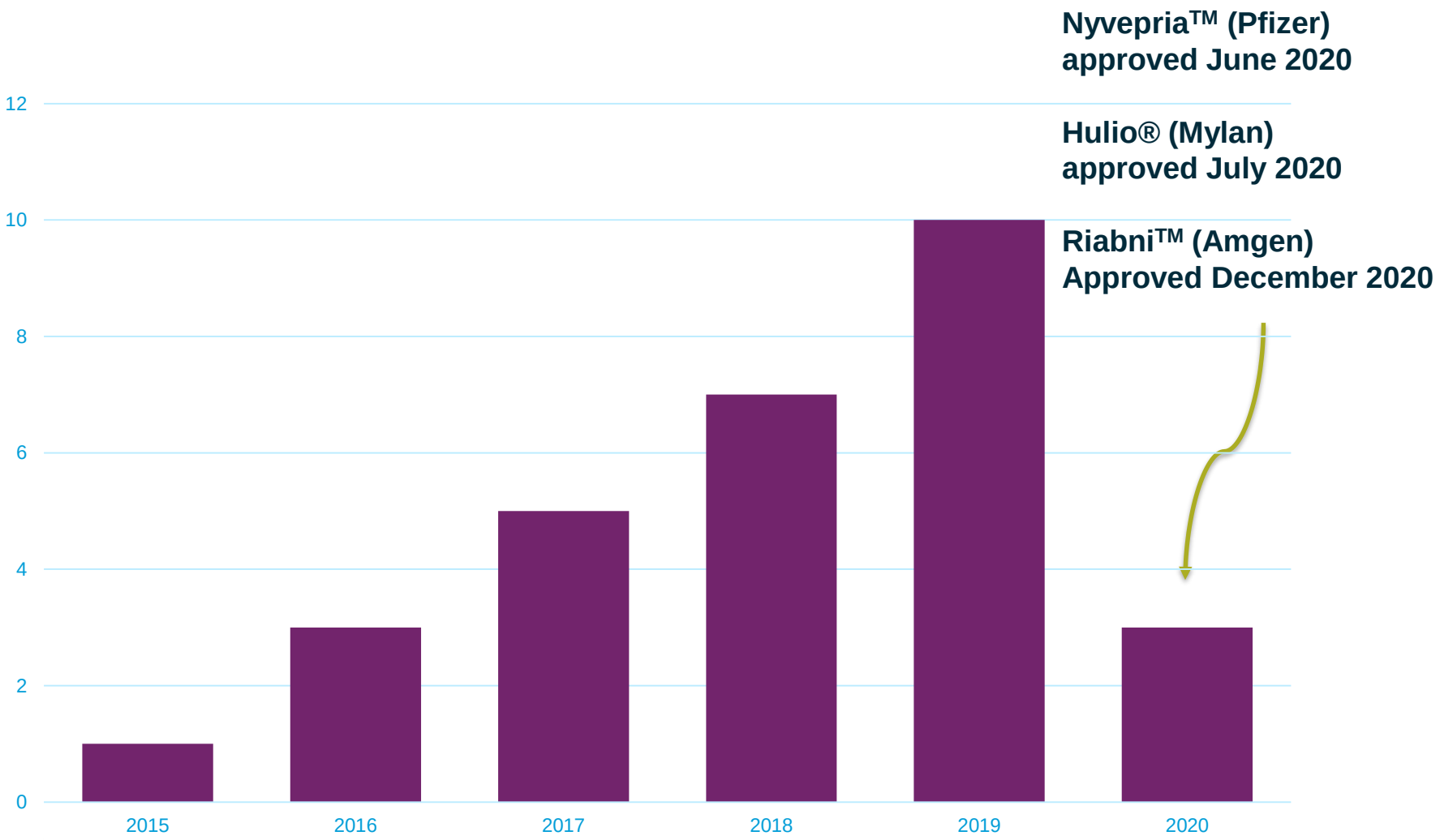
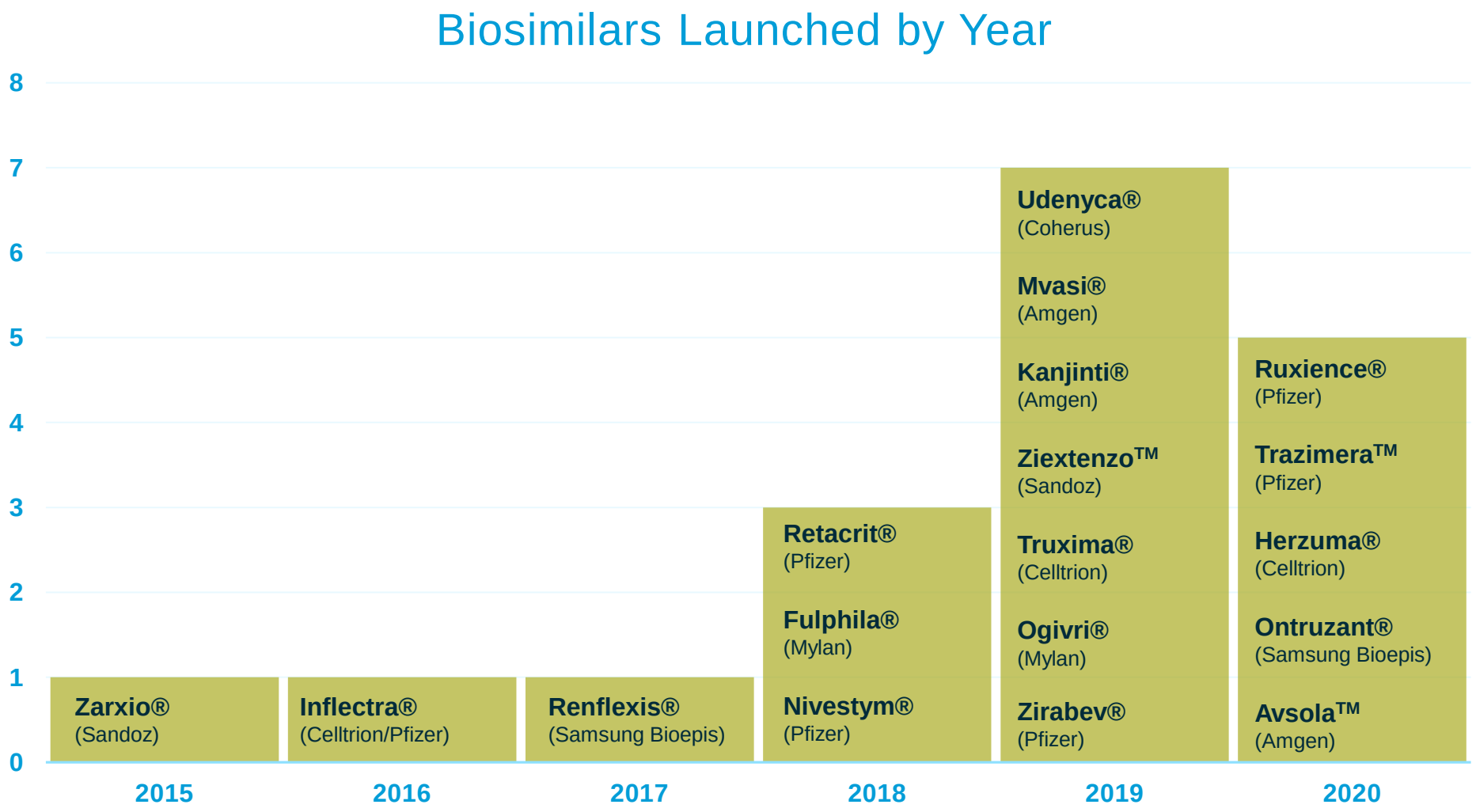
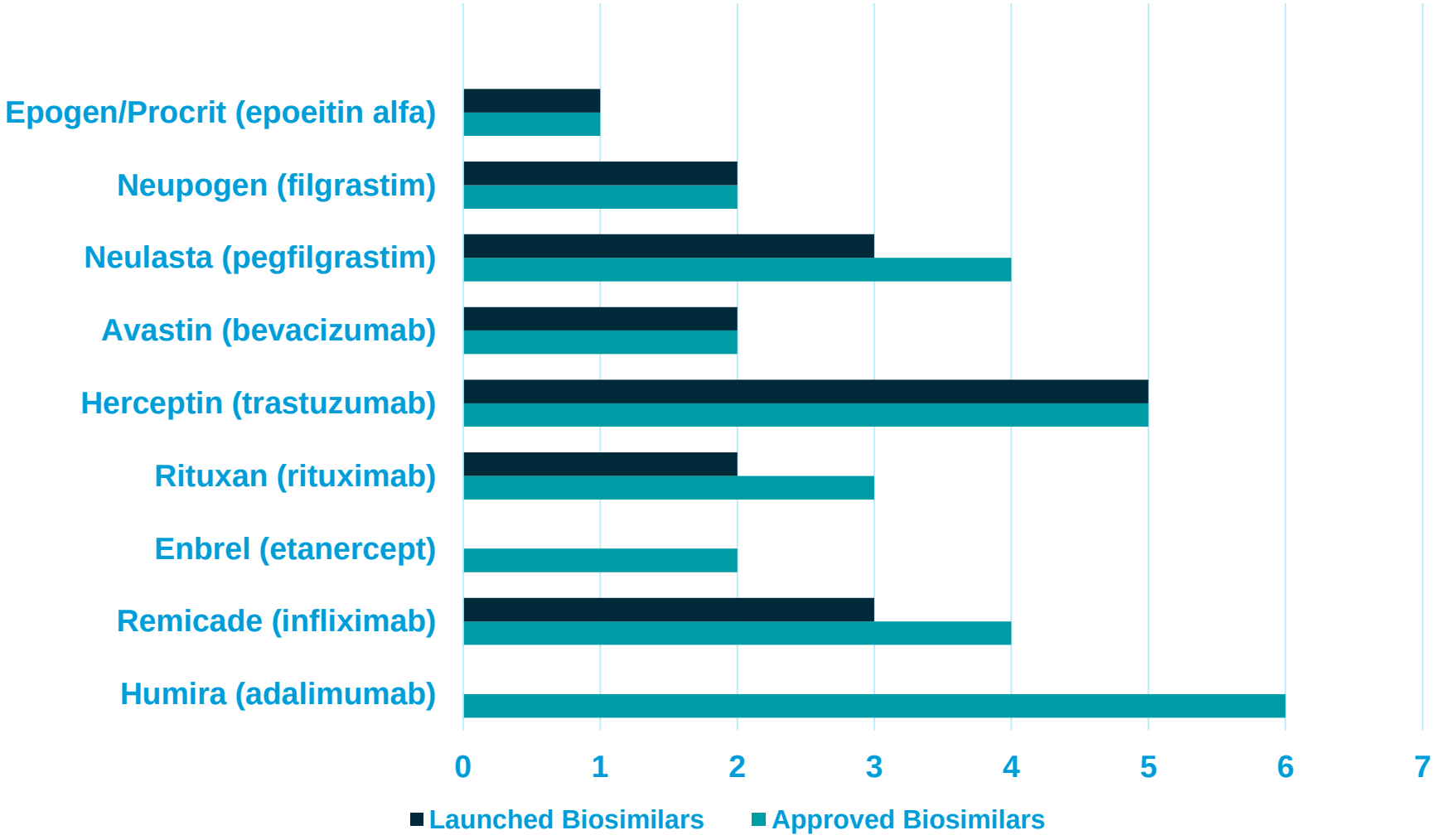
Only Three New Biosimilars Approved in 2020



Five Biosimilars Launched in 2020



Biosimilar Approvals Versus Launches through 2020



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	15%
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%
Avsola™	Remicade®	July 2020	57%

Biosimilar U.S. Market Share

Category	Reference Product	Number of Launched Biosimilars	Earliest Biosimilar Launch Date	Biosimilar Share by Volume
Oncology Therapeutics	Herceptin®	5	July 2019	40%
	Avastin®	2	July 2019	40%
	Rituxan®	2	Nov. 2019	20%
Supportive Care	Neulasta®	3	July 2018	28%
	Neupogen®	2	Sept. 2015	52%
	Epogen®/Procrit®	1	Nov. 2018	25%
Inflammation (anti-TNFα antibodies)	Remicade®	3	Nov. 2016	20%
	Humira®	0	Not yet launched	0%
	Enbrel®	0	Not yet launched	0%

Source: USA-CBU-80723-2020-Amgen-Biosimilar-Trends-Report.pdf (amgenbiosimilars.com) (market share data through 7/2020)

Regulatory Update

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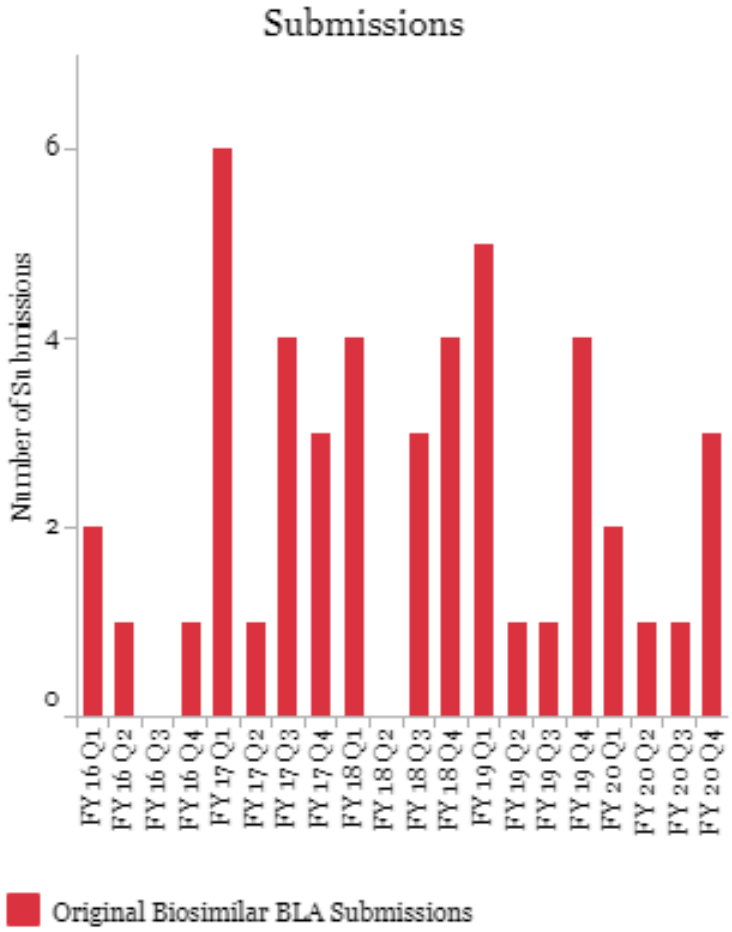
FDA Track – Biosimilars Dashboard



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

New Draft Guidance on Indications (Feb. 2020)

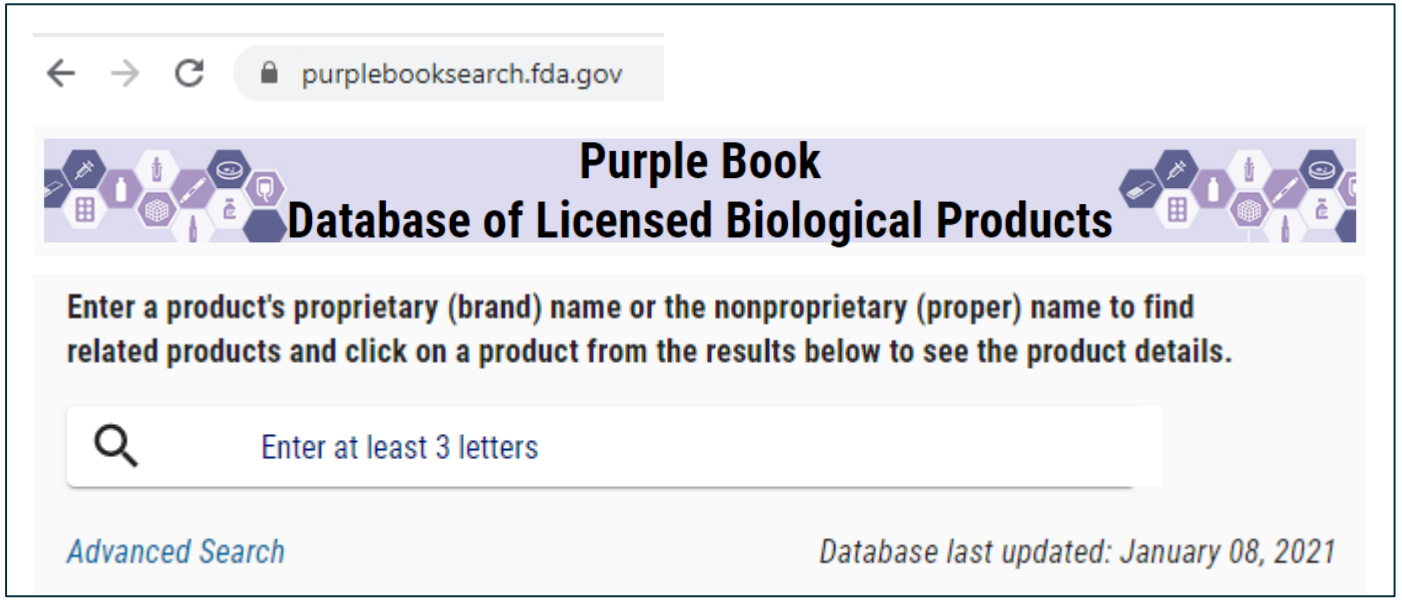
- "Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed"
  - "An applicant generally may obtain licensure of a biosimilar or interchangeable for *fewer* than all of the conditions of use for which the reference product 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."
  - Suggests that applicants wishing to delay licensure to avoid risk of patent infringement request that FDA refrain from acting until a specific date

“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 transitioned the Purple Book to a "searchable, public-facing online database"**
  - Goal: "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"
- **FDA released updates in several phases throughout 2020**



Purple Book Enhancements, Cont'd

- **Second COVID stimulus bill, signed into law on Dec. 27, 2020**
- **Amends the BPCIA**
  - Within 30 days of providing to a biosimilar during a patent dance, RPS must provide FDA with copies of any (l)(3)(A) or (l)(7) patent lists, along with patent expiration dates
  - FDA is to include the patent list and expiration dates in the Purple Book
  - FDA is also to include the following information for each approved biologic in the Purple Book: nonproprietary name, date of licensure and application number, licensure and marketing status, and exclusivities.

COVID-19 and Biologics/Biosimilars

- **Suspensions and Delays in Inspections**
  - Final decision on Biocon and Mylan's Avastin® biosimilar MYL-14020 was delayed because FDA was unable to conduct an inspection of the manufacturing facility due to COVID-19 travel restrictions.
- **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
  - August 2020: clarified how FDA is handling site inspections and provide insight into those inspections that are deemed "mission critical"
  - September 2020: describes "how to evaluate and prioritize remediation of current good manufacturing practice (CGMP) activities that were delayed, reduced, or otherwise modified" during the COVID-19 pandemic "in order to maintain production and the drug supply."
  - December 2020: addresses safety and compliance with good clinical practice (GCP) in clinical trials conducted during COVID-19

Litigation Update

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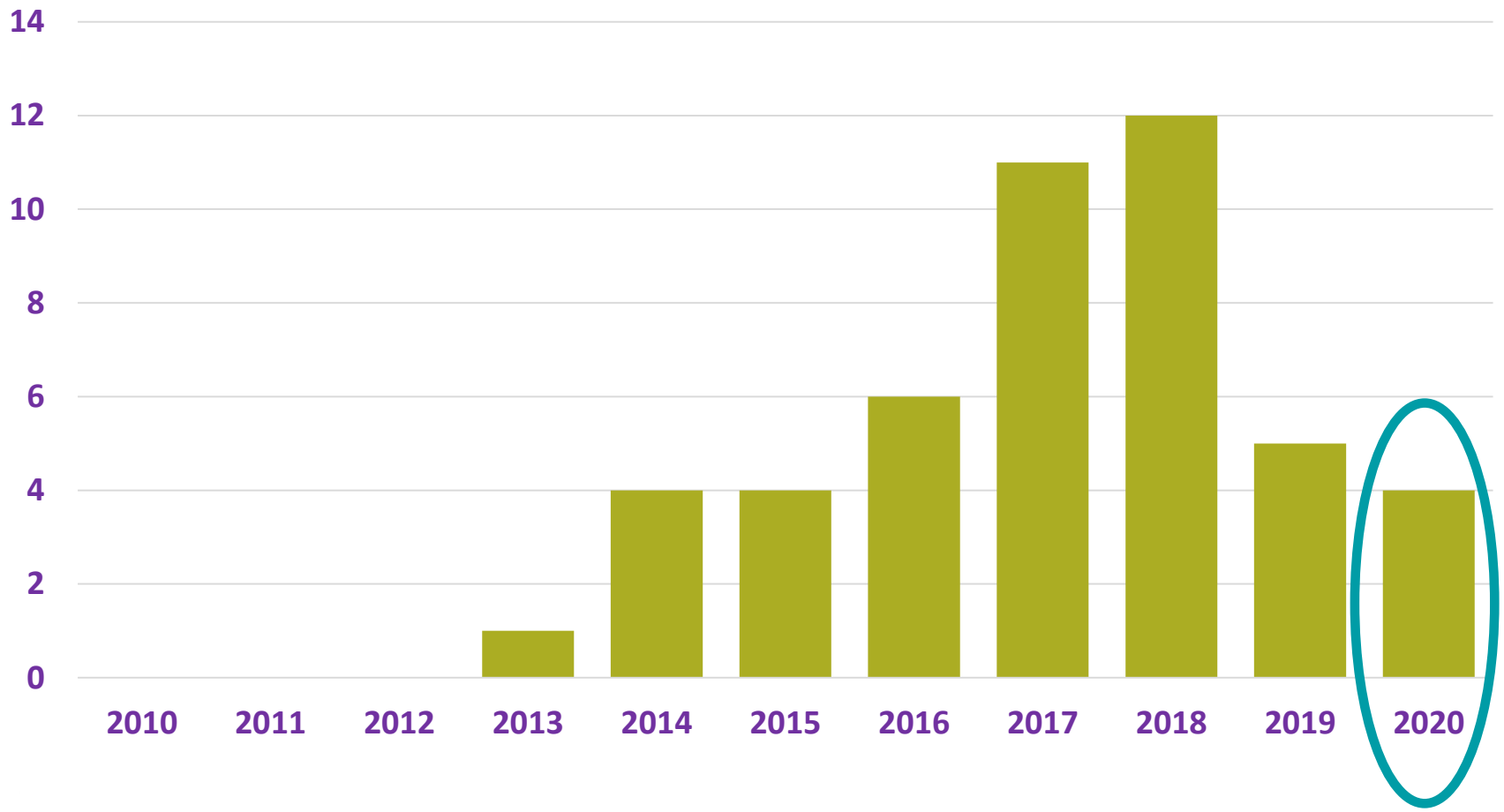
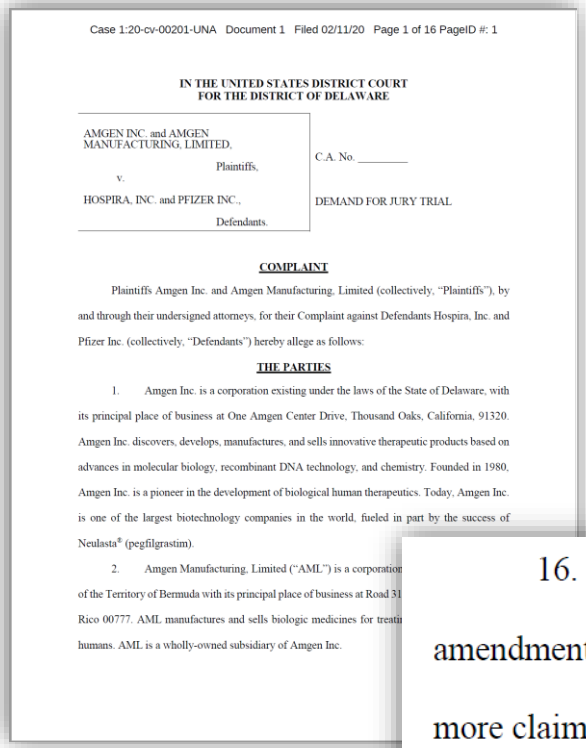
BPCIA District Court Cases By Year



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
Genentech v. Centus/Fujifilm	2-20-cv-00361 (E.D.Tex.)	Avastin®	Nov. 12, 2020

Amgen v. Hospira (D.Del.) - 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.

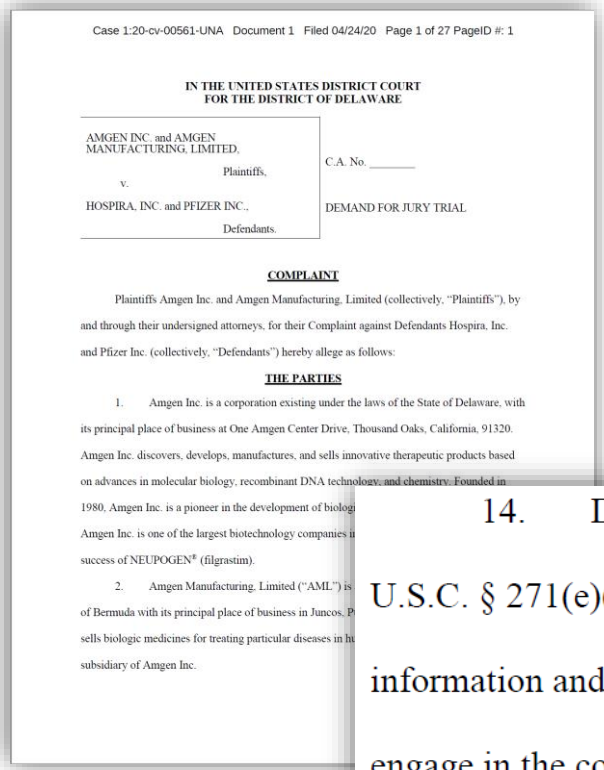
C.A. No. _____

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 (D.Del.) - 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 (D.Del.)

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC.

Plaintiff,

v.

SAMSUNG BIOEPIS CO. LTD.,

Defendant.

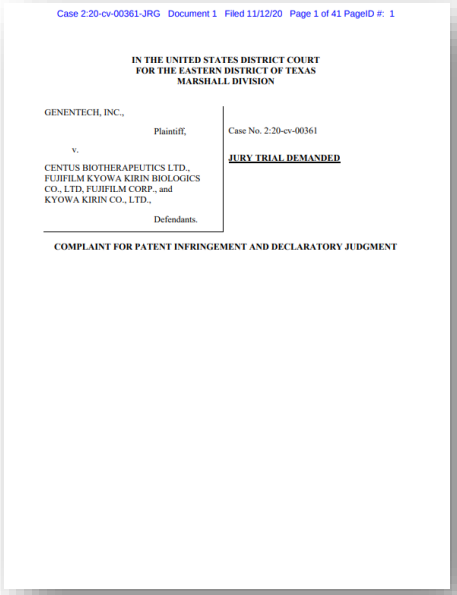
C. A. No. _____

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

Genentech v. Centus (E.D.Tex.)



Case 2:20-cv-00361-JRG Document 1 Filed 11/12/20 Page 1 of 41 PageID #: 1

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

GENENTECH, INC.,

Plaintiff,

v.

CENTUS BIOTHERAPEUTICS LTD., FUJIFILM KYOWA KIRIN BIOLOGICS CO., LTD, FUJIFILM CORP., and KYOWA KIRIN CO., LTD.,

Defendants.

Case No. 2:20-cv-00361

JURY TRIAL DEMANDED

COMPLAINT FOR PATENT INFRINGEMENT AND DECLARATORY JUDGMENT

Case 2:20-cv-00361-JRG Document 1 Filed 11/12/20 Page 1 of 41 PageID #: 1

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

GENENTECH, INC.,

Plaintiff,

v.

CENTUS BIOTHERAPEUTICS LTD., FUJIFILM KYOWA KIRIN BIOLOGICS CO., LTD, FUJIFILM CORP., and KYOWA KIRIN CO., LTD.,

Defendants.

Case No. 2:20-cv-00361

JURY TRIAL DEMANDED

COMPLAINT FOR PATENT INFRINGEMENT AND DECLARATORY JUDGMENT

8. This is an action for patent infringement arising under 35 U.S.C. § 271, including § 271(e)(2)(C)(ii), which was enacted in 2010 as part of the Biologics Price Competition and Innovation Act ("the BPCIA"), and for relief under the BPCIA. This action involves patents that cover bevacizumab (the active ingredient of the biologic drug product, Avastin®), its method of manufacture, certain materials used in its manufacture, and certain approved therapeutic uses of bevacizumab. Genentech brings this suit to enjoin Defendants from infringing its patents and to secure any recoverable damages resulting from Defendants' infringement.

BPCIA 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; attorney fee motion by Coherus denied
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; trial May 2021
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®	Stayed
Genentech v. Samsung Bioepis	20-cv-859 (D. Del.)	Avastin®	Motion to dismiss invalidity defenses and counterclaims pending
Genentech v. Centus/Fujifilm	2-20-cv-00361 (E.D.Tex.)	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.)**

- **Amgen 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 Disclosures - *Genentech v. Samsung Bioepis*

- **Genentech motion to dismiss affirmative defense and counterclaims re invalidity (Sept. 21, 2020)**
  - Samsung Bioepis did not provide invalidity statements for several asserted patents during the dance
  - Genentech argued that Samsung Bioepis cannot pursue patent invalidity arguments that were not identified in the patent dance
- **Parties dispute whether decision in *Genentech v. Amgen* broadly allows any new invalidity arguments**
  - Genentech argues that there should be a "good cause" requirement or else arguments are "forfeited"
- **Court has not yet ruled**

No Attorneys' Fees – Coherus and Amgen

- ***Coherus v. Amgen* (19-cv-00139 D. Del.)**
  - First biosimilar v. biosimilar litigation
  - Coherus asserted formulation patent against competitor biosimilar of Humira® (adalimumab)
  - Parties stipulated and agreed to dismissal
  - Amgen sought attorneys' fees because "Coherus "wrongful[ly], continued maintenance" of action for several months while allegedly knowing "its infringement claims were baseless"
  - June 11, 2020: motion for fees denied
- ***Amgen v. Coherus* (17-cv-00546 D. Del.)**
  - BPCIA litigation re Coherus' biosimilar Udenyca® (pegfilgrastim)
  - Dismissed at pleadings stage because of prosecution history estoppel; affirmed on appeal
  - Coherus sought attorneys' fees because of alleged weakness of Amgen's infringement case and Amgen's insistence on litigating all the way through appeal
  - Nov. 30, 2020: motion for fees denied

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, 19-1102)	Fed. Cir. **affirmed** (Dec. 16, 2019) Petition for rehearing *en banc* **denied** (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) Petition for rehearing *en banc* **denied** (Sept. 29, 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
  - July 2018: Judge Wolf of the District of Massachusetts granted Celltrion's motion for summary judgment of non-infringement based on ensnarement
- **Federal Circuit (CAFC 18-2321, 2350)**
  - Dec. 2018: Janssen appealed alleging district court engaged in hindsight in the obviousness analysis and failed to draw inferences in Janssen's favor
  - Feb. 2019: Celltrion cross-appealed on standing issues
  - March 4, 2020 – Oral Arguments
  - March 5, 2020 – Rule 36 Affirmance
- **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
- **Hospira appealed on multiple issues, including the safe harbor jury instructions and ruling**

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"**
  - 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
- **Petition for Rehearing En Banc denied Sept. 29, 2020**

IPR Update

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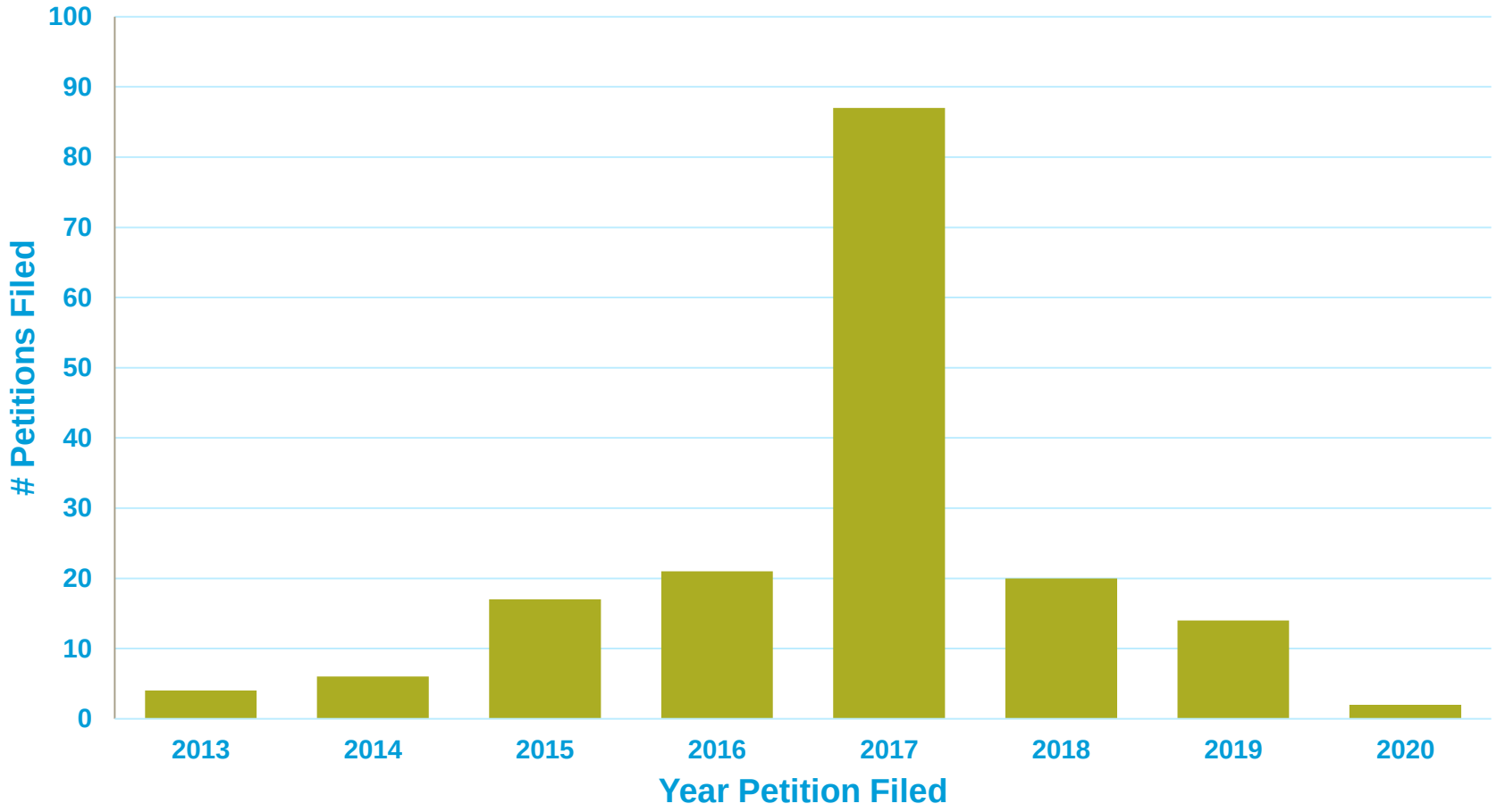
Only Two Biologic-Related IPRs in 2020



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**

Biologics IPRs at the Federal Circuit

- ***Genentech v. Hospira*, 946 F.3d 1333 (Fed. Cir. 2020)**
  - Affirmed IPR decision invalidating antibody manufacturing claims as anticipated and obvious
- ***Immunex v. Sanofi*, 977 F.3d 1212 (Fed. Cir. 2020)**
  - Affirmed IPR decision invalidating claims to isolated human antibodies for binding human IL-4 receptors as obvious
- ***Genentech v. Iancu*, 809 F. App'x 781 (Fed. Cir. 2020)**
  - Affirmed IPR decisions invalidating claims to methods of treatment using an anti-ErbB2 antibody
- ***AbbVie v. United States*, 789 F. App'x 879 (Mem), 2020 WL 91006 (Fed. Cir. 2020)**
  - Affirmed (Rule 36) IPR decisions invalidating claims to three patents directed to adalimumab as obvious
- ***Biogen, Inc. v. Iancu*, No. 2019-1364, 2020 WL 7381816 (Fed. Cir. Dec. 16, 2020)**
  - Affirmed (Rule 36) IPR decision invalidating method of treatment claim covering rituximab

Other Activity Related to Biosimilar Competition

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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 antitrust 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."

Humira® Antitrust Appeal (7th Cir. (20-2402))

STATEMENT OF THE ISSUES

1. Whether a global patent settlement wherein a brand manufacturer transfers hundreds of millions of dollars in overseas revenues to its biosimilar competitors in exchange for delayed domestic competition constitutes an unlawful restraint of trade under *Actavis*, 570 U.S. 136?

2. Whether asserting dozens of patents baselessly or meritlessly against competitors for the purpose of interfering with their business relations through the use of government processes constitutes sham petitioning under either *Professional Real Estate Investors, Inc. v. Columbia Pictures Industries, Inc.*, 508 U.S. 49 (1993) ("*PRE*") or *California Motor Transport Co. v. Trucking Unlimited*, 404 U.S. 508 (1972)?

Remicade® Antitrust Litigation Delayed

- **Multiple cases filed in 2017-2018 in E.D. Pa**
  - All allege that J&J/Janssen maintained market share and pricing for Remicade® through exclusionary contracts, anticompetitive bundling, and coercive rebates
- **In two cases (Pfizer and indirect purchasers as plaintiffs), fact discovery is ongoing and has been delayed due to COVID-19**
- **In third case (Walgreens plaintiff), Janssen/J&J did not answer until April 6, 2020**
  - Followed a granted motion to dismiss for lack of standing and reversal on appeal
  - Since then, delays to COVID-19

California Antitrust Bill (AB 824)

- Signed Oct. 2019, went into effect Jan. 1, 2020
- All settlements where biosimilar or generic receive "anything of value" are presumptively anticompetitive
- Provides for large civil penalties
- Challenged as unconstitutional and preempted by Federal law

Boehringer Ingelheim's Citizen Petition

VIA ELECTRONIC SUBMISSION

Boehringer Ingelheim

Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Citizen Petition Requesting the Food and Drug Administration to Make Strength Determinations for Parenteral Biologics Based Upon the Total Drug Content of the Container Without Regard to Concentration

On behalf of Boehringer Ingelheim Pharmaceuticals, Inc. ("Boehringer Ingelheim"), the undersigned hereby submits this Citizen Petition pursuant to 21 C.F.R. §§ 10.25 and 10.30 and section 351 of the Public Health Service Act ("PHS Act"), 42 U.S.C. § 262, to request the Commissioner of Food and Drugs to interpret the term "strength" in section 351(k) of the PHS Act for parenteral solutions to mean "total drug content," without regard to concentration. Such action is necessary to: (1) ensure the Food and Drug Administration's ("FDA's" or "the Agency's") interpretation is consistent with the clear meaning of the Biologics Price Competition and Innovation Act ("BPCIA"); (2) prevent abusive "evergreening" tactics from stifling competition of affordable biosimilar and interchangeable biological products; and (3) maintain fair and consistent treatment of all similarly situated parenteral biological products.

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 Labeling and Ads (Feb. 2020)

- Promotional material may be false or misleading if it 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

- 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 interchangeables

- 13 comments have been submitted

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.**

Federal Bills re Biosimilar Competition

- **Increasing Access to Biosimilars Act of 2020 (H.R. 6179 / S. 4134)**
  - "shared savings" model to encourage physicians to prescribe lower-cost biosimilars by offering providers a percentage of any net savings
- **ACCESS for Biosimilars Act of 2020 (S. 3466)**
  - waived all out-of-pocket expenses for biosimilar products for beneficiaries of Medicare Part B programs for the first 5 years that a biosimilar is on the market
- **Biosimilar Insulin Access Act of 2020 (H.R. 8190)**
  - allowed for biosimilar insulins to automatically be granted interchangeability designations to their reference products

Looking to 2021

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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.

New Biosimilar BLA Approvals?

Proposed Biosimilar	Reference Product	Nonproprietary Name	FDA Status
AVT02 (Alvotech)	Humira® (AbbVie)	adalimumab	BLA Accepted: November 2020
SB11 (Samsung Bioepis/Biogen)	Lucentis® (Roche)	ranibizumab	BLA Accepted: November 2020
MYL-14020 (Mylan/Biocon)	Avastin® (Roche)	bevacizumab	BLA Accepted: March 2020 FDA Goal Date: December 27, 2020, but delayed due to COVID-19 pandemic
SB8 (Samsung Bioepis)	Avastin® (Roche)	bevacizumab	BLA Accepted: November 2019
MSB11455 (Fresenius Kabi)	Neulasta® (Amgen)	pegfilgrastim	BLA Accepted: May 2020

First Interchangeable?

- **Semglee™, an insulin product comparable to Sanofi's Lantus®, was originally reviewed under an NDA**
- **In March 2020 it was "deemed" to be a BLA**
- **FDA approved Semglee™ in June 2020**
- **Biocon and Mylan launched Semglee™ in August 2020**
- **Mylan stated it filed "all necessary documentation" to the FDA for biosimilar approval under the 351(k) pathway**
- **Mylan stated it "remains confident in seeking an interchangeability designation" for the product as well.**

Source: https://www.centerforbiosimilars.com/view/biocon-launches-semglee-and-seeks-biosimilar-interchangeable-status

Thank You!

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