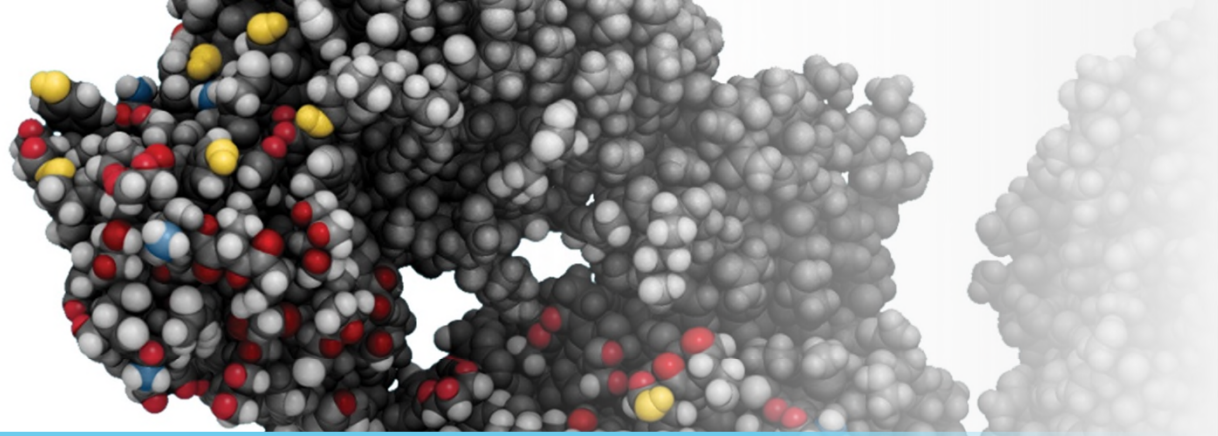
Morgan Lewis



BLOCKBUSTER BIOLOGICS REVIEW

Quarterly Update – April 2019

Christopher J. Betti, Ph.D.
Robin Silva
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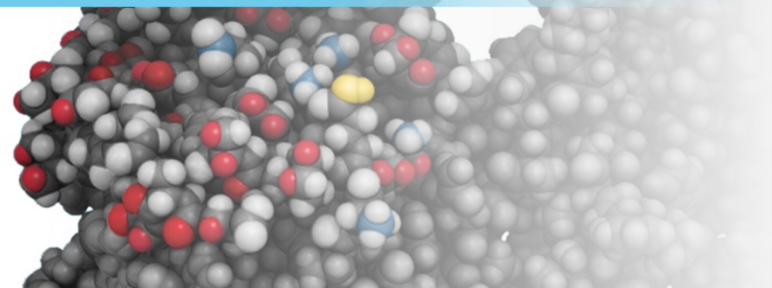

Quarterly Post-Grant and Patent Litigation Update

Welcome to our ongoing updates relating to biologics and biosimilars, including post-grant and patent litigation challenges to blockbuster biologics. We hope you find this 1Q 2019 update informative. As always, please feel free to reach out to us with any questions.

Chris, Robin, and Jennifer

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INTER PARTES REVIEWS

IPRs: Developments

- **Quick statistics:**
  - The current institution rate for IPR challenges to patents that claim biologics is 45% (excludes IPRs that have settled or otherwise been terminated)
  - Of those IPRs instituted and that have gone to final written decision (FWD), 47% have resulted in the challenged claims being held unpatentable, with 22% having mixed results

IPRs: Developments (cont.)

- **NEUPOGEN/NEULASTA IPR Update:**
  - Kashiv Biosciences (formerly Adello Biologics) filed two IPR petitions, IPR 2019-00791 and IPR 2019-00797, against two process patents owned by Amgen, US Patent Nos. 8,940,878 and 9,643,997
    - The patents are directed to methods to purify proteins expressed in a non-native soluble form in a non-mammalian expression system
  - Fresenius Kabi submitted an IPR petition (IPR 2019-00971) against US Patent No. 9,856,287 – a method patent owned by Amgen
    - Patent is directed to method for refolding proteins expressed in a non-mammalian expression system

IPRs: Developments (cont.)

- **RITUXAN IPR Update:**
  - Pfizer and Biogen terminated IPR 2018-00285 regarding US Patent No. 8,329,172 (the ’172 Patent) due to a settlement
    - The IPR was instituted in July 2018
    - The ’172 Patent is directed to methods for treating low-grade B-cell non-Hodgkin’s lymphoma
    - Although the ’172 Patent has been subjected to four IPRs including IPRs filed by Celltrion and Boehringer Ingelheim, none of them have reached an FWD

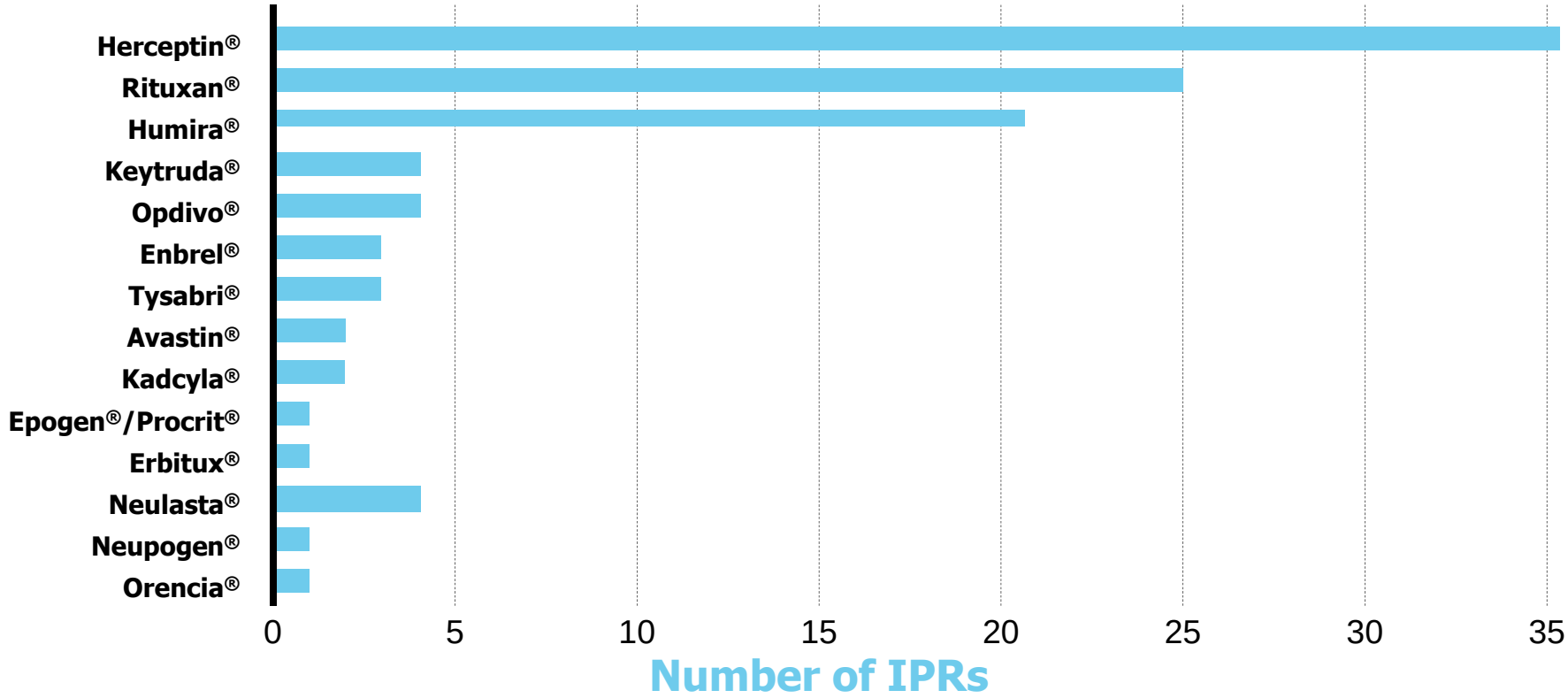
IPRs: Developments (cont.)

- **RITUXAN IPR Update:**
  - After successfully invalidating claims 1-5 of US Patent No. 8,821,873 (the ’873 Patent) in IPR No. 2017-01168, Pfizer filed notice that it will not participate in Biogen’s appeal of the FWD
    - Biogen’s appeal questions the constitutionality of IPRs
    - The United States has filed a notice to intervene in the appeal to defend the constitutionality of IPRs
    - The claims of the ’873 Patent are generally drawn to methods of treating patients with diffuse large B-cell lymphoma by administering an anti-CD20 antibody and CHOP (cyclophosphamide, hydroxydaunorubicin/doxorubicin, vincristine, and prednisone/prednisolone)

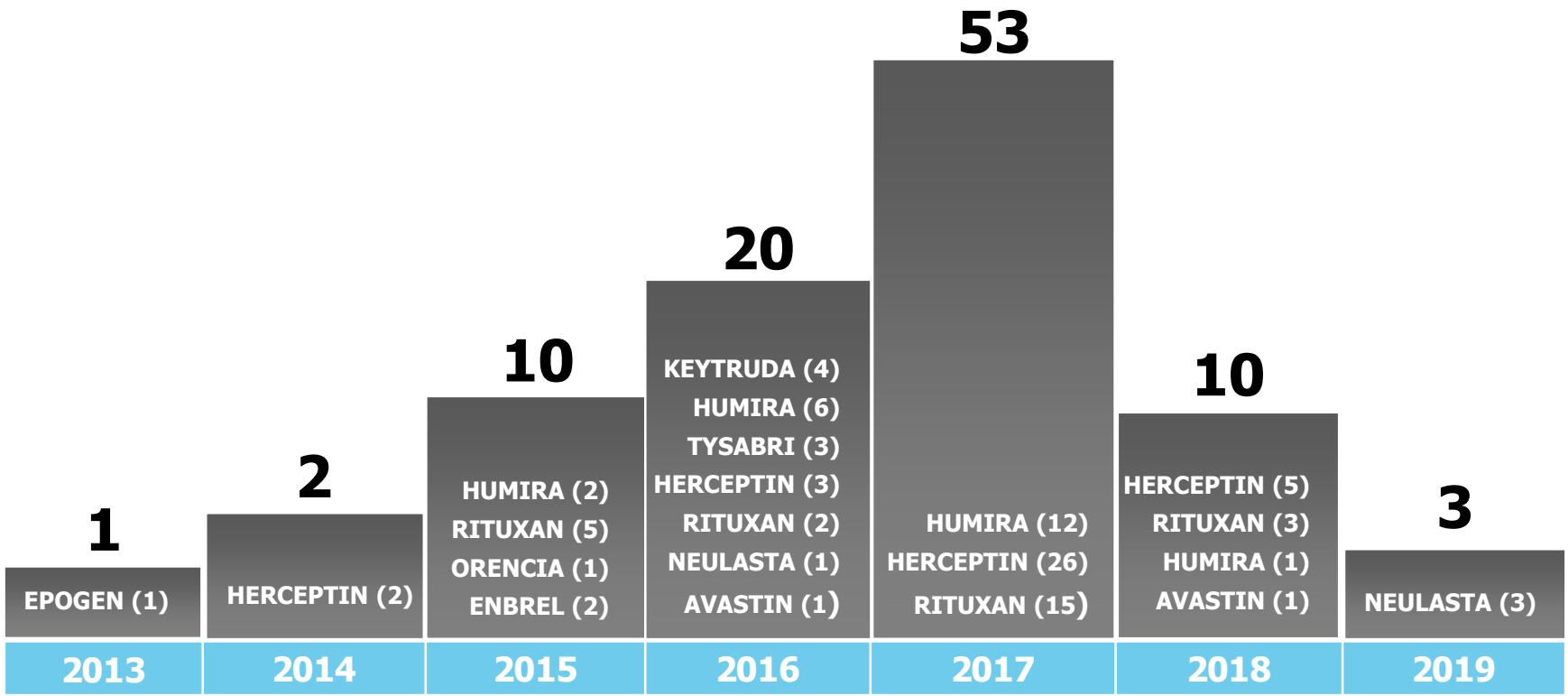
IPRs: Developments (cont.)

- **ORENCIA IPR Update:**
  - Federal Circuit dismissed Momenta's appeal of the FWD upholding the claims of US Patent No. 8,476,239 for lack of standing/jurisdiction and for mootness
    - BMS filed a letter with the court in December 2018, including documents that Momenta has filed with the SEC stating that it terminated its collaboration with Mylan to develop a biosimilar to Orencia

IPRs by Reference Product

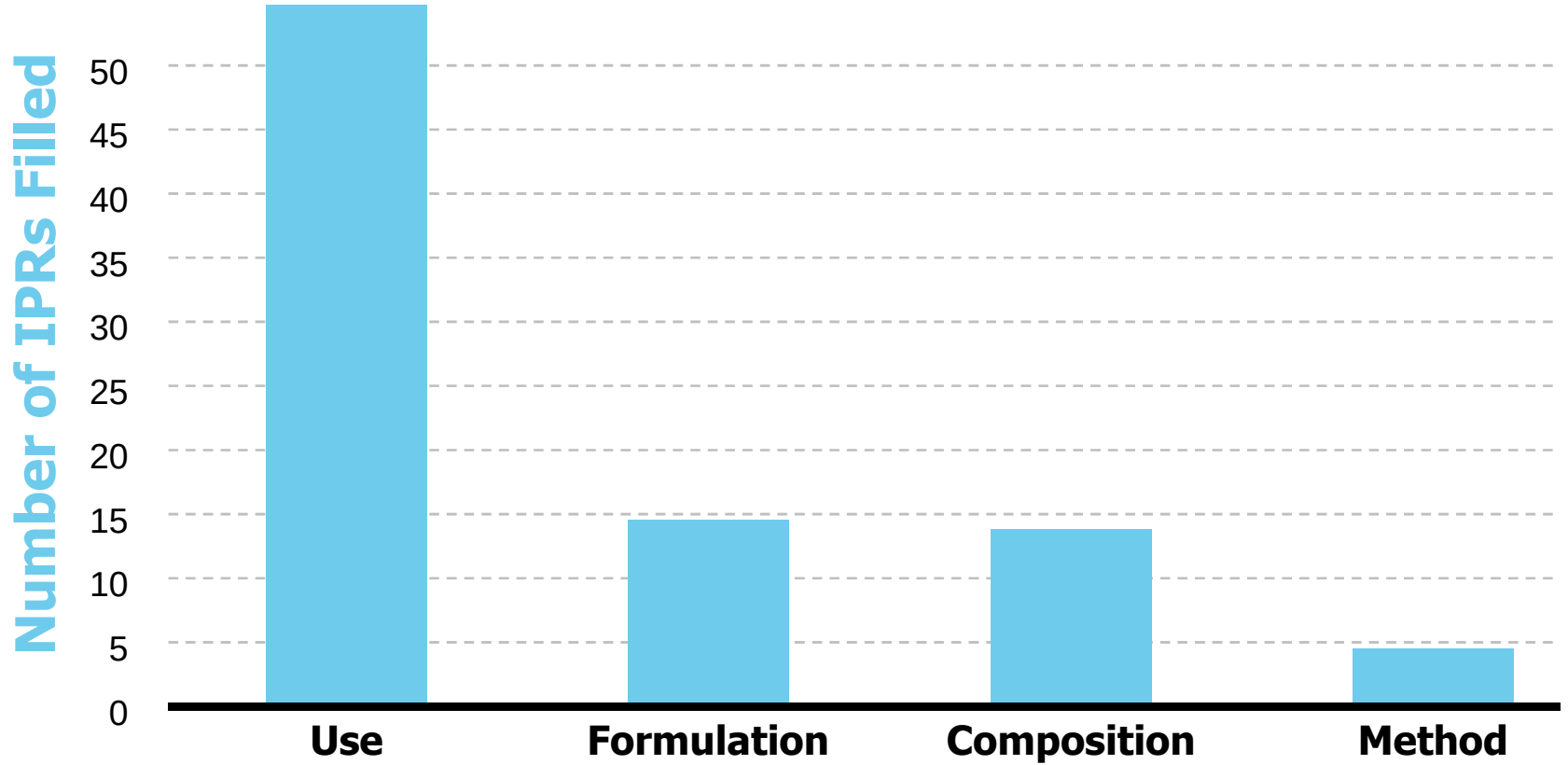


IPR Timeline



PTO Fiscal Year
(September–October)

Types of Claims Being Challenged



IPR Scorecard – Institution

Product (# IPRs)	Challenger	Pend. Inst.	Pet. Not Inst.	Sett. Term.	Inst.*
Humira (22)	Amgen	0	2	-	-
	BI	0	-	-	2
	Coherus	0	5	2	3
	Sandoz	0	6	2	-
Rituxan (27)	BI	0	1	2	-
	Celltrion	0	6	2	3
	Pfizer	0	5	3	3
	Sandoz	0	2	-	-
Herceptin (36)	Phigenix	0	1	-	1
	Mylan	0	-	2	-
	Hospira	0	1	-	5
	Celltrion	0	-	1	6
	Pfizer	0	5	2	4
	Samsung	0	1	-	5
	BI	0	-	2	-
Tysabri (3)	Swiss Pharma	0	3	-	-

Institution rate* = 35/78 = 45%

**** IPRs instituted but later settled or otherwise terminated are not included***

IPR Scorecard – Institution (cont.)

Product (# IPRs)	Challenger	Pend. Inst.	Pet. Not Inst.	Sett. Term.	Inst.*
Avastin (2)	Hospira	0	1	-	1
Orencia (1)	Momenta	0	-	-	1
Neulasta (4)	Apotex	0	-	-	1
	Fresenius Kabi	1	-	-	-
	Kashiv Biosciences	2	-	-	-
Enbrel (3)	Kyle Bass	0	1	-	-
	Coherus	0	2	-	-
Epogen (1)	Hospira	0	-	1	-
Keytruda (4)	Merck	0	0	4	-
TOTALS		3	42	23	35

Institution rate* = 35/78 = 45%

**** IPRs instituted but later settled or otherwise terminated are not included***

IPR Scorecard – FWDs

Product (# IPRs)	**Challenger**	**Inst.***	**FWD** (invalid)	**FWD** (upheld)	**Mixed**
Humira (22)	Amgen	-	-	-	-
	BI	**2**	**2**	-	-
	Coherus	**3**	**3**	-	-
	Sandoz	-	-	-	-
Rituxan (27)	BI	-	-	-	-
	Celltrion	**3**	**1**	**1**	-
	Pfizer	**3**	**1**	**1**	-
	Sandoz	-	-	-	-
Herceptin (36)	Phigenix	**1**	-	**1**	-
	Mylan	-	-	-	-
	Hospira	**5**	**3**	**2**	-
	Celltrion	**6**	**2**	**2**	**2**
	Pfizer	**4**	**1**	-	**2**
	Samsung	**5**	**1**	**2**	**2**
	BI	-	-	-	-

Invalidation rate = 15/32 = 47%, w/ mixed results 22%

**** IPRs instituted but later settled or otherwise terminated are not included***

IPR Scorecard – FWDs (cont.)

Product (# IPRs)	Challenger	Inst.*	FWD (invalid)	FWD (upheld)	Mixed
Tysabri (3)	Swiss Pharma	-	-	-	-
Avastin (2)	Hospira	1	1	-	-
Orencia (1)	Momenta	1	-	1	-
Neulasta (4)	Apotex	1	-	-	1
Enbrel (3)	Kyle Bass	-	-	-	-
	Coherus	-	-	-	-
Epogen (1)	Hospira	-	-	-	-
Keytruda (4)	Merck	-	-	-	-
TOTALS		35	15	10	7

Invalidation rate = 15/32 = 47%, w/ mixed results 22%

**** IPRs instituted but later settled or otherwise terminated are not included***

Blockbuster Biologics: IPR Appeals (Humira)

Patent Owner	Challenger	Patent No.	Biologic	IPR No. (Appeal No.)	Decision Appealed	Status of Appeal
AbbVie	Coherus	8,889,135	**Humira**	2016-00172 (2017-2304)	Claims Invalid	• All of these appeals have been consolidated • AbbVie challenged the constitutionality of the application of the America Invents Act (AIA) in these cases • US Attorney General has intervened • Coherus withdrew as party due to settlement • Patent and Trademark Office (PTO) intervened
AbbVie	Boehringer Ingelheim	8,889,135	**Humira**	2016-00408 (2017-2362)	Claims Invalid	
AbbVie	Boehringer Ingelheim	8,889,135	**Humira**	2016-00409 (2017-2363)	Claims Invalid	
AbbVie	Coherus	9,017,680	**Humira**	2016-00188 (2017-2305)	Claims Invalid	
AbbVie	Coherus	9,017,987	**Humira**	2016-00189 (2017-2306)	Claims Invalid	

Blockbuster Biologics: IPR Appeals (Rituxan)

Patent Owner	Challenger	Patent No.	Biologic	IPR No. (Appeal No.)	Decision Appealed	Status of Appeal
Genentech	Celltrion	7,820,161	**Rituxan**	2016-1614 (2018-1885) 2017-01115 joined (2018-1924)	Claims Valid	• Issues briefed – Motion to Strike Pfizer's Reply Brief pending • Appeal No. 2018-1924 dismissed as part of litigation settlement (Case No. 18-574-RMB-KMW (D.N.J.)) • Appeal No. 2016-1614 voluntarily dismissed
Biogen	Pfizer	8,821,873	**Rituxan**	2017-01168 (2018-1885)	Claims Invalid	• Biogen challenging constitutionality of IPRs • Pfizer not participating in appeal • United States intervening in appeal • Parties voluntarily dismissed appeal

Blockbuster Biologics: IPR Appeals (Herceptin)

Patent Owner	Challenger	Patent No.	Biologic	IPR No. (Appeal No.)	Decision Appealed	Status of Appeal
Genentech	Hospira	7,807,799	**Herceptin**	2016-01837 (2018-1933)	Claims Invalid	• Includes constitutional challenge regarding retroactive application of IPR to pre-AIA patent • United States intervened • Issues have been briefed
Genentech	Hospira	7,846,441	**Herceptin**	2017-00731 (2019-1263)	Claims Invalid	• Hospira moved to withdraw as party due to settlement • PTO allowed to intervene
Genentech	Celltrion	7,846,441	**Herceptin**	2017-01121 (2019-1267)	Claims Invalid	• Briefing not yet started • PTO allowed to intervene
Genentech	Hospira	6,627,196	**Herceptin**	2017-00804/ No. 2017-01958 joined (2019-1173)	Claims Valid	• Lead case – consolidated with 2019-1174 • Briefing not yet started

Blockbuster Biologics: IPR Appeals (Herceptin) (cont.)

Patent Owner	Challenger	Patent No.	Biologic	IPR No. (Appeal No.)	Decision Appealed	Status of Appeal
Genentech	Hospira	7,371,379	**Herceptin**	2017-00805/ No. 2017-01959 joined (2019-1174)	Claims Valid	• Consolidated with 2019-1173 • Briefing not yet started
Genentech	Celltrion	6,627,196	**Herceptin**	2017-01139 (2019-1258)	Claims Valid	• Consolidated with 2019-1259 • Parties dismissed appeal
Genentech	Celltrion	7,371,379	**Herceptin**	2017-01140 (2019-1259)	Claims Valid	• Consolidated with 2019-1258 • Parties dismissed appeal
Genentech	Hospira	7,892,549	**Herceptin**	2017-00737/ No. 2017-01960 joined (2019-1265)	Claims Invalid	• Hospira withdrew as party due to settlement
Genentech	Celltrion	7,892,549	**Herceptin**	2017-01122 (2019-1270)	Claims Invalid	• Briefing not yet started • PTO allowed to intervene

Blockbuster Biologics: IPR Appeals (Avastin)

Patent Owner	Challenger	Patent No.	Biologic	IPR No. (Appeal No.)	Decision Appealed	Status of Appeal
Genentech	Hospira	7,622,115	**Avastin**	2016-01771 (2018-1959)	Claims Invalid	• Includes constitutional challenge regarding retroactive application of IPR to pre-AIA patent • United States intervened • Issues have been briefed

Blockbuster Biologics: IPR Appeals (Orencia)

Patent Owner	Challenger	Patent No.	Biologic	IPR No. (Appeal No.)	Decision Appealed	Status of Appeal
Bristol-Myers Squibb	Momenta	8,476,239	Orencia	2015-01537 (2017-1694)	Claims Valid	• Federal Circuit dismissed appeal for lack of standing/jurisdiction and for mootness

Post-Grant Reviews (PGRs)

> Only one PGR has been filed to date in connection with a blockbuster biologic

Product (# IPRs)	**Challenger**	**Pend. Inst.**	**Pet. Not Inst.**	**Sett. Term.**	**Inst.**
Neupogen (1)	Adello/Apotex	1	-	-	**-**

US BIOSIMILAR-RELATED PATENT LITIGATIONS

US Biosimilar Litigations: Developments

- **HUMIRA Litigation:**
  - Coherus and AbbVie entered into a settlement agreement granting Coherus a global, non-exclusive, royalty-bearing license to AbbVie's intellectual property to commercialize its Humira biosimilar
    - The settlement resolved all disputes pending between the parties related to Coherus's Humira biosimilar
    - Coherus's US license will begin December 15, 2023
    - Coherus anticipates filing an aBLA for its biosimilar in late 2019
  - Coherus filed a complaint and an amended complaint against Amgen, No. 19-00139 (D. Del.), alleging infringement of US Patent Nos. 10,155,039, 10,159,732, and 10,159,733 through the commercial manufacture of Amgevita in the United States
    - The patents claim stable aqueous pharmaceutical compositions comprising adalimumab and other components
    - Litigation underscores the importance of biosimilars developing robust patent positions

US Biosimilar Litigations: Developments (cont.)

> Summary of Humira Biosimilar Settlements

Party	US Market Entry	EP Market Entry
Amgen	January 31, 2023	October 16, 2018
Biogen and Samsung Bioepis	June 30, 2023	October 16, 2018
Mylan	July 31, 2023	– – –
Sandoz	September 30, 2023	October 16, 2018
Fresenius Kabi	September 30, 2023	Upon approval
Momenta	November 20, 2023	– – –
Pfizer	November 20, 2023	– – –
Coherus	December 15, 2023	– – –

US Biosimilar Litigations: Developments (cont.)

HUMIRA Litigation:

- Three antitrust lawsuits have been filed against AbbVie accusing the company of illegally shielding Humira from competition through its creation of a thicket of more than 100 "overlapping and unoriginal" patents and of entering into unlawful pay-for-delay agreements to keep biosimilars of Humira off of the market
  - *UFCW Local 1500 Welfare Fund v. AbbVie, et al.*, No. 19-01873 (N.D. Ill.) – Class Action Suit
  - *Fraternal Order of Police, Miami Lodge 20, Insurance Trust Fund v. AbbVie, et al.*, No. 19-01933 (N.D. Ill.) – Class Action Suit
  - *Mayor and City Council of Baltimore v. AbbVie, et al.*, No. 19-02015 (N.D. Ill.) – Class Action Suit

US Biosimilar Litigations: Developments (cont.)

- **NEUPOGEN/NEULASTA Litigation:**
  - *Sandoz v. Amgen*, No. 19-00977 (N.D. Cal.)
    - Sandoz filed a complaint for declaratory judgment of noninfringement and invalidity of US Patent No. 9,643,997 directed to capture purification processes for proteins expressed in a non-mammalian system
- **NEULASTA Litigation:**
  - *Amgen v. Apotex*, No. 18-61828 (S.D. Fla.) – Apotex's Motion to Dismiss Amgen's Complaint based on collateral estoppel and prosecution history disclaimer was denied
    - District court found that it was inappropriate to apply collateral estoppel to preclude Amgen from arguing a different meaning for claim terms previously construed in a different case because the claim language in the newly asserted patent was different
    - District court also found that the prosecution statements cited by Apotex did not show a clear and unmistakable surrender of subject matter
- **AVASTIN Litigation:**
  - *Genentech v. Pfizer*, No. 19-00638 (D. Del.) – New lawsuit filed by Genentech on April 5, 2019

US Biosimilar Litigations: Developments (cont.)

- Products in patent litigation that we are monitoring include:
  - Humira
  - Rituxan
  - Herceptin
  - Neupogen
  - Neulasta
  - Enbrel
  - Epogen
  - Avastin
  - Remicade
- These litigations are summarized on the following slides

Blockbuster Biologics: US Litigation Scorecard – Humira

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Humira (4)	*AbbVie v. Amgen*	No. 16-666-MSG (D. Del.)	10	M, F, U, C	• Settled – US launch of Amjevita expected January 31, 2023
	AbbVie v. Boehringer Ingelheim	No. 17-1065-SLR (D. Del.)	8	M, F, U, C	• In discovery – Expert discovery will close on May 29, 2020 • Claim construction briefing filed
	AbbVie v. Sandoz	No. 18-12668 (D.N.J.)	2	U, F	• Settled – US launch of Hyrimoz expected September 20, 2023
	Coherus v. Amgen	No. 19-00139 (D. Del.)	3	C	• Amended complaint filed March 5, 2019

Blockbuster Biologics: US Litigation Scorecard – Rituxan

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Rituxan (4)	*Genentech v. Sandoz*	No. 17-13507-RMB-KMW (D.N.J.)	24	M, U, C	• Stipulated Dismissal without prejudice • Sandoz decided not to pursue its FDA submission for its biosimilar
	Celltrion v. Genentech	No. 18-276-JSW (N.D. Cal.) No. 18-2161 (Fed. Cir.) (consolidated with No. 18-2160)	37	M, U	• Genentech's Motion to Dismiss granted • Final Judgment appealed to Federal Circuit • Appeal voluntarily dismissed
	Genentech v. Celltrion	No. 18-574-RMB-KMW (D.N.J.)	40	M, U, C	• Settled
	Genentech v. Celltrion	No. 18-11553 (D.N.J.) (consolidated with No. 18-574-RMB-KMW)	18 (Claims mirror those of No. 18-574 – filed to ensure compliance with BPCIA)	M, U, C	• Settled

Blockbuster Biologics: US Litigation Scorecard – Herceptin

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Herceptin (6)	*Celltrion v. Genentech*	No. 18-274-JSW (N.D. Cal.) No. 18-2160 (Fed. Cir.)	38	M, U, C	• Genentech's Motion to Dismiss granted • Final Judgment appealed to Federal Circuit • Appeal voluntarily dismissed
	Genentech v. Celltrion	No. 18-095-CFC (D. Del.)	40	M, U, C	• All of the Delaware cases are before Judge Connolly and being coordinated • *Markman* hearing April 2019 • Trial set for December 2019 • Lead case • Settled
	Genentech v. Pfizer	No. 17-1672-CFC (D. Del.)	40	M, U, C	• Settled

Blockbuster Biologics: US Litigation Scorecard – Herceptin (cont.)

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Herceptin (6)	*Genentech v. Amgen*	No. 18-924-CFC (D. Del.)	37	M, U, C	• Early discovery • Claim Construction being briefed
	Genentech v. Celltrion	No. 18-1025-CFC (D. Del.)	40	M, U, C	• Settled
	Genentech v. Samsung Bioepis	No. 18-01363-CFC (D. Del.)	21	M, U, C	• Answer to Complaint filed • Motion to Dismiss Unenforceability Count for Failure to State a Claim filed • Claim Construction being briefed

Blockbuster Biologics: US Litigation Scorecard – Neupogen

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Neupogen (5)	*Amgen v. Sandoz*	No. 14-04741-RS (N.D. Cal.) No. 15-1499 (Fed. Cir.) Nos. 15-1039, 15-1195 (Supreme Court) No. 18-1551 (Fed. Cir.)	1	M	• Complaint alleged Sandoz violated the BPCIA by (1) failing to provide its aBLA and manufacturing information within 20 days of FDA acceptance and (2) providing notice of commercial marketing before FDA approval of its aBLA • District Court ruled in favor of Sandoz; on appeal, Federal Circuit and Supreme Court did the same • District Court subsequently granted Sandoz's Motion for Summary Judgment of Non-infringement, currently on appeal
	Amgen v. Apotex	No. 15-62081-JIC (S.D. Fla.)	2	M, C	• Consolidated with *Amgen v. Apotex* pegfilgrastim (Neulasta) litigation, No. 15-61631, where District Court entered judgment of non-infringement for Sandoz • Affirmed

Blockbuster Biologics: US Litigation Scorecard – Neupogen (cont.)

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Neupogen (5)	*Amgen v. Adello*	No. 18-3347-JMV-SCM (D.N.J.)	17	M	• Amended Complaint filed, reducing number of patents to four and naming Amneal Pharmaceuticals as co-defendant • Amneal moved to dismiss Amended Complaint for failure to state a claim and lack of subject matter jurisdiction
	Amgen v. Hospira	No. 18-1064 (D. Del.)	1	M	• Scheduling Order issued: Close of fact discovery is August 23, 2019 • *Markman* hearing is set for May 15, 2019 • Trial is set for June 15, 2020
	Sandoz v. Amgen	No. 19-00977 (N.D. Cal.)	1	M	• Complaint filed February 2019

Blockbuster Biologics: US Litigation Scorecard – Neulasta

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Neulasta (6)	*Amgen v. Apotex*	No. 15-61631-JIC (S.D. Fla.) No. 16-1308 (Fed. Cir.) No. 17-1010 (Fed. Cir.) No. 16-332 (Supreme Court)	2	M, F	• Amgen found not to infringe • Supreme Court denied Apotex's Petition for Certiorari • Federal Circuit affirmed district court ruling • District Court: 1) Granted Amgen's Motion for Summary Judgment re: invalidity defenses except non-enablement 2) Awarded judgment of non-infringement for Apotex 3) Dismissed Apotex's non-enablement defense without prejudice
	Amgen v. Sandoz	No. 16-1276-SRC-CLW (D.N.J.)	Litigation over whether Sandoz violated BPCIA	NA	• Dismissed after Sandoz restarted patent dance negotiations

Blockbuster Biologics: US Litigation Scorecard – Neulasta (cont.)

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Neulasta (6)	*Amgen v. Sandoz*	No. 16-02581-RS (N.D. Cal.) No. 18-1552 (Fed. Cir.) consolidated with No. 18-1551	2	M, F	• On appeal, fully briefed, pending scheduling of oral argument • Summary Judgment of Non-infringement granted for Sandoz • Oral argument held March 4, 2019
	Amgen v. Coherus	No. 17-546-LPS (D. Del.) No. 18-1993 (Fed. Cir.)	1	M	• Court granted Coherus's Motion to Dismiss for Failure to State a Claim • Judgment entered against Amgen and case dismissed • On appeal, briefing stage • Oral argument scheduled for May 8, 2019

Blockbuster Biologics: US Litigation Scorecard – Neulasta (cont.)

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Neulasta (6)	*Amgen v. Mylan*	No. 17-1235-MRH (W.D. Pa.)	2	M	• Claim Construction Order issued • Amgen ordered to file with infringement contentions a statement identifying facts relied on outside of Mylan's FDA filings • Motion for Summary Judgment of Non-infringement of US Patent No. 9,643,997 filed
	Amgen v. Apotex	No. 18-61828 (S.D. Fla.)	1	M	• District Court denied Apotex's motion to dismiss Amgen's complaint for failure to state a claim

Blockbuster Biologics: US Litigation Scorecard – Enbrel

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Enbrel (1)	*Immunex v. Sandoz*	No. 16-01118-CCC-JBC (D.N.J.)	5	C, F, U	• Before trial, Sandoz stipulated to infringement to certain asserted claims of two of the five patents-in-suit • Bench trial held September 2018

Blockbuster Biologics: US Litigation Scorecard – Epogen

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Epogen (1)	*Amgen v. Hospira*	No. 15-839-RGA (D. Del.) No. 16-2179 (Fed. Cir.) (appeal was dismissed) No. 19-1067 and No. 19-1102 (Fed. Cir.)	2	C, M	• Jury found infringement and awarded $70M in damages • Final judgment entered with pre- and post-judgment interest • Hospira appealed, arguing that all of its batches of product should be subject to the safe harbor provision about which the jury was given erroneous instructions • Amgen responded that there was sufficient evidence supporting the jury's finding that only 7 of the 21 drug batches qualified for safe harbor

Blockbuster Biologics: US Litigation Scorecard – Avastin

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Avastin (5)	*Genentech v. Amgen*	No. 17-165-GMS (D. Del.)	Litigation over violations of the BPCIA	NA	• Dismissed Complaint without prejudice
	Amgen v. Genentech	No. 17-7349-GW-AGR (C.D. Cal.)	27	M, C, F, U	• Genentech's Motion to Dismiss for Lack of Subject Matter Jurisdiction granted
	Genentech v. Amgen	No. 17-1407-CFC (D. Del.)	24	M, C, F, U	• Early pleadings and discovery • Consolidated with No. 17-1471 • Lead case • Post-*Markman* Claim Construction Brief filed • Trial set for July 13, 2020 • Hearing scheduled for April 23, 2019 regarding discovery dispute related to Amgen's proposed expert
	Genentech v. Amgen	No. 17-1471-CFC (D. Del.)	25	M, C, F, U	• Consolidated with No. 17-1407
	Genentech v. Pfizer	No. 19-00638-CFC (D. Del.)	22	M, C, F, U	• Complaint filed April 5, 2019

Blockbuster Biologics: US Litigation Scorecard – Remicade

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Remicade (5)	*Janssen v. Celltrion*	No. 15-10698-MLW (D. Mass.) No. 17-1120 (Fed. Cir.)	2	C, U	• Partial Summary Judgment of Invalidity granted with respect to one patent ('471 patent) • Federal Circuit dismissed appeal as moot upon affirming decision in appeal (No. 17-1257) from ex parte reexamination ruling by USPTO that same patent's claims are unpatentable for double patenting • Dismissed without prejudice in favor of Case No. 17-11008
	Janssen v. Celltrion	No. 16-11117-MLW (D. Mass.)	1	M (cell culture media)	• Dismissed without prejudice in favor of Case No. 17-11008
	Janssen v. HyClone	No. 16-00071-BCW (D. Utah)	1	M (cell culture media)	• Stayed pending resolution of D. Mass. case

Blockbuster Biologics: US Litigation Scorecard – Remicade (cont.)

Product (# litigations)	Case Name	Case No. (Jurisdiction)	# of Asserted Patents	Types of Claims	Status
Remicade (5)	*Janssen v. Celltrion*	No. 17-11008 (D. Mass.) No. 18-2350 (Fed. Cir.) Lead appeal (No. 18-2321)	1	M (cell culture media)	• Judgment entered for defendants after court allowed Motion for Summary Judgment of Non-infringement based on ensnarement • On appeal (both parties)
	Janssen v. Samsung Bioepis	No. 17-3524-MCA-SCM (D.N.J.)	3	M	• Janssen voluntarily dismissed its patent infringement claims • Suit dismissed with prejudice

LEGISLATIVE UPDATES

Legislative Updates

- **Proposed Legislation:**
  - FDA Naming Guidance
    - FDA will add unique suffixes to the active-ingredient names of interchangeable as well as regular biosimilars
    - FDA will not require suffixes for originator biologics already approved without suffixes, but has been requiring suffixes for newer originator biologics and will continue to do so going forward

Legislative Updates (cont.)

- **Proposed Legislation:**
  - Biologic Patent Transparency Act (BPTA) introduced in March 2019
    - Will require holders of approved products, including biosimilars, to disclose for publication in the Purple Book the patents that they believe could be asserted as infringed by the holder
    - The Purple Book would include patents listed during the patent dance
    - The Purple Book would be a single searchable list also including information on biosimilarity and interchangeability, approved indications, and information on exclusivities
    - Certain claims of infringement related to late-filed patents by the biologic manufacturer would be barred if the patents are not timely disclosed where a biosimilar application has already been filed

BIOSIMILAR APPROVALS AND LAUNCHES

US Biosimilar Approvals – 18 total

Drug Name	Approval Date
Trazimera (trastuzumab-qyyp)	March 2019
Ontruzant (trastuzumab-dttb)	January 2019
Herzuma (trastuzumab-pkrb)	December 2018
Truxima (rituximab-abbs)	November 2018
Udenyca (pegfilgrastim-cbqv)	November 2018
Hyrimoz (adalimumab-adaz)	October 2018
Nivestym (filgrastim-aafi)	July 2018
Fulphila (pegfilgrastim-jmdb)	June 2018
Retacrit (epoetin alfa-epbx)	May 2018

Drug Name	Approval Date
Ixifi (infliximab-qbtx)	December 2017
Ogivri (trastuzumab-dkst)	December 2017
Mvasi (bevacizumab-awwb)	September 2017
Cyltezo (adalimumab-adbm)	August 2017
Renflexis (infliximab-abda)	May 2017
Amjevita (adalimumab-atto)	September 2016
Erelzi (etanercept-szzs)	August 2016
Inflectra (infliximab-dyyb)	April 2016
Zarxio (filgrastim-sndz)	March 2015

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Our Global Reach

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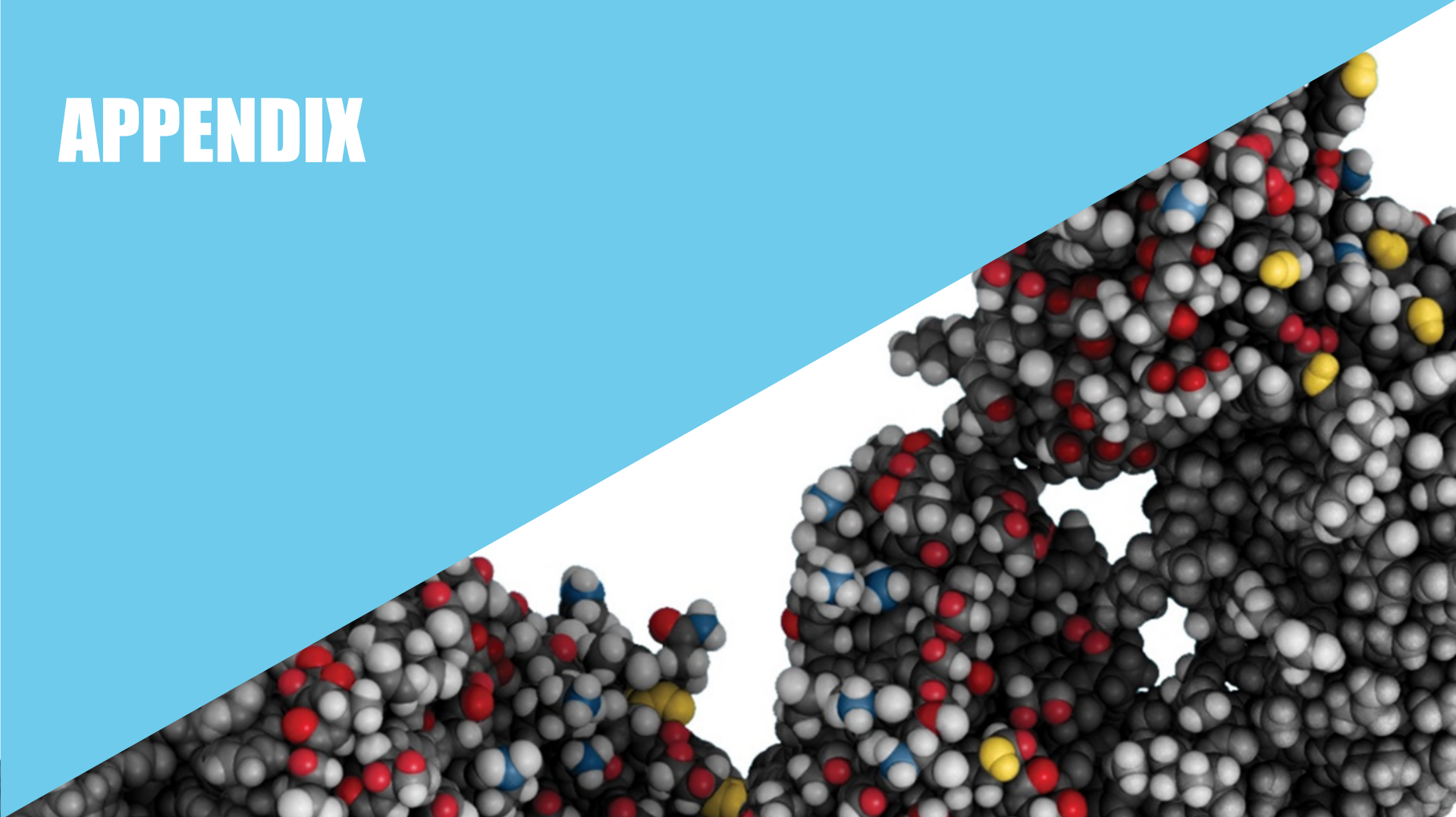
THANK YOU

APPENDIX



Legend

P	Petitioner
PO	Patent Owner
2-Consid.	Secondary Considerations raised by Patent Owner to support nonobviousness
U	Use
F	Formulation
C	Composition
M	Method
FWD	Final Written Decision
Pending	IPR has been instituted and is pending an FWD
Pending Inst. Dec.	IPR has been filed and is pending a decision on institution
Institution Denied	PTAB has denied institution of IPR
J/W	Joined with
NA	Not Applicable
Y/N	Yes / No

HUMIRA

Humira-Related IPRs

> 22 IPRs filed challenging 14 different patents

AbbVie Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,916,157	Amgen	2015-01514	1/0	Y	F (20-150 mg)	Institution Denied
8,916,158	Amgen	2015-01517	1/0	Y	F (20-150 mg)	Institution Denied
8,889,135	1) Coherus	1) 2016-00172	1) 2/5	1) Y	1) U (RA)	1) FWD – Claims Invalid (Appealed)
	2) Boehringer Ingelheim	2) 2016-00408	2) 2/5	2) Y	2) U	2) FWD – Claims Invalid (Appealed)
	3) Boehringer Ingelheim	3) 2016-00409	3) 2/5	3) Y	3) U	3) FWD – Claims Invalid (Appealed)
9,017,680	Coherus	2016-00188	3/5	Y	U (RA)	FWD – Claims Invalid (Appealed)
9,073,987	Coherus	2016-00189	3/5	Y	U (RA)	FWD – Claims Invalid (Appealed)

Humira-Related IPRs

> 22 IPRs filed challenging 14 different patents

AbbVie Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
9,114,166	Coherus	2016-01018	2/0	Y	F (50 mg)	Institution Denied
9,085,619	Coherus	1) 2017-00822 2) 2017-00823 3) 2017-00826 4) 2017-00827 5) 2017-01008 6) 2017-01009	1) 1/0 2) 1/0 3) 2/NA 4) 2/NA 5) 2/0 6) 2/0	1) Y 2) N 3) Y 4) Y 5) Y 6) Y	F (Bufferless)	1-2) Institution Denied 3-4) IPRs Dismissed April 11, 2017 * 5-6) Institution Denied
9,067,992	Sandoz	2017-02106	1/1	Y	U (Psoriatic arthritis)	Terminated due to settlement
8,911,737	Sandoz	2017-01987	6/0	Y	U (Crohn's)	Institution Denied
8,974,790	Sandoz	2017-01988	6/0	Y	U (Ulcerative colitis)	Institution Denied
9,090,689	Sandoz	2017-02105	3/2	Y	U (Plaque psoriasis)	Terminated due to settlement

*** IPRs 2017-01008 & 2017-01009 replaced IPRs 2017-00826 & 2017-00827**

Humira-Related IPRs

> 22 IPRs filed challenging 14 different patents

AbbVie Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,802,100	Sandoz	2017-01823	1/0	N	F (45-150 mg)	Institution Denied
9,512,216	Sandoz	1) 2017-01824 2) 2018-00002	1) 2/0 2) 2/0	1) Y 2) Y	U (Plaque psoriasis)	1) Institution Denied 2) Institution Denied
9,187,559	Sandoz	2018-00156	2/0	Y	U (IBD)	Institution Denied

8,916,157 Patent IPR

Representative Claim

1. A stable liquid aqueous pharmaceutical formulation comprising
   a) a human IgG1 anti–human Tumor Necrosis Factor alpha (TNFα) antibody, or an antigen-binding portion thereof, at a concentration of 20 to 150 mg/ml,
   b) a tonicity agent,
   c) a surfactant, and
   d) a buffer system having a pH of 4.0 to 8.0, wherein the antibody comprises the light chain variable region (LCVR) and the heavy chain variable region (HCVR) of D2E7.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Amgen	2015-01514	1-8, 10-13, 15-30	None	1/0	Y	F	Institution Denied

8,916,158 Patent IPR

Representative Claim

1. A stable liquid aqueous pharmaceutical formulation comprising
   a) a human IgG1 anti–human TNFα antibody, or an antigen-binding portion thereof, at a concentration of 20 to 150 mg/ml,
   b) a tonicity agent,
   c) a surfactant, and
   d) a buffer system having a pH of 4.0 to 8.0, wherein the antibody comprises the LCVR and HCVR of D2E7.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Amgen	2015-01517	1-8, 10-13, 15-30	None	1/0	Y	F	Institution Denied

8,889,135 Patent IPRs

Representative Claim

1. A method for treating rheumatoid arthritis in a human subject by administering subcutaneously a total body dose of 40 mg of a human anti-TNFα antibody once every 13–15 days for a period sufficient to treat the rheumatoid arthritis, wherein the anti-TNFα antibody comprises an IgG1 heavy chain constant region; a variable light (V_L) chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:7, a CDR2 having the amino acid sequence of SEQ ID NO:5, and a CDR3 having the amino acid sequence of SEQ ID NO:3; and a variable heavy (V_H) chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:8, a CDR2 having the amino acid sequence of SEQ ID NO:6, and a CDR3 having the amino acid sequence of SEQ ID NO:4.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coherus	2016-00172	1-5	§ 103 for all claims	2/5	N	U	FWD – Claims Invalid (Appealed)
Boehringer Ingelheim	2016-00408	1-5	§ 103 for all claims	2/5	Y	U	FWD – Claims Invalid (Appealed)
Boehringer Ingelheim	2016-00409	1-5	§ 103 for all claims	2/5	Y	U	FWD – Claims Invalid (Appealed)

9,017,680 Patent IPR

Representative Claim

1. A method of reducing signs and symptoms in a patient with moderately to severely active rheumatoid arthritis, comprising:

   a) administering to said patient, in combination with methotrexate, a human anti-TNFα antibody,

   b) wherein the human anti-TNFα antibody is administered subcutaneously in a total body dose of 40 mg once every 13–15 days, and

   c) wherein the anti-TNFα antibody comprises an IgG1 heavy chain constant region; a VL chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:7, a CDR2 having the amino acid sequence of SEQ ID NO:5, and a CDR3 having the amino acid sequence of SEQ ID NO:3; and a VH chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:8, a CDR2 having the amino acid sequence of SEQ ID NO:6, and a CDR3 having the amino acid sequence of SEQ ID NO:4.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coherus	2016-00188	1-4	§ 103 for all claims	3/5	N	U	FWD – Claims Invalid (Appealed)

9,073,987 Patent IPR

Representative Claim

1. A method of reducing signs and symptoms in a patient with moderately to severely active rheumatoid arthritis, comprising:

   a) administering to said patient a total body dose of 40 mg of a human anti-TNFα antibody,

   b) wherein the dose is administered subcutaneously from a 40 mg dosage unit form once every 13–15 days, and

   c) wherein the anti-TNFα antibody comprises an IgG1 heavy chain constant region; a V_L chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:7, a CDR2 having the amino acid sequence of SEQ ID NO:5, and a CDR3 having the amino acid sequence of SEQ ID NO:3; and a V_H chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:8, a CDR2 having the amino acid sequence of SEQ ID NO:6; and a CDR3 having the amino acid sequence of SEQ ID NO:4.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coherus	2016-00189	1-2	§ 103 for all claims	3/5	N	U	FWD – Claims Invalid (Appealed)

9,114,166 Patent IPR

Representative Claim

1. A stable liquid aqueous pharmaceutical formulation comprising a human anti–human TNFα IgG1 antibody at a concentration of 50 mg/ml, wherein the antibody comprises the LCVR and HCVR of D2E7, and a buffer system; wherein the formulation is isotonic, suitable for single-use subcutaneous injection, and has a pH of 4.0 to 8.0.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coherus	2016-01018	1-4, 6-10, 13-16, 23-26, 28	None	2/0	Y	F	Institution Denied

9,085,619 Patent IPRs

Representative Claim

16. An aqueous pharmaceutical formulation comprising:

a) an anti-TNFα antibody comprising an LCVR having a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7; and an HCVR having a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, wherein the concentration of the antibody is 50 to 200 mg/ml; and

b) water; wherein the formulation does not comprise a buffering system.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coherus	2017-00822	16-19, 24-30	NA	1/0	Y	F	Institution Denied
Coherus	2017-00823	16-19, 24-30	NA	1/0	N	F	Institution Denied

9,085,619 Patent IPRs (cont.)

Representative Claim

16. An aqueous pharmaceutical formulation comprising:

a) an anti-TNFα antibody comprising an LCVR having a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7; and an HCVR having a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, wherein the concentration of the antibody is 50 to 200 mg/ml; and

b) water; wherein the formulation does not comprise a buffering system.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coherus	2017-00826	16-19, 24-30	NA	2/NA	Y	F	Dismissed
Coherus	2017-00827	16-19, 24-30	NA	2/NA	Y	F	Dismissed
Coherus	2017-01008	16-19, 24-30	NA	2/1	Y	F	Institution Denied
Coherus	2017-01009	16-19, 24-30	NA	2/1	Y	F	Institution Denied

9,067,992 Patent IPR

Representative Claim

1. A method of treatment of moderate to severe active psoriatic arthritis in adult patients, wherein each said patient has ≧3 swollen and ≧3 tender joints prior to the treatment and has failed NSAID therapy, comprising subcutaneously administering to each said patient 40 mg of adalimumab every other week, wherein 23% of said patients achieve 70% reduction in American College of Rheumatology (ACR) score at week 24 of the treatment.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2017-02106	1, 2, 5-7	§ 102 for claims 1, 5, 6 § 103 for all claims	1/1	Y	U	Terminated

8,911,737 Patent IPR

Representative Claim

1. A method for treating Crohn's disease in a human subject by administering subcutaneously a total body dose of 40 mg of a human anti-TNFα antibody once every 13–15 days for a period sufficient to treat Crohn's disease, wherein the anti-TNFα antibody comprises an IgG1 heavy chain constant region; a VL chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:7, a CDR2 having the amino acid sequence of SEQ ID NO:5, and a CDR3 having the amino acid sequence of SEQ ID NO:3; and a VH chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:8, a CDR2 having the amino acid sequence of SEQ ID NO:6, and a CDR3 having the amino acid sequence of SEQ ID NO:4.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2017-01987	1-6	NA	6/0	Y	U	Institution Denied

8,974,790 Patent IPR

Representative Claim

1. A method for treating ulcerative colitis in a human subject by administering subcutaneously a total body dose of 40 mg of a human anti-TNFα antibody once every 13–15 days for a period sufficient to treat the ulcerative colitis, wherein the anti-TNFα antibody comprises an IgG1 heavy chain constant region; a VL chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:7, a CDR2 having the amino acid sequence of SEQ ID NO:5, and a CDR3 having the amino acid sequence of SEQ ID NO:3; and a VH chain region comprising a CDR1 having the amino acid sequence of SEQ ID NO:8, a CDR2 having the amino acid sequence of SEQ ID NO:6, and a CDR3 having the amino acid sequence of SEQ ID NO:4.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2017-01988	1-6	NA	6/0	Y	U	Institution Denied

9,090,689 Patent IPR

Representative Claim

1. A method of administering adalimumab for treatment of moderate to severe chronic plaque psoriasis by filling adalimumab into vessels and subcutaneously administering 40 mg of said adalimumab every other week.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2017-02105	1, 4, 7, 10, 13, 16, 19	§ 103 for all claims	3/2	Y	U	Terminated

8,802,100 Patent IPR

Representative Claim

1. A stable liquid aqueous pharmaceutical formulation comprising
   a) a human IgG1 anti–human TNFα antibody, or an antigen-binding portion thereof, at a concentration of 45 to 150 mg/ml,
   b) a polyol,
   c) a polysorbate at a concentration of 0.1 to 10 mg/ml, and
   d) a buffer system having a pH of 4.5 to 7.0, wherein the antibody comprises the LCVR and HCVR of D2E7.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2017-01823	1-29	NA	1/0	N	F	Institution Denied

9,512,216 Patent IPRs

Representative Claim

1. A method for treating moderate to severe chronic plaque psoriasis by subcutaneously administering to an adult patient an initial dose of 80 mg of adalimumab, followed by 40 mg of adalimumab every other week, starting one week after said first dosing, wherein the patient achieves at least Psoriasis Area and Severity Index (PASI) 75 response at week 12 of the treatment.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2017-01824	1-16	NA	2/0	Y	U	Institution Denied
Sandoz	2018-00002	1-16	NA	2/0	Y	U	Institution Denied

9,187,559 Patent IPR

Representative Claim

1. A multiple-variable dose method for treating idiopathic inflammatory bowel disease in a human subject in need thereof, comprising subcutaneously administering to the human subject:

    a) a first dose of 160 mg of adalimumab administered to the human subject within a day; and

    b) a second dose of 80 mg of adalimumab administered to the human subject within a day, wherein the second dose is administered two weeks following administration of the first dose.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2018-00156	1-30	NA	2/0	Y	U	Institution Denied

RITUXAN

Rituxan-Related IPRs

> 27 IPRs filed challenging 10 different patents

Genentech/ Biogen Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
7,820,161	1) BI	1) 2015-00415	1) 1/0	1) Y	1) U (RA)	1) Petitioner's adverse judgment
	2) Celltrion	2) 2015-01744	2) 1/0	2) Y	2) U	2) Petitioner filed Motion to Dismiss
	3) Celltrion	3) 2016-01614	3) 2/1	3) Y	3) U	3) FWD – Claims Valid
	4) Pfizer	4) 2017-01115	4) 3/NA	4) Y	4) U	4) FWD – Claims Valid (J/W '614)
7,976,838	1) BI	1) 2015-00417	1) 1/0	1) Y	1) U (RA)	1) Petitioner's adverse judgment
	2) Celltrion	2) 2015-01733	2) 1/0	2) Y	2) U	2) Petition filed Motion to Dismiss
	3) Celltrion	3) 2016-01667	3) 2/0	3) Y	3) U	3) Institution Denied
	4) Pfizer	4) 2017-01923	4) 3/1	4) Y	4) U	4) Terminated - Settled
	5) Sandoz	5) 2017-02042	5) 2/0	5) Y	5) U	5) Institution Denied
	6) Sandoz	6) 2017-02036	6) 2/0	6) Y	6) U	6) Institution Denied
	7) Celltrion	7) 2018-01019	7) 3/0	7) Y	7) U	7) Instituted

Rituxan-Related IPRs

> 27 IPRs filed challenging 10 different patents

Genentech/ Biogen Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,329,172	1) BI 2) Celltrion 3) Pfizer 4) Pfizer	1) 2015-00418 2) 2017-01093 3) 2017-01166 4) 2018-00285	1) 1/0 2) 2/0 3) 2/0 4) 2/1	1) Y 2) Y 3) Y 4) Y	1) U (lymphoma) 2) U 3) U 4) U	1) Institution Denied 2) Institution Denied 3) Institution Denied 4) Terminated - Settled
8,557,244	1) Celltrion 2) Pfizer	1) 2017-01094 2) 2017-01167	1) 2/0 2) 2/0	1) Y 2) Y	1) U (lymphoma) 2) U	1) Institution Denied 2) Institution Denied
9,296,821	1) Celltrion 2) Pfizer	1) 2017-01095 2) 2018-00186	1) 2/0 2) 2/1	1) Y 2) Y	1) U (lymphoma) 2) U	1) FWD – Claims Invalid 2) Terminated

Rituxan-Related IPRs

> 27 IPRs filed challenging 10 different patents

Genentech/ Biogen Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
7,682,612	1) Celltrion 2) Celltrion 3) Pfizer	1) 2017-01227 2) 2017-01230 3) 2017-02126	1) 1/0 2) 1/0 3) 2/0	1) Y 2) Y 3) Y	1) U (leukemia) 2) U 3) U	1) Institution Denied 2) Institution Denied 3) Institution Denied
8,206,711	1) Celltrion 2) Pfizer	1) 2017-01229 2) 2017-02127	1) 1/0 2) 2/0	1) Y 2) Y	1) U (leukemia) 2) U	1) Institution Denied 2) Institution Denied
8,821,873	Pfizer	2017-01168	2/1	Y	U (lymphoma)	FWD – Claims Invalid
8,545,843	Pfizer	2018-00086	2/0	Y	U (vasculitis)	Institution Denied
9,504,744	Pfizer	2018-00231	2/0	Y	U (lymphoma)	Terminated

7,820,161 Patent IPRs

Representative Claim

1. A method of treating rheumatoid arthritis in a human by administering:
   a) more than one intravenous dose of a therapeutically effective amount of rituximab; and
   b) methotrexate.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Boehringer Ingelheim	2015-00415	1-12	§ 103 for claims 1, 2, 5, 6, 9, and 10	1/0	Y	U	Adverse Judgment
Celltrion	2015-01744	1, 2, 5, 6, 9, and 10	None	1/0	Y	U	Dismissed

7,820,161 Patent IPRs

Representative Claim

1. A method of treating rheumatoid arthritis in a human by administering:
   a) more than one intravenous dose of a therapeutically effective amount of rituximab; and
   b) methotrexate.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Celltrion	2016-01614	1-12	§ 103 for claims 1-3, 5-7, 9-11	2/1	Y	U	FWD – Claims Valid Celltrion's appeal dismissed as part of litigation settlement (Case No. 18-574-RMB-KMW (D.N.J.))
Pfizer	2017-01115	1-12	§ 103	3/NA	Y	U	FWD – Claims Valid (J/W '614)

7,976,838 Patent IPRs

Representative Claim

1. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor by administering an antibody that binds to CD20, wherein the antibody is administered as two intravenous doses of 1,000 mg.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Boehringer Ingelheim	2015-00417	1-14	§ 103 for all claims	1/0	Y	U	Adverse Judgment
Celltrion	2015-01733	1-14	NA	1/0	Y	U	Dismissed
Celltrion	2016-01667	1-14	NA	2/0	Y	U	Institution Denied
Pfizer	2017-01923	1-14	§ 103 for all claims	3/1	Y	U	Terminated - Settled

7,976,838 Patent IPRs

Representative Claim

1. A method of treating rheumatoid arthritis in a human patient who experiences an inadequate response to a TNFα-inhibitor by administering an antibody that binds to CD20, wherein the antibody is administered as two intravenous doses of 1,000 mg.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Sandoz	2017-02036	1-14	NA	2/0	Y	U	Institution Denied
Sandoz	2017-02042	1-14	NA	2/0	Y	U	Institution Denied
Celltrion	2018-01019	1-14	§ 103 for all claims	3/0	Y	U	Instituted

8,329,172 Patent IPRs

Representative Claim

1. A method of treating low-grade B-cell non-Hodgkin's lymphoma (NHL) in a human patient by administering chemotherapy consisting of cyclophosphamide, vincristine, and prednisone (CVP therapy) to which the patient responds, followed by rituximab maintenance therapy, wherein the maintenance therapy comprises four weekly administrations of rituximab at a dose of 375 mg/m^2 every six months, and wherein the maintenance therapy is provided for two years.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Boehringer Ingelheim	2015-00418	1	NA	1/0	N	U	Institution Denied
Celltrion	2017-01093	1	NA	2/0	Y	U	Institution Denied
Pfizer	2017-01166	1	NA	2/0	Y	U	Institution Denied
Pfizer	2018-00285	1	§ 103	2/1	Y	U	Terminated - Settled

8,557,244 Patent IPRs

Representative Claim

1. A method of treating a patient with diffuse large-cell lymphoma by administering an unlabeled chimeric anti-CD20 antibody and CHOP (cyclophosphamide, hydroxydaunorubicin/doxorubicin, vincristine, and prednisone/prednisolone) chemotherapy to the patient, wherein the patient is >60 years old and has bulky disease (tumor >10 cm in diameter).

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Celltrion	2017-01094	1-2	NA	2/0	Y	U	Institution Denied (Request for Rehearing Denied)
Pfizer	2017-01167	1-2	NA	2/0	Y	U	Institution Denied

9,296,821 Patent IPRs

Representative Claim

1. A method for treating low-grade or follicular NHL by administering to a patient a therapeutically effective amount of rituximab during a chemotherapeutic regimen, wherein the chemotherapeutic regimen consists of CVP therapy, wherein the method comprises administering 375 mg/m^2 of rituximab, and wherein the method provides a beneficial synergistic effect in the patient.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Celltrion	2017-01095	1-6	§ 102 for all claims § 103 for all claims	2/0	Y	U	FWD – Claims Invalid
Pfizer	2018-00186	1-6	§ 102 for claims 4-6 § 103 for all claims	2/1	Y	U	Terminated

7,682,612 Patent IPRs

Representative Claim

1. A method of treating chronic lymphocytic leukemia (CLL) in a human patient by administering an anti-CD20 antibody in an amount effective to treat the CLL, wherein the method does not include treatment with a radiolabeled anti-CD20 antibody.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Celltrion	2017-01227	23-57	NA	1/0	Y	U	Institution Denied
Celltrion	2017-01230	1-22, 58-60	NA	1/0	Y	U	Institution Denied
Pfizer	2017-02126	1-13, 15-35, 37-60	NA	2/0	Y	U	Institution Denied

8,206,711 Patent IPRs

Representative Claim

1. A method of treating CLL in a human patient by administering rituximab in an amount effective to treat the CLL, wherein the rituximab is administered to the patient at a dosage of 500 mg/m^2.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Celltrion	2017-01229	1-9	NA	1/0	Y	U	Institution Denied
Pfizer	2017-02127	1-9	NA	2/0	Y	U	Institution Denied

8,821,873 Patent IPR

Representative Claim

1. A method of treating a patient with diffuse large-cell lymphoma by administering anti-CD20 antibody and chemotherapy, wherein the patient is >60 years old, wherein the chemotherapy comprises CHOP, and wherein the anti-CD20 antibody is administered in combination with a stem cell transplantation regimen.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2017-01168	1-5	§ 103	2/1	Y	U (lymphoma)	FWD – Claims Invalid

8,545,843 Patent IPR

Representative Claim

1. A method of treating vasculitis in a human who does not have rheumatoid arthritis or cancer comprising administering to the human a therapeutically effective amount of rituximab, wherein the administration of the rituximab consists of intravenous administration.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2018-00086	1-12	NA	2/0	Y	U (vasculitis)	Institution Denied

9,504,744 Patent IPR

Representative Claim

1. A method of treating a >60-year-old diffuse large-cell lymphoma patient comprising administering anti-CD20 antibody and CHOP chemotherapy to the patient, wherein the anti-CD20 antibody is administered to the patient in combination with a transplantation regimen.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2018-00231	1-16	NA	2/0	Y	U (vasculitis)	Terminated

HERCEPTIN

Herceptin-Related IPRs

> 36 IPRs filed challenging 12 different patents

Genentech Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,337,856 (Kadcyla)	Phigenix	2014-00676	1/4	Y	C	FWD – Claims Valid
7,575,748	Phigenix	2014-00842	1/0	Y	U	Institution Denied
6,407,213	1) Mylan 2) Mylan 3) Celltrion 4) Celltrion 5) Pfizer 6) Pfizer 7) BI 8) BI 9) Samsung Bioepis 10) Samsung Bioepis	1) 2016-01693 2) 2016-01694 3) 2017-01373 4) 2017-01374 5) 2017-01488 6) 2017-01489 7) 2017-02032 8) 2017-02031 9) 2017-02139 10) 2017-02140	1) 2/0 2) 2/0 3) 2/4 4) 2/4 5) 2/1 6) 2/1 7) 1/0 8) 1/0 9) 4/NA 10) 4/NA	1) Y 2) Y 3) Y 4) Y 5) Y 6) Y 7) Y 8) Y 9) Y 10) Y	1) C 2) C 3) C 4) C 5) C 6) C 7) C 8) C 9) C 10) C	1) Terminated (Settled) 2) Terminated (Settled) 3) FWD – Claims Invalid (some) 4) FWD – Claims Invalid (some) 5) FWD – Claims Invalid (some) 6) FWD – Claims Invalid (some) 7) Adverse Judgment 8) Adverse Judgment 9) FWD – Claims Invalid (some) (J/W '488) 10) FWD – Claims Invalid (some) (J/W '489)

Herceptin-Related IPRs

> 36 IPRs filed challenging 12 different patents

Genentech Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
7,807,799	Hospira	2016-01837	1/2	Y	M	FWD – Claims Invalid (Appealed)
7,846,441	1) Hospira 2) Celltrion 3) Pfizer 4) Pfizer 5) Samsung Bioepis	1) 2017-00731 2) 2017-01121 3) 2017-02063 4) 2018-00016 5) 2018-00192	1) 4/2 2) 3/2 3) 1/NA 4) 1/1 5) 2/0	1) Y 2) Y 3) Y 4) Y 5) Y	1) U 2) U 3) U 4) U 5) U	1) FWD – Claims Invalid (Appealed) 2) FWD – Claims Invalid (Appealed) 3) FWD – Claims Invalid (J/W '121) 4) Institution Denied 5) Institution Denied
6,627,196	1) Hospira 2) Samsung Bioepis 3) Celltrion	1) 2017-00804 2) 2017-01958 3) 2017-01139	1) 2 2) 3/NA 3) 1/2	1) Y 2) Y 3) Y	1) U 2) U 3) U	1) FWD – Claims Valid (Appealed) 2) FWD – Claims Valid (J/W '804) 3) FWD – Claims Valid (Appealed)
7,371,379	1) Hospira 2) Samsung Bioepis 3) Celltrion	1) 2017-00805 2) 2017-01959 3) 2017-01140	1) 2 2) 2/NA 3) 1/0	1) Y 2) Y 3) Y	1) U 2) U 3) U	1) FWD – Claims Valid (Appealed) 2) FWD – Claims Valid (J/W '805) 3) FWD – Claims Valid (Appealed)

Herceptin-Related IPRs

> 36 IPRs filed challenging 12 different patents

Genentech Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,591,897	1) Pfizer 2) Pfizer 3) Celltrion	1) 2017-01726 2) 2017-01727 3) 2017-00959	1) 3/NA 2) 3/NA 3) 1/NA	1) Y 2) Y 3) Y	1) U 2) U 3) U	1) Institution Denied 2) Institution Denied 3) Terminated
6,339,142	1) Pfizer 2) Pfizer	1) 2017-02019 2) 2018-00330	1) 2/3 2) 3/0	1) Y 2) Y	1) C 2) C	1) Terminated 2) Institution Denied
9,249,218	1) Pfizer 2) Pfizer	1) 2017-02020 2) 2018-00331	1) 2/3 2) 1/0	1) Y 2) Y	1) F 2) F	1) Terminated 2) Institution Denied
7,892,549	1) Hospira 2) Hospira 3) Celltrion 4) Samsung Bioepis	1) 2017-00737 2) 2017-00739 3) 2017-01122 4) 2017-01960	1) 1/2 2) 1/0 3) 1/2 4) 2/NA	1) Y 2) N 3) Y 4) Y	1) U 2) U 3) U 4) U	1) FWD – Claims Invalid (Appealed) 2) Institution Denied 3) FWD – Claims Invalid (Appealed) 4) FWD – Claims Invalid (J/W '737)

Herceptin-Related IPRs

> 36 IPRs filed challenging 12 different patents

Genentech Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,314,225* *Also being asserted regarding Rituxan	Pfizer	2018-01219	1/0	Y	C	Instituted Roche disclaimed all claims except claim 20 and argued that institution should be denied because the patent is under ex parte reexamination

8,337,856 Patent IPR

Representative Claim

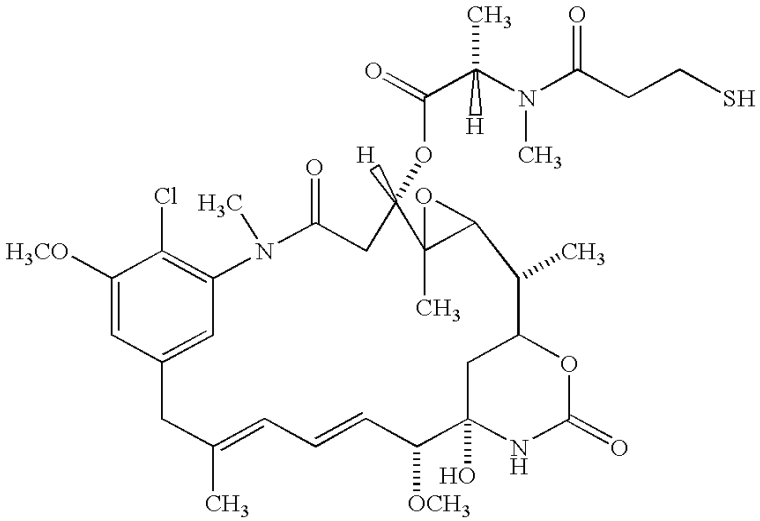
1. An immunoconjugate comprising an anti-ErbB2 antibody conjugated to a maytansinoid, wherein the antibody is huMAb4D5-8.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Phigenix	2014-00676	1-8	§ 103 for all claims	1/4	N	C	FWD – Claims Valid

7,575,748 Patent IPR

Representative Claim

1. A method for the treatment of a tumor in a mammal, comprising the steps of (i) identifying said tumor as being characterized by overexpression of an ErbB2 receptor and as being a tumor that does not respond, or responds poorly, to treatment with an anti-ErbB antibody, and (ii) intravenously administering to the mammal a therapeutically effective amount of a conjugate of a humanized antibody huMab 4D5-8 covalently linked via a thioether linking group with a maytansinoid DM1 having the structure at a dose of between about 0.2 mg/kg and about 10 mg/kg (antibody-maytansinoid conjugate weight/body weight) and at a frequency of dosing selected from the group of dosing frequencies consisting of bolus, less than about one time per week, one time per week, two times per week, more than two times per week, and continuous infusion, whereby said tumor characterized by overexpression of an ErbB2 receptor and that does not respond, or responds poorly, to treatment with an anti-ErbB antibody, is treated.



Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Phigenix	2014-00842	1-20, 25-27	NA	1/0	N	U	Institution Denied

6,407,213 Patent IPRs (cont.)

Representative Claim

1. A humanized antibody variable domain comprising non-human Complementarity Determining Region (CDR) amino acid residues that bind an antigen incorporated into a human antibody variable domain, and further comprising a Framework Region (FR) amino acid substitution at a site selected from the group consisting of 4L, 38L, 43L, 44L, 58L, 62L, 65L, 66L, 67L, 68L, 69L, 73L, 85L, 98L, 2H, 4H, 36H, 39H, 43H, 45H, 69H, 70H, 74H, and 92H, utilizing the numbering system set forth in Kabat.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Mylan	2016-01693	1, 2, 4, 12, 25, 29-31, 33, 42, 60, 62-67, 69, 71-81	NA	2/4	Y	C	Settled
Mylan	2016-01694	1, 2, 4, 12, 25, 29-31, 33, 42, 60, 62-67, 69, 71-81	NA	2/4	Y	C	Settled
Celltrion	2017-01374	1-2, 4, 12, 25, 29-31, 33, 42, 60, 62-67, 69, 71-81	§ 102 for claims 1, 2, 4, 25, 29, 62-64, 66, 67, 71, 72, 75, 76, 80, 81 § 103 for claims 1, 2, 4, 12, 25, 29, 30, 31, 33, 42, 60, 62-67, 69, 71-81	2/4	Y	C	FWD – Claims Invalid (1, 2, 4, 25, 29, 30, 31, 33, 62-64, 66, 67, 69, 72, 78, 80, 81)
Celltrion	2017-01373	1-2, 4, 12, 25, 29-31, 33, 42, 60, 62-67, 69, 71-81	§ 103 for all claims	2/4	Y	C	FWD – Claims Invalid (1, 2, 4, 12, 25, 29, 30, 31, 33, 42, 60, 62-64, 66, 67, 69, 71, 73, 74, 78, 80, 81)

6,407,213 Patent IPRs

Representative Claim

1. A humanized antibody variable domain comprising non-human Complementarity Determining Region (CDR) amino acid residues that bind an antigen incorporated into a human antibody variable domain, and further comprising a Framework Region (FR) amino acid substitution at a site selected from the group consisting of 4L, 38L, 43L, 44L, 58L, 62L, 65L, 66L, 67L, 68L, 69L, 73L, 85L, 98L, 2H, 4H, 36H, 39H, 43H, 45H, 69H, 70H, 74H, and 92H, utilizing the numbering system set forth in Kabat.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2017-01488	1-2, 4, 12, 25, 29-31, 33, 42, 60, 62-67, 69, 71-81	§ 102 for daims 1, 2, 4, 25, 29, 62-64, 66, 67, 71, 72, 75, 76, 80, 81 § 103 for daims 1, 2, 4, 12, 25, 29, 30, 31, 33, 42, 60, 62-67, 69, 71-81	2/1	Y	C	FWD – Claims Invalid (1, 2, 4, 25, 29, 30, 31, 33, 62-64, 66, 67, 69, 72, 78, 80, 81)
Pfizer	2017-01489	1-2, 4, 12, 25, 29, 62-67, 69, 71-81	§ 103 for all daims	2/1	Y	C	FWD – Claims Invalid (1, 2, 4, 12, 25, 29, 30, 31, 33, 42, 60, 62-64, 66, 67, 69, 71, 73, 74, 78, 80, 81)
BI	2017-02032	1-2, 4, 25, 29, 62-64, 66-67, 71-73, 75-78, 80-81	§ 102 for daims 1-2, 4, 25, 62-64, 66, 67, 69, 71, 73, 75, 78, 80, 81 § 103 for daims 1, 2, 4, 25, 29, 62-64, 66, 67, 69, 71-73, 75-78, 80-81	1/0	Y	C	Adverse Judgment

6,407,213 Patent IPRs

Representative Claim

1. A humanized antibody variable domain comprising non-human CDR amino acid residues that bind an antigen incorporated into a human antibody variable domain, and further comprising an FR amino acid substitution at a site selected from the group consisting of 4L, 38L, 43L, 44L, 58L, 62L, 65L, 66L, 67L, 68L, 69L, 73L, 85L, 98L, 2H, 4H, 36H, 39H, 43H, 45H, 69H, 70H, 74H, and 92H, utilizing the numbering system set forth in Kabat.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
BI	2017-02031	1-2, 4, 25, 29, 62-64, 66-67, 69, 71, 75-76, 78, 8-81	§ 102 for claim 63 § 103 for claims 1, 2, 4, 25, 29, 62, 64, 66, 69, 71, 73, 75-78, 80, 81	1/0	Y	C	Adverse Judgment
Samsung Bioepsis	2017-02140	1-2, 4, 12, 25, 29, 62-67, 69, 71-81	NA	4/NA	Y	C	FWD – Claims Invalid (1, 2, 4, 12, 25, 29, 30, 31, 33, 42, 60, 62-64, 66, 67, 69, 71, 73, 74, 78, 80, 81) (J/W '489)
Samsung Bioepsis	2017-02139	1-2, 4, 12, 25, 29, 62-64, 66-67, 69, 71-72, 75-76, 80-81	§ 102 for claims 1, 2, 4, 25, 29, 62-64, 66, 67, 71, 72, 75, 76, 80, 81 § 103 for claims 1, 2, 4, 12, 25, 29, 30, 31, 33, 42, 60, 62-67, 69, 71-81	4/NA	Y	C	FWD – Claims Invalid (1, 2, 4, 25, 29, 30, 31, 33, 62-64, 66, 67, 69, 72, 78, 80, 81) (J/W '488)

7,807,799 Patent IPR

Representative Claim

1. A method of purifying a protein that comprises a CH2/CH3 region by subjecting a composition of said protein to protein A affinity chromatography at a temperature in the range from about 10°C to about 18°C.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Hospira	2016-01837	1-3, 5-11	§ 102 for claims 1, 2, and 5 § 103 for claims 1-3, 5-11	1/2	Y	M	FWD – Claims Invalid Genentech appealed; includes a constitutional challenge

7,892,549 Patent IPRs

Representative Claim

1. A method for the treatment of a human patient with breast cancer that overexpresses ErbB2 receptor, comprising administering a combination of an antibody that binds ErbB2, a taxoid, and a further growth inhibitory agent to the human patient in an amount effective to extend the time to disease progression in the human patient, wherein the antibody binds to epitope 4D5 within the ErbB2 extracellular domain sequence.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Hospira	2017-00737	1-17	§ 103	1/2	Y	U	FWD – Claims Invalid (Appealed) Denied PO's Motion to Amend
Hospira	2017-00739	1-11, 14-17	NA	1/0	N	U	Institution Denied

7,892,549 Patent IPRs

Representative Claim

1. A method for the treatment of a human patient with breast cancer that overexpresses ErbB2 receptor, comprising administering a combination of an antibody that binds ErbB2, a taxoid, and a further growth inhibitory agent to the human patient in an amount effective to extend the time to disease progression in the human patient, wherein the antibody binds to epitope 4D5 within the ErbB2 extracellular domain sequence.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Celltrion	2017-01122	1-11, 14-17	§ 103	1/2	Y	U	FWD – Claims Invalid (Appealed)
Samsung Bioepis	2017-01960	1-17	§ 103	2/NA	Y	U	FWD – Claims Invalid (J/W '737)

7,846,441 Patent IPRs (cont.)

Representative Claim

1. A method for the treatment of a human patient with a malignant progressing tumor or cancer characterized by overexpression of ErbB2 receptor by administering a combination of an intact antibody that binds to epitope 4D5 within the ErbB2 extracellular domain sequence and a taxoid, in the absence of anthracycline derivative, to the human patient in an amount effective to extend the time to disease progression in said human patient, without increase in overall severe adverse events.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Hospira	2017-00731	1-14	§ 103	4/2	Y	U	FWD – Claims Invalid (Appealed)
Celltrion	2017-01121	1-14	§ 103	3/2	Y	U	FWD – Claims Invalid (Appealed)
Pfizer	1) 2017-02063 2) 2018-00016	1) 1-14 2) 1-14	1) § 103 2) NA	1/3 1/1	1) Y 2) Y	1) U 2) U	1) FWD – Claims Invalid (J/W '121) 2) Institution Denied
Samsung Bioepsis	2018-00192	1-14	NA	2/0	Y	U	Institution Denied

6,627,196 Patent IPRs

Representative Claim

1. A method for the treatment of a human patient diagnosed with cancer characterized by overexpression of ErbB2 receptor by administering an effective amount of an anti-ErbB2 antibody to the human patient, giving:
   a) an initial dose of at least approximately 5 mg/kg of the anti-ErbB2 antibody; and
   b) a plurality of subsequent doses of the antibody in an amount that is approximately the same or less than the initial dose, wherein the subsequent doses are separated in time from each other by at least two weeks.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Hospira	2017-00804	1-3, 5, 7, 9-11, 17-33	§ 103	2	Y	U	FWD – Claims Valid (Appealed)
Samsung Bioepis	2017-01958	1-3, 5, 7, 9-11, 17-33	§ 103	3/NA	Y	U	FWD – Claims Valid (J/W '804)
Celltrion	2017-01139	1-3, 5, 7, 9-11, 17-33	§ 103	1/2	Y	U	FWD – Claims Valid (Appealed)

7,371,379 Patent IPRs

Representative Claim

1. A method for the treatment of a human patient diagnosed with cancer characterized by overexpression of ErbB2 receptor by administering an effective amount of an anti-ErbB2 antibody to the human patient, giving:
   a) an initial dose of at least approximately 5 mg/kg of the anti-ErbB2 antibody;
   b) a plurality of subsequent doses of the antibody in an amount that is approximately the same or less than the initial dose, wherein the subsequent doses are separated in time from each other by at least two weeks; and
   c) an effective amount of a chemotherapeutic agent.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Hospira	2017-00805	1-3, 5, 7, 9-11, 16-28, 30-40	§ 103	2/NA	Y	U	FWD – Claims Valid (Appealed)
Celltrion	2017-01140	1-3, 5, 7, 9-11, 13-28, 30-40	§ 103	1/0	Y	U	FWD – Claims Valid (Appealed)

7,371,379 Patent IPRs

Representative Claim

1. A method for the treatment of a human patient diagnosed with cancer characterized by overexpression of ErbB2 receptor by administering an effective amount of an anti-ErbB2 antibody to the human patient, giving:
   a) an initial dose of at least approximately 5 mg/kg of the anti-ErbB2 antibody;
   b) a plurality of subsequent doses of the antibody in an amount that is approximately the same or less than the initial dose, wherein the subsequent doses are separated in time from each other by at least two weeks; and
   c) an effective amount of a chemotherapeutic agent.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Samsung Bioepis	2017-01959	1-3, 5, 7, 9-11, 16-28, 30-40	NA	2/NA	Y	U	FWD – Claims Valid (J/W '805)

8,591,897 Patent IPRs

Representative Claim

1. A method of adjuvant therapy by administering to a human subject with nonmetastatic HER2 positive breast cancer, following definitive surgery, anthracycline/cyclophosphamide (AC) based chemotherapy, followed by sequential administration of a taxoid and trastuzumab, or an antibody that blocks binding of trastuzumab to HER2.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2017-01726	1-13	NA	3/NA	Y	U	Institution Denied
Pfizer	2017-01727	1-13	NA	3/NA	Y	U	Institution Denied
Celltrion	2017-00959	1-13	NA	1/NA	Y	U	Terminated – Adverse Judgment

6,339,142 Patent IPRs

Representative Claim

1. A composition of a mixture of anti-HER2 antibody and one or more acidic variants thereof, wherein the amount of the acidic variant(s) is less than about 25%.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2017-02019	1-3	NA	2/3	Y	C	Terminated
Pfizer	2018-00330	1-3	NA	3/0	Y	C	Institution Denied

9,249,218 Patent IPRs

Representative Claim

1. A therapeutic composition of a mixture of anti-HER2 antibody and one or more acidic variants thereof, wherein:
   a) the amount of the acidic variant(s) is less than about 25%,
   b) the acidic variant(s) are predominantly deamidated variants, wherein one or more asparagine residues of the anti-HER2 antibody have been deamidated,
   c) the anti-HER2 antibody is humMAb4D5-8,
   d) the deamidated variants have Asn30 in CDR1 of either or both VL regions of humMAb4D5-8 converted to aspartate, and
   e) a pharmaceutically acceptable carrier.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2017-02020	1, 5-7	NA	2/3	Y	C	Terminated
Pfizer	2018-00331	1-20	NA	1/0	Y	C	Institution Denied

8,314,225 Patent IPR*

Representative Claim

1. A nucleic acid encoding the amino acid sequence of the C-terminal part of the CH3-domain of an immunoglobulin of the class IgA or IgG, or the amino acid sequence of the C-terminal part of the CH4-domain of an immunoglobulin of the class IgE or IgM, wherein the glycine-lysine-dipeptide comprised in said amino acid sequence of the C-terminal part of the CH3- or CH4-domain is encoded by one of the following nucleic acid sequences: ggaaca, ggcaac, gggaaa, ggaaag, ggcaag, and gggaag; the nucleic acid ggaaaa; or the nucleic acid ggcaaa.

*Also being asserted regarding Rituxan

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2018-01219	1-5, 10-12, 20	§§ 102, 103 for claim 20	1/0	Y	C	Instituted Roche disclaimed all claims except claim 20 and argued that institution should be denied because the patent is under ex parte reexamination

TYSABRI

Tysabri-Related IPRs

> Three IPRs filed challenging three different patents

Biogen Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,815,236	Swiss Pharma	2016-00912	5/0	N	U	Institution Denied
8,349,321	Swiss Pharma	2016-00915	4/0	N	F	Institution Denied
8,900,577	Swiss Pharma	2016-00916	4/0	N	F	Institution Denied

8,815,236 Patent IPR

Representative Claim

1. A method of treatment by administering to a patient with multiple sclerosis a therapeutic amount of a stable, aqueous pharmaceutical formulation of about 20 mg/ml to about 150 mg/ml of natalizumab, about 10 mM phosphate buffer, about 140 mM sodium chloride, and polysorbate 80 present in an amount of about 0.001% to 2% (w/v).

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Swiss Pharma	2016-00912	1-16, 21-22	None	5/0	Y	U	Institution Denied

8,349,321 Patent IPR

Representative Claim

1. A stable, aqueous pharmaceutical formulation of 20 mg/ml of natalizumab, about 10 mM sodium phosphate buffer, 8.18 mg/ml of sodium chloride, and 0.2 mg/ml of polysorbate 80, and wherein the formulation has a pH of 6.1.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Swiss Pharma	2016-00915	1-4	None	4/0	Y	F	Institution Denied

8,900,577 Patent IPR

Representative Claim

1. A stable, aqueous pharmaceutical formulation of about 20 mg/ml to about 150 mg/ml of natalizumab, polysorbate 80 present in an amount of about 0.001% to 2% (w/v), about 10 mM phosphate buffer, and about 140 mM NaCl.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Swiss Pharma	2016-00916	1, 3-7, 9-12	None	4/0	Y	F	Institution Denied

KEYTRUDA

Keytruda-Related IPRs

> Four IPRs filed challenging two patents

Ono Pharm. Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
9,067,999	1) Merck 2) Merck	1) 2016-01217 2) 2016-01218	1) 1/NA 2) 1/NA	1) NA 2) NA	1) U 2) U	1) Settled 2) Settled
9,073,994	1) Merck 2) Merck	1) 2016-01219 2) 2016-01221	1) 1/NA 2) 1/NA	1) NA 2) NA	1) U 2) U	1) Settled 2) Settled

9,067,999 Patent IPRs

Representative Claim

1. A method of treating a lung cancer comprising administering a composition comprising a human or humanized anti-PD-1 monoclonal antibody to a human with the lung cancer, wherein the administration of the composition treats the lung cancer in the human.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Merck	2016-01217	1, 6-14, 19-20, 24-27, and 29-30	§§ 102, 103 for all claims	1/NA	NA	U	Settled
Merck	2016-01218	1, 6-14, 19-20, and 24-27, and 29-30	§§ 102, 103 for all claims	1/NA	NA	U	Settled

9,073,994 Patent IPRs

Representative Claim

1. A method of treating a metastatic melanoma comprising intravenously administering an effective amount of a composition comprising a human or humanized anti-PD-1 monoclonal antibody and a solubilizer in a solution to a human with the metastatic melanoma, wherein the administration of the composition treats the metastatic melanoma in the human.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Merck	2016-01219	1-3, 8-9, 14-15, 19-22 and 25-26	§§ 102, 103 for all claims	1/NA	NA	U	Settled
Merck	2016-01221	1-3, 8-9, 14-15, 19-22, and 25-26	§§ 102, 103 for all claims	1/NA	NA	U	Settled

AVASTIN

Avastin-Related IPRs

> Two IPRs filed challenging two patents

Genentech Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
7,622,115	Hospira	2016-01771	1/2	Y	U	FWD – Claims Invalid, Genentech appealed
9,795,672	Pfizer	2018-00373	1/0	Y	U	Institution Denied

7,622,115 IPR

Representative Claim

1. A method for treating cancer in a patient by administering an effective amount of bevacizumab and assessing the patient for gastrointestinal perforation.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Hospira	2016-01771	1-5	§§ 102, 103 for all claims	1/2	Y	U	FWD – Claims Invalid Genentech appealed, includes a constitutional challenge

9,795,672 IPR

Representative Claim

1. A method for treating cancer in a patient by administering an effective amount of bevacizumab and assessing the patient for gastrointestinal perforation.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Pfizer	2018-00373	1-18	NA	1/0	Y	U	Institution Denied

EPOGEN

6,747,002 IPR

> One IPR filed challenging one patent

Representative Claim

1. A method of administering at least one EPO dose to a patient according to an EPO dosing regimen, wherein said regimen maintains at least a serum EPO concentration above a predose level for about five to about 30 days between doses.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Hospira	2013-00365	1-7, 12, 14-28	NA	3/0	NA	U	Not instituted; Janssen disclaimed all of the challenged claims

ORENCIA

8,476,239 IPR

> One IPR filed challenging one patent

Representative Claim

1. A stable formulation suitable for subcutaneous administration of at least 100mg/ml CTLA4Ig molecule, a sugar selected from the group consisting of sucrose, lactose, maltose, mannitol and trehalose and mixtures thereof, and a pharmaceutically acceptable aqueous carrier, wherein the formulation has a pH range of from 6 to 8, viscosity from 9 to 20 cps, and the weight ratio of sugar:protein of 1.1:1 or higher.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Momenta	2015-01537	1-15	§ 103	1/2	Y	F	FWD – Claims Valid Momenta Appealed (Case No. 17-1694) Momenta ordered to show cause as to why appeal should not be dismissed as moot due to lack of Article III standing

NEULASTA

Neulasta-Related IPRs

> Four IPRs filed challenging four patents

Amgen Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,952,138	Apotex	2016-01542	1/1	N	M	FWD – Claims 1-17 and 19-24 unpatentable Claim 18 patentable (non-aerobic) Additional briefing regarding Request for Rehearing filed per PTAB request March 2019
9,856,287	Fresenius Kabi	2019-00971	N/A	Y	M	Pending
8,940,878	Kashiv Biosciences	2019-00791	N/A	Y	M	Pending
9,643,997	Kashiv Biosciences	2019-00797	N/A	Y	M	Pending

Representative Claim

1. A method of refolding a protein expressed in a nonmammalian expression system and present in a volume at a concentration of 2.0 g/L or greater that includes:
   a) contacting the protein with a refold buffer that has a redox component with a final thiol-pair ratio in the range of 0.001 to 100, a redox buffer strength of 2 mM or greater, and one or more of:
      i. a denaturant;
      ii. an aggregation suppressor; and
      iii. a protein stabilizer;
      iv. to form a refold mixture;
   b) incubating the refold mixture; and
   c) isolating the protein from the refold mixture.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Apotex	2016-01542	1-24	§ 103 for all claims	1/1	N	M	FWD – Claims 1-17 and 19-24 unpatentable Claim 18 patentable (non-aerobic) Additional briefing regarding Request for Rehearing filed per PTAB request March 2019

9,856,287 IPR

Representative Claim

1. A method of refolding proteins expressed in a non-mammalian expression system, the method comprising:
   a) contacting the proteins with a preparation that supports the renaturation of at least one of the proteins to a biologically active form, to form a refold mixture, the preparation comprising:
      i. at least one ingredient selected from the group consisting of a denaturant, an aggregation suppressor and a protein stabilizer;
      ii. an amount of oxidant; and
      iii. an amount of reductant,
      iv. wherein the amounts of the oxidant and the reductant are related through a thiol-pair ratio and a thiol-pair buffer strength,
      v. wherein the thiol-pair ratio is in the range of 0.001-100; and
      vi. wherein the thiol-pair buffer strength maintains the solubility of the preparation; and
      vii. incubating the refold mixture so that at least about 25% of the proteins are properly refolded.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Fresenius Kabi	2019-00971	1, 4-6, 8-10, 12, 14-16, 19-21, 23-26, 29-30	N/A	N/A	Y	M	Pending

8,940,878 IPR

Representative Claim

1. A method of purifying a protein expressed in a non-native soluble form in a non-mammalian expression system comprising:
   a) lysing a non-mammalian cell in which the protein is expressed in a non-native soluble form to generate a cell lysate;
   b) contacting the cell lysate with a separation matrix under conditions suitable for the protein to associate with the separation matrix;
   c) washing the separation matrix; and
   d) eluting the protein from the separation matrix, wherein the separation matrix is an affinity resin selected from the group consisting of Protein A, Protein G and a synthetic mimetic affinity resin.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Kashiv Biosciences	2019-00791	7-8, 11-13, 15-19, 21	N/A	N/A	Y	M	Pending

9,643,997 IPR

Representative Claim

1. A method of purifying a protein expressed in a non-native soluble form in a non-mammalian expression system comprising:
   a) lysing a non-mammalian cell in which the protein is expressed in a nonnative soluble form to generate a cell lysate;
   b) contacting the cell lysate with a separation matrix under conditions suitable for the protein to associate with the separation matrix;
   c) washing the separation matrix; and
   d) eluting the protein from the separation matrix.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Kashiv Biosciences	2019-00797	9-10, 13-15, 17-21, 23, 26-30	N/A	N/A	Y	M	Pending

ENBREL

Enbrel-Related IPRs

> Three IPRs filed challenging two patents

Hofmann-LaRoche Patent	Challenger(s)	IPR No.	# P / PO Experts	2-Consid.	Claim Type	Status
8,163,522	Coalition for Affordable Drugs (Kyle Bass)	2015-01792	1/0	Y	M	Institution Denied
	Coherus	2017-01916	1/2	Y	M	Institution Denied
8,063,182	Coherus	2017-02066	1/2	Y	C	Institution Denied

8,163,522 Patent IPR

Representative Claim

1. A method comprising the steps of:
   a) culturing a host cell with a polynucleotide, wherein the polynucleotide encodes a protein consisting of:
      i. the extracellular region of an insoluble human TNF receptor, wherein the insoluble human TNF receptor has an apparent molecular weight of about 75 kilodaltons as determined on a nonreducing SDS-polyacrylamide gel and the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO:10), and
      ii. all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region, and
   b) purifying an expression product of the polynucleotide from the cell mass or the culture medium.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coalition for Affordable Drugs (Kyle Bass)	2015-01792	1-10	NA	1/0	Y	M	Institution Denied
Coherus	2017-01916	1-10	NA	1/2	Y	M	Institution Denied

8,063,182 Patent IPR

Representative Claim

1. An isolated antibody that binds specifically to the polypeptide of SEQ ID NO:548.

Challenger(s)	IPR No.	Challenged Claims	Instituted Grounds	# P / PO Experts	2-Consid.	Claim Type	Status
Coherus	2017-02066	2-36	NA	1/2	Y	C	Institution Denied