No. 2019-2156

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

GENENTECH, INC.,

Plaintiff-Appellant,

CITY OF HOPE,

Plaintiff,

v.

AMGEN INC.,

Defendant-Appellee.

On Appeal from the United States District Court
for the District of Delaware, No. 1:18-cv-00924-CFC, Judge Colm F. Connolly

NON-CONFIDENTIAL REPLY OF PLAINTIFF-APPELLANT GENENTECH, INC. IN SUPPORT OF ITS EMERGENCY MOTION FOR AN INJUNCTION PENDING RESOLUTION OF APPEAL AND MOTION TO EXPEDITE BRIEFING ON APPEAL

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August 1, 2019

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CONFIDENTIAL MATERIAL OMITTED

The confidential information that has been deleted on pages 6-9 and 11 and Exhibits 33, 35, and 38 describes highly confidential, competitively sensitive information relating to the Herceptin biosimilar market including market entry, forecast planning, competitive intelligence, the terms of third party license agreements, and confidential FDA labeling strategy.

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INTRODUCTION

Amgen's opposition only serves to highlight the need for interim relief while this Court considers Genentech's appeal. Amgen chose to deliberately infringe Genentech's patents by launching a competing product. When Genentech learned of Amgen's launch decision, it immediately sought relief in the district court and this Court, and self-expedited its opening brief, filing 53 days early and three days before Amgen filed its opposition to this motion. *See* ECF No. 20. Unless enjoined pending appeal, the immediate and irreversible consequences of Amgen's launch will deprive Genentech of the opportunity for meaningful appellate review.

Genentech is likely to prevail in this appeal because the district court's determination of no irreparable harm rested on legal errors. Amgen cites no authority finding a supposed delay in seeking relief where, as here, the patentee sought to enjoin the irreparable harms ***before*** they commenced. Nor has Amgen identified any case holding that litigation settlements allowing ***future*** entry defeat a claim of irreparable harm from a different party's ***earlier*** entry. The irreparable harm Genentech will suffer if Amgen continues to infringe while the Court considers this appeal dovetails with the harm that Genentech showed below, that Amgen did not dispute, and that the district court erroneously ignored: price erosion and lost market share that cannot be fully compensated by damages.

Amgen cannot claim any cognizable injury from a brief injunction pending this self-expedited appeal. Any purported hardship to Amgen is the result of its calculated choice to proceed at risk despite knowing Genentech's intent to seek expedited relief from this Court.

The public interest also favors an injunction pending appeal. Genentech undisputedly remains able to supply the market in full, and the Court may enter an appropriately-tailored injunction to avoid disrupting any current patient treatment.

Genentech therefore respectfully requests that the Court enter an injunction pending appeal.

ARGUMENT

I. GENENTECH HAS MADE A STRONG SHOWING THAT IT WILL SUCCEED ON APPEAL AND THAT AN INTERIM INJUNCTION IS NEEDED TO PREVENT IRREPARABLE HARM.

The district court's order rested on two legal errors contrary to governing precedent. Because the district court based its order on irreparable harm, Genentech presents the first two factors for an injunction pending appeal together (*i.e.*, Genentech's "strong showing that [it] is likely to succeed on the merits" and its proof that it "will be irreparably injured absent the requested relief"). *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 897 F.2d 511, 512 (Fed. Cir. 1990). Both elements are clearly met, and Amgen's opposition does not show otherwise.

A. Genentech Is Likely To Succeed In Showing That The District Court Assessed Irreparable Harm Under An Erroneous Legal Standard.

1. An injunction motion presented *before* the harm to be enjoined even begins does not show a lack of irreparable harm.

The district court's ruling that the timing of Genentech's injunction request defeated its showing of irreparable harm is contrary to this Court's precedents. Although a patentee's claim to irreparable harm may be undermined where it has long suffered the harm without complaint, *see Nutrition 21 v. United States*, 930 F.2d 867, 872 (Fed. Cir. 1991), such an inference cannot be drawn when the patentee moves before the harm has even begun. This Court has never held, as the district court concluded here, that a party that seeks an injunction ***before*** the harm to be enjoined even begins—as Genentech did—somehow forfeits the ability to show irreparable harm. This Court's analysis has focused on delay ***after*** the harm commences—and even then, has found no undue delay even when the patentee waits until months afterwards. *Polymer Techs., Inc. v. Bridwell*, 103 F.3d 970, 976 (Fed. Cir. 1996) (no undue delay four months after infringement began); *see Pfizer, Inc. v. Teva Pharm., USA, Inc.*, 429 F.3d 1364, 1382 (Fed. Cir. 2005) (no undue delay two months after generic launch). Amgen never engages with this issue or attempts to reconcile the district court's analysis with this Court's precedents.

Amgen (Opp. 11) cites two district court opinions, but neither supports it. In *Immunomedics, Inc. v. Venbio Select Advisor LLC*, 2017 WL 822800 (D. Del. Mar. 2, 2017), a plaintiff seeking to enjoin a shareholder vote knew about the alleged violations for six months and had already delayed the annual meeting twice. *Id.* at *3. And the court in *Graceway Pharmaceuticals LLC v. Perrigo Co.*, 722 F. Supp. 2d 566 (D.N.J. 2010), was "unwilling to conclude that [Graceway's] conduct was dilatory," in part because it "brought suit (although not its TRO motion) prior to Nycomed's launch," *id.* at 570—which if anything supports Genentech.

Nor does Amgen even acknowledge, much less explain, its repeated representations to Genentech and the district court that—even as late as June 2019—it had still not decided whether to launch, much less when. *See* Ex.[1] 38 (Appx4838(353:12-19)) (June 27, 2019) (Amgen's Rule 30(b)(6) witness: "So as of today, no decision has been made on launching either Mvasi or Kanjinti at all."); Mot. 3, 11. Amgen's plan to be "ready" to launch in July 2019 (Opp. 6) is beside the point; Amgen itself repeatedly distinguished between being "ready" to launch and actually deciding to launch. Even after receiving FDA approval, Amgen insisted that an actual launch could still be a year away, well after the scheduled December 2019 trial. Ex. 23 (30:3-8) (June 18, 2019) ("[I]f we were to launch in ***two months***

[1] "Ex." are the exhibits to Genentech's motion and reply. "Amgen Ex." are the exhibits to Amgen's opposition.

versus six months versus a year, the company would still need to make the preparation to be in a position to launch[.]" (emphasis added)). Genentech cannot be faulted for taking Amgen at its word.

Amgen decided on July 8 to launch within a week, and Genentech immediately sought injunctive relief upon learning of those plans—five days before Amgen's launch. There was no delay here, let alone delay refuting Genentech's proof of irreparable harm.

2. The timing of Genentech's motion is consistent with the BPCIA.

Nor was the timing of Genentech's motion inconsistent with the "spirit and purpose of the BPCIA." Opp. 12. Nothing in 42 U.S.C. § 262(*l*)(8) required Genentech to seek an injunction immediately following Amgen's notice of commercial marketing; even Amgen concedes that "there [was] no statutory mandate" to do so (Opp. 14).

Amgen asserts that Genentech should have sought injunctive relief even while "the scope of Amgen's label was in flux." Opp. 14. But such a blanket rule would force potentially unnecessary motion practice and is contrary to the requirement of an imminent, irreparable injury necessary to obtain a preliminary injunction. *See Cordis Corp. v. Medtronic, Inc.*, 780 F.2d 991, 996 (Fed. Cir. 1985) ("A preliminary injunction will not issue simply to prevent a mere possibility of injury, even where prospective injury is great."). Here, for example, even after Amgen reverted to

seeking approval for the infringing indications in March 2019, Amgen continued to consider whether to [redacted] and [redacted] in an effort to avoid infringement. Amgen Ex. 2, AMGKAN02908379.

3. Genentech did not disclaim preliminary injunctive relief.

Contrary to Amgen's assertion (Opp. 6-7), Genentech never represented that it would forgo injunctive relief if Amgen decided to launch at risk. Genentech, in fact, said the opposite: "Your Honor, if there's a launch, we're going to request a preliminary injunction." Ex. 32 (87:20-21). Neither Amgen nor the district court raised a concern about such timing. At the May 16, 2019 hearing, Genentech merely reiterated the status quo: Amgen had affirmatively disclaimed having made a launch decision, and Genentech observed as a consequence that "[w]e're not presently seeking injunctive relief." Amgen Ex. 4 (26:3-4). Genentech's observation in May that it had not filed for a preliminary injunction when it would have been premature to do so should not foreclose it from seeking relief when Amgen later made a launch decision in July.[2]

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[2] Although Amgen relies on a prior discovery dispute regarding Genentech's settlement agreements (Opp. 7, 17-18), the district court did not base its injunction decision on that dispute. Rather, the court recognized the third-party licensees' legitimate interest against having their "highly sensitive" licensing terms disclosed prematurely. Amgen Ex. 4 (70:11-24). Now that Genentech has moved for a preliminary injunction, Genentech has produced all terms of its U.S. settlements with Mylan, Pfizer, Celltrion, and Samsung Bioepis to Amgen's outside counsel.

B. The District Court Committed Legal Error In Applying A Categorical Rule That Genentech's Settlements With Others Defeated Irreparable Harm.

Genentech's settlement licenses with others for ***future*** entry dates do not diminish the irreparable harm to Genentech of Amgen's infringement ***now***. Amgen's argument that "the fact that Genentech licensed others to enter … undermines its protestation of grave and irreparable harm" (Opp. 17) merely reiterates the district court's error of assuming a categorical rule contrary to *eBay*.

The cases cited by Amgen and the district court (Opp. 18-19; Ex. 17 at 7) only show that a patentee's licensing history may defeat irreparable harm when it affirmatively demonstrates a willingness to license the patent for money or a desire to provide immediate widespread use of its invention by others. For example, *Cordance Corp. v. Amazon.com, Inc.*, 730 F. Supp. 2d 333, 341 (D. Del. 2010)—Amgen's sole cited authority (Opp. 18-19)—involved a patentee who had ceded any exclusivity years ago by licensing its patent to a nonprofit seeking to make an open-access platform. Genentech's conduct here shows the opposite: Genentech settled litigation by ensuring that others would not enter the market until after a negotiated period of exclusivity, at which time the licenses would be [redacted] precisely because Genentech could not put a price on infringement and negotiated for that period of market exclusivity instead. Genentech's decision to allow market entry

beginning [redacted] prior to patent expiration does not diminish the value of Genentech maintaining exclusivity now.

This Court has held that licenses for future entry do not negate irreparable harm in the present. *See AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1061-1063 (Fed. Cir. 2010); *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1361-1362 (Fed. Cir. 2008). Although Amgen seeks to distinguish *Abbott* on the theory that it involved other harms (*e.g.*, layoffs), Opp. 19, the only injuries that this Court discussed when addressing the licensing history were price erosion and lost market share, 544 F.3d at 1361-1362—exactly what Genentech has alleged here.

C. Absent An Injunction Pending Appeal, Genentech Will Suffer Irreparable Price Erosion And Lost Market Share.

Amgen does not dispute that Genentech will suffer price erosion and lost market share due to Amgen's infringement during the pendency of this appeal. *See* Mot. 16-21; Opp. 19-20. Amgen seeks to cast those harms as compensable because they are "financial in nature." Opp. 19. But as Amgen has admitted in other cases and this Court's precedents hold, price erosion and loss of market share are irreparable (*see* Mot. 16-19), and Amgen provided no evidence to dispute that its infringement would cause those harms here.[3] Unsurprisingly, then, Amgen also

[3] Even Amgen's cited authority recognizes that price erosion and lost market share are irreparable and specifically distinguishes them from mere "lost sales," *Automated Merchandising Sys., Inc. v. Crane Co.*, 357 F. App'x 297, 301 (Fed. Cir. 2009), which are the subject of the passage that Amgen quotes (Opp. 19-20).

submitted no evidence purporting to show how those harms could be quantifiable (Opp. 16), and the district court cited none (Ex. 17 at 8). The fact that trial is scheduled four months from now (Opp. 16; Ex. 17 at 8 (citing *King Pharmaceuticals, Inc. v. Sandoz Inc.*, 2010 WL 1957640 (D.N.J. May 17, 2010))) does not make the full extent of Genentech's injuries—which will persist even if Amgen were later removed from the market (Ex. 28 (¶¶67-68))—any more quantifiable.

Amgen asserts that Genentech has forecast that the financial impact of its infringement before trial "will be '[c]onsiderably' less than [redacted]." Opp. 20. But that is not supported by the record, nor did the district court accept that characterization. That forecast assumed no trastuzumab biosimilar market entry before [redacted]. Ex. 33 (Appx4738(¶9)). It does not address the effects of Amgen launching now. *Id.*

Amgen's assertion (Opp. 1, 16-17) that its infringement now will cause the same harms that Genentech will experience from the eventual licensed launch of other trastuzumab biosimilars is wrong. As Genentech explained (Mot. 16-17)—and Amgen does not dispute—Amgen's unique market position makes Amgen's current infringement a more formidable competitive threat. Ex. 3 (¶¶47-54). And Genentech's future loss of exclusivity does not deprive Genentech of its right to

enjoy that exclusivity while it lasts or make the harm caused by Amgen's present infringement any less irreparable.

A brief injunction is essential to preserving Genentech's ability to obtain meaningful review on appeal. Unless Amgen is immediately enjoined, during the pendency of this appeal Genentech will already suffer the very irreparable price erosion and lost market share that it sought a preliminary injunction to avoid.

D. Genentech Is Likely To Succeed On The Remaining Elements Of Its Preliminary Injunction Request.

Although the district court did not reach the underlying patent merits, they overwhelmingly favor Genentech too. Amgen concedes infringement, and its invalidity defense has already been rejected in multiple IPRs. Amgen's sole "new" reference (Opp. 21 n.5)—the Hellmann patent—is just more of the same; it discloses the weekly administration of Herceptin that the PTAB already concluded was insufficient to invalidate Genentech's patents (even on a lower standard of proof). Ex. 34 (Appx4742(¶9), Appx4748(¶25)). And the "testimony from the inventors and Genentech's consultant" that Amgen hints at (Opp. 20), but never discusses, does not support obviousness either. Amgen's reliance on such evidence simply reinforces its improper use of hindsight to retrace the inventors' path.

II. AN INJUNCTION PENDING APPEAL WILL NOT "SUBSTANTIALLY INJURE" AMGEN IN ANY COGNIZABLE WAY.

Amgen has not contested the adequacy of Genentech's proposed $10 million bond as security, and any purported hardships to Amgen at this point are self-inflicted. After Genentech's motion for a preliminary injunction was denied, Genentech immediately informed Amgen that it would seek an injunction pending appeal. Ex. 35 (Appx4945(32:2-13); Appx4950(37:9-15)). Amgen nevertheless commenced with its launch. Any harm to Amgen stemming from "its own calculated risk to launch its product pre-judgment" cannot defeat an injunction, *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383 (Fed. Cir. 2006)—a point Amgen itself has argued elsewhere. Ex. 36 (Appx4877) (such harm "weighs against the infringer in the balance of the hardships analysis").

III. THE PUBLIC INTEREST FAVORS AN INJUNCTION PENDING APPEAL.

Amgen does not dispute that the public interest favors the enforcement of patent rights to encourage innovation—a position that Amgen itself has repeatedly espoused. Ex. 37 (Appx1924-1925); Ex. 25 at 19.

Amgen asserts that an injunction would deprive the public of Kanjinti's non-infringing uses. Opp. 22-23. But by Amgen's own estimation, Genentech's patents cover [redacted] of patient use; non-infringing uses are minor by comparison. Ex. 30, AMGKAN2727080. If Amgen wants to market Kanjinti's non-infringing uses, it

can attempt to carve-out the infringing uses from its product label, as it once planned to do.

Contrary to Amgen's assertion (Opp. 23), Genentech does not seek to deprive patients of lifesaving medicine. Genentech undisputedly can continue to supply the market with Herceptin so that no patient is denied therapy. Nor does Genentech intend to force treatment interruptions for the few patients who may have already received Kanjinti due to Amgen's infringement. Genentech has no objection to excluding from the scope of the injunction the treatment of patients who have already begun Kanjinti therapy.

CONCLUSION

Genentech respectfully requests that the Court grant its motion.

Respectfully submitted,

/s/ William F. Lee

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Attorneys for Plaintiff-Appellant Genentech, Inc.

August 1, 2019

CERTIFICATE OF INTEREST

Counsel for Plaintiffs-Appellant Genentech, Inc. certifies the following:

1. The full name of every party or *amicus* represented by me is:

Genentech, Inc.

2. The names of the real party in interest represented by me is:

Not applicable.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

Genentech, Inc. is a wholly-owned subsidiary of Roche Holdings Inc. Roche Holdings Inc.'s ultimate parent, Roche Holdings Ltd, is a publicly held Swiss corporation traded on the Swiss Stock Exchange. Upon information and belief, more than 10% of Roche Holdings Ltd's voting shares are held either directly or indirectly by Novartis AG, a publicly held Swiss corporation.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

WILMER CUTLER PICKERING HALE AND DORR LLP: Timothy Cook, Robert J. Gunther Jr., William F. Lee, Jason H. Liss, Mark D. McBriar, Helena Million-Perez, Kevin S. Prussia, Rana Sawaya, Nancy L. Schroeder

DURIE TANGRI LLP: Adam R. Brausa, Daralyn J. Durie, Eneda Hoxha, Eric C. Wiener

MCCARTER & ENGLISH, LLP: Alexandra M. Joyce, Michael P. Kelly, Daniel M. Silver

WILLIAMS & CONNOLLY LLP: David I. Berl, Thomas S. Fletcher, Paul B. Gaffney, Teagan J. Gregory, Kathryn S. Kayali, Charles L. McCloud, Jonathan S. Sidhu, Kyle E. Thomason

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal:

Genentech, Inc. v. Amgen, Inc., No. 18-cv-924-CFC (D. Del.)

Dated: August 1, 2019

/s/ William F. Lee

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CERTIFICATE OF SERVICE

I hereby certify that, on this 1st day of August, 2019, I filed the foregoing Non-Confidential Reply of Plaintiff-Appellant Genentech, Inc. in Support of Its Emergency Motion for an Injunction Pending Resolution of Appeal and Motion to Expedite Briefing on Appeal with the Clerk of the United States Court of Appeals for the Federal Circuit via the CM/ECF system, which will send notice of such filing to all registered CM/ECF users.

/s/ William F. Lee

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CERTIFICATE OF COMPLIANCE

Pursuant to Fed. R. App. P. 27(d) and 32(g), the undersigned hereby certifies that this reply complies with the type-volume limitation of Circuit Rule 27(d).

1. Exclusive of the accompanying documents as authorized by Fed. R. App. P. 27(a)(2)(B) and the exempted portions of the reply as provided by Fed. R. App. P. 27(d)(2) and 32(f), the reply contains 2,598 words.

2. The reply has been prepared in proportionally spaced typeface using Microsoft Word 2010 in 14 point Times New Roman font as provided by Fed. R. App. P. 32(a)(5)-(6). As permitted by Fed. R. App. P. 32(g), the undersigned has relied upon the word count feature of this word processing system in preparing this certificate.

/s/ William F. Lee
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August 1, 2019

No. 2019-2156

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

GENENTECH, INC., CITY OF HOPE,

Plaintiff-Appellant,

CITY OF HOPE,

Plaintiff,

v.

AMGEN INC.,

Defendant-Appellee.

On Appeal from the United States District Court,
for the District of Delaware, No. 18-cv-00924-CFC, Judge Colm F. Connolly

NON-CONFIDENTIAL DECLARATION OF ANDREW J. DANFORD IN SUPPORT OF THE REPLY OF PLAINTIFF-APPELLANT GENENTECH, INC. IN SUPPORT OF ITS EMERGENCY MOTION FOR AN INJUNCTION PENDING RESOLUTION OF APPEAL AND MOTION TO EXPEDITE BRIEFING ON APPEAL

I, Andrew J. Danford, pursuant to 28 U.S.C. § 1746, declare as follows:

1. I am a partner at Wilmer Cutler Pickering Hale and Dorr LLP ("WilmerHale"), counsel to Plaintiff-Appellant Genentech, Inc. in the above captioned appeal. I have personal knowledge of the facts set forth below.

2. Attached hereto as Exhibit 32 is a true and correct excerpt of the transcript of the October 16, 2018 status conference in *Genentech, Inc. and City of Hope v. Amgen Inc.*, No. 18-00924-CFC (D. Del.).

3. Attached hereto as Exhibit 33 is a true and correct copy of the Reply Declaration of Christy Oliger in Support of Genentech's Emergency Motions for Temporary Restraining Order and Preliminary Injunction, in *Genentech, Inc. and City of Hope v. Amgen Inc.*, No. 18-00924-CFC (D. Del. July 10, 2019), ECF No. 278. This exhibit is marked Confidential.

4. Attached hereto as Exhibit 34 is a true and correct excerpt of the Expert Declaration of George M. Grass, Ph.D., in Support of Genentech's Combined Reply Brief in Support of its Emergency Motions for a Temporary Restraining Order and a Preliminary Injunction, in *Genentech, Inc. and City of Hope v. Amgen*, No. 18-00924-CFC (D. Del. July 10, 2019), ECF No. 277.

5. Attached hereto as Exhibit 35 is a true and correct excerpt of the July 19, 2019 telephonic hearing transcript in *Genentech, Inc. and City of Hope v. Amgen*, No. 18-00924-CFC (D. Del.). This exhibit is marked Confidential.

6. Attached hereto as Exhibit 36 is a true and correct excerpt of Amgen's Opening Brief in Support of its Motion for Permanent Injunctive Relief in *Amgen, Inc. et al. v. Sanofi et al.*, C.A. No.: 14-1317-SLR (D. Del. April 27, 2016), ECF No. 340.

7. Attached hereto as Exhibit 37 is a true and correct excerpt of Amgen's Opening Brief in Support of its Motion for Permanent Injunctive Relief in *Amgen, Inc. et al. v. Sanofi et al.*, C.A. No.: 14-1317-SLR (D. Del. April 27, 2016), ECF No. 340.

8. Attached hereto as Exhibit 38 is a true and correct excerpt of the transcript of the deposition of Amgen's Rule 30(b)(6) witness Molly Benson, dated June 27, 2019. This exhibit is marked Confidential.

Executed on: August 1, 2019

/s/ Andrew J. Danford
Andrew J. Danford

EXHIBIT 32

IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

- - -

GENENTECH, INC., and CITY OF HOPE, Plaintiffs and Counterclaim Defendants, vs. PFIZER INC., Defendant and Counterclaim Plaintiff.	:	CIVIL ACTION NO. 17-1672-CFC
GENENTECH, INC., and CITY OF HOPE, Plaintiffs and Counter Defendants, vs. CELLTRION, INC., CELLTRION HEALTHCARE CO., LTD., TEVA PHARMACEUTICALS USA, INC., and TEVA PHARMACEUTICALS INTERNATIONAL GMBH, Defendants and Counterclaim Plaintiffs.	:	CIVIL ACTION NO. 18-95-CFC

- - -

Wilmington, Delaware
Tuesday, October 16, 2018
2:07 o'clock, p.m.

- - -

BEFORE: HONORABLE COLM F. CONNOLLY, U.S.D.C.J.

16:41:13 1 October is really, really quick given everything we have to
16:41:16 2 do.
16:41:17 3 THE COURT: How many days of trial do you think
16:41:19 4 it will be?
16:41:20 5 MR. GUNTHER: You know, Your Honor, it depends.
16:41:23 6 I think we'll -- if nobody launches and we're at a trial and
16:41:27 7 we're -- you know, if nobody has done acts of infringement
16:41:31 8 that we have to worry about damages or things like that and
16:41:34 9 we're down to, you know, a relatively small number of
16:41:37 10 patents, I could imagine, you know, sort of five-day trials
16:41:41 11 against each defendant maybe. Maybe we would be able to put
16:41:44 12 some together. I don't know at this point. That's a very
16:41:47 13 hard thing to say.
16:41:47 14 THE COURT: All right. And it's a bench trial?
16:41:51 15 MR. GUNTHER: Assuming nobody launches and
16:41:53 16 nobody commits acts of infringement, I think it would be a
16:41:55 17 bench trial.
16:41:56 18 THE COURT: All right.
16:41:56 19 MR. GUNTHER: And that to me is really
16:41:58 20 important. Even December I think is really important that
16:42:01 21 we're in that world in order to get this done.
16:42:03 22 THE COURT: Well, for the launch, I told you all
16:42:05 23 bets are off on the schedule.
16:42:07 24 Ms. Rhyu, you asked for at least leave or
16:42:13 25 permission to ask leave to file a dispositive motion. I

16:42:17 1 have to tell you based on ANDA experience, if it's a bench
16:42:21 2 trial --
16:42:23 3 MS. RHYU: I understand.
16:42:24 4 THE COURT: -- we're not going to hear any
16:42:25 5 dispositive motions because I'm going to as a fact-finder --
16:42:29 6 and there was another party who also brought up dispositive
16:42:32 7 motions. Which party was that?
16:42:34 8 MR. THAKORE: Samsung also had the same
16:42:35 9 proposal.
16:42:36 10 THE COURT: Okay. You have to understand that's
16:42:37 11 what we do here.
16:42:39 12 MS. RHYU: But the reason that we made that
16:42:40 13 proposal was that we do think there's a chance this becomes
16:42:44 14 a jury trial, and we're not completely convinced a
16:42:47 15 preliminary injunction would be in order because we don't
16:42:49 16 think irreparable harm would be demonstrated here. So even
16:42:52 17 if we do launch, it may or may not happen that we have a
16:42:55 18 P.I. hearing. So we want to keep this date on the calendar
16:42:59 19 potentially as a jury trial.
16:43:02 20 MS. DURIE: Your Honor, if there's a launch,
16:43:03 21 we're going to request a preliminary injunction.
16:43:05 22 THE COURT: I'm shocked.
16:43:09 23 MS. RHYU: We did want to leave open the
16:43:11 24 possibility for a jury trial.
16:43:12 25 THE COURT: I get that. So the current schedule

16:43:15 1 though is assuming a bench trial. All right. And we
16:43:19 2 will -- I understand that, you know, if the damages come
16:43:21 3 into play, we have a jury trial. I will think about that
16:43:25 4 one second.
16:43:28 5 Now, we will leave it to be decided, the trial
16:43:31 6 date. Now, you also, Ms. Rhyu, originally had proposed a
16:43:36 7 December date.
16:43:37 8 MS. RHYU: Yes.
16:43:44 9 THE COURT: And then through the questioning you
16:43:46 10 were kind enough to agree to move it up to October.
16:43:50 11 Would Pfizer be prejudiced -- I don't think so.
16:43:53 12 Right? Why don't we move it to December? That's still four
16:43:56 13 months earlier than the plaintiffs want. I assume the
16:44:00 14 defendants as a whole would think that was still a
16:44:05 15 beneficial ruling for them. Right?
16:44:07 16 MS. RHYU: The problem I'm having, Judge, if you
16:44:09 17 are setting start dates, are you contemplating that Pfizer
16:44:12 18 and Celltrion would go first, and then --
16:44:14 19 THE COURT: I don't know who would go first.
16:44:16 20 That's why I want to pick a date that any defendant or group
16:44:20 21 of defendants could go forward, and that's why you all have
16:44:23 22 to commit to it.
16:44:24 23 MS. RHYU: Which is why I was wondering if it
16:44:26 24 makes more sense to have Celltrion and Teva secure that
16:44:30 25 October 28th start date, and then in sequence --

EXHIBIT 33

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC. and CITY OF HOPE,	)	
Plaintiffs,	)	
v.	)	C.A. No. 18-924-CFC
AMGEN, INC.,	)	**CONFIDENTIAL - FILED UNDER SEAL**
Defendant.	)	

REPLY DECLARATION OF CHRISTY OLIGER IN SUPPORT OF GENENTECH'S MOTION FOR TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

CONFIDENTIAL MATERIAL FILED UNDER SEAL REDACTED

1. My name is Christy Oliger. I am employed by Genentech, Inc. as Senior Vice President of BioOncology, in which role I manage the company's United States commercial operations for its oncology products. I submitted a declaration dated July 10, 2019 in support of Genentech's emergency motion for a temporary restraining order and a preliminary injunction.

2. I make this declaration to address certain points in Amgen's Opposition to Genentech's motion.

I. FORECASTED IMPACT OF AMGEN'S BIOSIMILAR TRASTUZUMAB ON HERCEPTIN REVENUES

3. I understand that in its Opposition, Amgen asserts that [redacted] and that as support for this assertion, Amgen relies in part on my deposition testimony. Amgen's assertion is mistaken in several respects.

4. During my deposition, I was asked about a document titled [redacted] labeled GNE-HER_002948730-70 ("[redacted]").[1] In particular, I was asked about the page labeled GNE-HER_002948733, which refers to a forecasted loss of Herceptin revenue in 2019 of [redacted].[2]

5. For the reasons explained in my original Declaration, forecasting the potential impact of biosimilar trastuzumab on Herceptin revenues and market share, as well as those of other Genentech products, involves numerous complex variables and a high degree of uncertainty.[3] Accordingly, Genentech's forecasts regarding the potential impact of biosimilar trastuzumab are essentially "best guesses."

6. [redacted]

[1] This document was cited as Exhibit 52 in my Declaration in Support of Genentech's Motion for Preliminary Injunction ("original Declaration").

[2] Ex. 241 [Oliger Dep. Tr.] at 107-11.

[3] Original Declaration § V.

[4] Original Declaration ¶¶ 36-37, 44, 46.

[5] Ex. 52 at GNE-HER_002948751.

[redacted]

7. [redacted] Instead, Genentech has not increased the price of Herceptin at all in 2019, [redacted]

8. Amgen's suggestion that the [redacted] figure shown in the [redacted] represents a definitive expectation of quantifiable harm is also mistaken. In addition to the fact that Genentech's forecasts are simply highly variable best guesses, Amgen's introduction of Kanjinti will have far-reaching effects that will are likely to change the dynamics of the entire oncology biologics market. Accordingly, as discussed in my original Declaration, [redacted]

9. Amgen also misunderstands my deposition testimony regarding the forecast of the impact of biosimilar trastuzumab in 2019 being [redacted] Amgen, a traditional innovator with extensive biologics experience and well-established relationships with clinics and payers.

II. POTENTIAL IMPACT OF AMGEN'S BIOSIMILAR TRASTUZUMAB ON OTHER GENENTECH PRODUCTS

10. I understand that Amgen also asserts that the potential impact of Kanjinti on other Genentech products, such as Perjeta, Kadcyla, Avastin, and Rituxan, should be disregarded because [redacted].

---

[6] Original Declaration ¶¶ 41, 47-48, 50, 53-54, 76.

[7] Ex. 52 at GNE-HER_002948753.

[8] Original Declaration §§ V-VII.

[9] During my deposition, Amgen's counsel did not ask me when I expected biosimilar trastuzumab competition to begin.

CONFIDENTIAL MATERIAL FILED UNDER SEAL REDACTED

11. In my original Declaration, I discussed several reasons that biosimilar trastuzumab is likely to adversely affect Genentech's sales of those other products.[10] [redacted]

12. These considerations do not lend themselves to forecasting, especially in light of their interrelated nature, the numerous variables involved in forecasting discussed in my original Declaration, and Genentech's lack of information regarding the price at which Amgen will offer Kanjinti.[11] Nevertheless, Amgen's suggestion that [redacted],[12] and for the reasons discussed in my original Declaration, the launch of biosimilar trastuzumab—especially by Amgen, in light of its relationships and experience—is likely to have a pronounced adverse effect on these other Genentech products.[13]

III. POTENTIAL IMPACT OF AMGEN'S BIOSIMILAR TRASTUZUMAB ON GENENTECH SPENDING

13. I understand that Amgen also asserts that the launch of Kanjinti will not force Genentech to reduce staff, or to reduce research and development ("R&D") expenditures. [redacted]

14. [redacted]

IV. POTENTIAL IMPACT OF AMGEN'S BIOSIMILAR TRASTUZUMAB ON GENENTECH'S REPUTATION AND GOODWILL

15. I understand that Amgen also asserts that the launch of Kanjinti will not adversely affect Genentech's reputation and goodwill [redacted]

---

[10] Original Declaration §§ III, VI.B.

[11] Original Declaration § V.

[12] Original Declaration ¶¶ 59, 61 (citing Ex. 53 at GNE-HER_001378974-75).

[13] Original Declaration §§ VI.B.

CONFIDENTIAL MATERIAL FILED UNDER SEAL REDACTED

[redacted]

16. [redacted]

Date: July 16, 2019

Christy Oliger

[14] Original Declaration ¶ 67.

CERTIFICATE OF SERVICE

The undersigned counsel hereby certifies that true and correct copies of the foregoing document were caused to be served on July 16, 2019 on the following counsel in the manner indicated:

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Dated: July 16, 2019

/s/ Michael P. Kelly
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EXHIBIT 34

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GENENTECH, INC. and CITY OF HOPE,	)	
Plaintiffs,	)	
v.	)	C.A. No. 18-924-CFC
AMGEN, INC.,	)	**CONFIDENTIAL - FILED UNDER SEAL**
Defendant.	)	

EXPERT DECLARATION OF GEORGE M. GRASS, Ph.D.
IN SUPPORT OF GENENTECH'S EMERGENCY MOTION FOR
TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

this research, I was the co-recipient of the 1989 Ebert Prize, awarded by the American Pharmacists Association Academy of Pharmaceutical Research and Sciences, for a series of manuscripts published in the *Journal of Pharmaceutical Sciences* entitled "Mechanisms of Corneal Drug Penetration." I obtained a M.S. degree in Pharmaceutics at the University of Wisconsin, Madison in 1983. I obtained a Pharm. D. degree from the University of Nebraska in 1980, and was formerly licensed to practice pharmacy in the state of Nebraska.

6. I have spent more than thirty years working in the pharmaceutical industry. From 1985 to 1991, I worked as a Research Scientist at Syntex Research in Palo Alto, where I was responsible for formulation development and research in oral drug absorption, including methods to orally deliver peptides. Since 1991, I have been a pharmaceutical industry consultant. In 1991, I started my own company, Precision Instrument Design Inc., and, in 1997, another company, NaviCyte, Inc. In 1999, NaviCyte, Inc. was acquired by Trega Biosciences, and I served as Chief Technology Officer at Trega Biosciences, Inc. until 2001. In 2001, I founded G2 Research, Inc., and also founded RaptorGraphics, Inc., a computer graphics and simulation business. From 2005 to 2007, I was Vice President of Product Development and Chief Technology Officer for PDxRx, Inc., a specialty-focused pediatrics company. From 2007 to 2010, I was Senior Vice President of Research and Development for Sorbent Therapeutics, Inc., a company developing novel polymer therapeutics for sodium fluid removal. From January 2016 until May 2017, I was Senior Vice President of non-clinical development and founder for NeuroVia, Inc., a company developing a novel compound for childhood cerebral adrenoleukodystrophy.

7. I am the author or co-author of more than 30 published scientific articles, primarily in the areas of models to predict drug pharmacokinetics, corneal permeability and drug

transport, and intestinal transport and drug absorption. I have authored book chapters related to drug delivery and have been an invited speaker at multiple scientific meetings, including meetings of the American Association of Pharmaceutical Scientists. I have been a peer reviewer for a number of journals such as *Pharmaceutical Research* and *Journal of Pharmaceutical Sciences*. I have presented technical information and development plans to the FDA. I am an inventor or co-inventor on eight U.S. patents and four additional U.S. patent applications and several foreign patents. My curriculum vitae is attached as **Appendix A**.

8. I have been retained and provided declarations in other proceedings related to the asserted patents. I provided declarations in the following proceedings: prosecution of the '811 patent (U.S. Patent Application No. 14/073,659) before the U.S. Patent and Trademark Office; *inter partes* review proceedings ("IPRs") related to the '196 and '379 patents (IPR2017-00804, -00805, -01139, -01140); and foreign counterpart proceedings in Japan, South Africa, Europe, and Mexico. I provided deposition testimony in IPR2017-00804, -00805, -01139, -01140.

III. Summary of Opinions

9. The principal prior art references upon which Amgen relies to support its obviousness claims report on studies in which trastuzumab was administered at weekly dosing intervals. The Watanabe Abstract describes a Phase I study in which a first dose of either 1 mg/kg, 2 mg/kg, 4 mg/kg, or 8 mg/kg of trastuzumab was administered and then followed in three weeks by nine weekly doses in the same amount as the first. Based on this study, Watanabe concluded that further clinical trials with "2-4 mg/kg weekly intravenous infusions is warranted." Baselga '96 and Pegram '98 likewise describe Phase II studies of trastuzumab in which patients were given a 250 mg loading dose of trastuzumab followed by weekly doses of 100 mg. The Herceptin Label describes the first FDA-approved dosing regimen for Herceptin, a 4 mg/kg loading dose followed by weekly doses of 2 mg/kg. This is significant not only because

it suggests that skilled artisans at the time of the invention would have known that weekly dosing worked, but also because the prior art did not include pharmacokinetic data with respect to intervals of longer than one week. The "different prior art" cited by Amgen, U.S. Patent No. 8,309,087 (the "Hellmann patent") also describes the weekly FDA approved dosing regimen for Herceptin, a 4 mg/kg loading dose followed by weekly doses of 2 mg/kg, but does not describe extended dosing intervals or include any pharmacokinetic data for trastuzumab. In my opinion, the Hellmann patent does not provide any relevant information that was not provided in Watanabe, Baselga '96, Pegram '98 and the Herceptin Label.

10. It is also my opinion that a skilled artisan would conclude that it was not possible to reliably model a new dosing regimen based on the limited pharmacokinetic data in the references upon which Amgen relies. I base this opinion on two key pharmacokinetic properties of trastuzumab that were expressly described in the prior art. First, the prior art reported that trastuzumab had dose-dependent, non-linear kinetics, which means that the half-life of the drug varied with dose amount and dose interval. A skilled artisan at the time of the invention would have known that reliably modeling a dosing regimen for a drug with non-linear kinetics would require more data than one would need to model a dosing regimen for a drug with linear kinetics, *i.e.*, a half-life that remained constant regardless of the dose amount or interval. For example, the prior art upon which Amgen relies reported many different half-lives for trastuzumab, depending on the dose administered. The half-life reported in the Amgen prior art includes 1.7 days, 5.8 days, and 12 days in the Herceptin Label, 1.8, 8.3, and 9.1 days in Baselga '96, and 2.9, 4.0, 9.2, and 11.0 days in Pegram '98.

11. The prior art disclosure that trastuzumab had non-linear pharmacokinetics would have injected substantial uncertainty into modeling a dosing regimen for trastuzumab because the

serum half-life of 8.3 +/- 5.0 days. (*Id.* at AMGKAN01191051). Baselga '96 sought to achieve trough concentrations of at least 10 µg/mL based on preclinical studies. (*Id.* at AMGKAN01191050.) Baselga '96 reported that over 90% of patients had trough serum concentrations above the 10 µg/mL target, and that patients with trough concentrations below 10 µg/mL did not demonstrate a therapeutic response. (*Id.* at AMGKAN01191051, AMGKAN01191053-54.)

3. Pegram '98

23. Pegram '98 describes the results of a Phase II clinical study in which 39 patients with metastatic breast cancer received trastuzumab in combination with the chemotherapeutic agent cisplatin. (Amgen Ex. 5, at AMGKAN01193130.) Patients were treated with a loading dose of 250 mg of trastuzumab followed by weekly doses of 100 mg for nine weeks. Patients also received 75 mg/m^2 doses of cisplatin about every four weeks. (*Id.* at AMGKAN01193130-32.) Pegram '98 provides only limited pharmacokinetic information on trastuzumab. Specifically, Table 6 of Pegram '98 reports a half-life of 11.0 ± 4.0 days for patients treated with trastuzumab and cisplatin. (*Id.* at AMGKAN01193136, Table 6.) Pegram '98 also includes results from Baselga '96, reporting that when administered alone, trastuzumab had a mean half-life of 9.2 ± 5.3 days. Pegram '98 further reports that mean maximum trough serum concentrations reached 54 µg/mL when trastuzumab was administered without chemotherapy, and 85 µg/mL when trastuzumab was administered with cisplatin. (*Id.*)

4. Herceptin Label

24. The Herceptin Label describes the initial FDA-approved indications and dosing regimen for trastuzumab. (Ex. 40 at AMGKAN02731815.) Based on Phase III clinical trials, the FDA approved a regimen of a loading dose of 4 mg/kg followed by weekly maintenance doses of 2 mg/kg to treat HER2 positive metastatic breast cancer. (*Id.*) The Label contains

limited pharmacokinetic data. For example, the Label states that trastuzumab exhibited dose-dependent kinetics and reports that in dose-rising studies, 10 mg doses administered weekly had an average half-life of 1.7 days and 500 mg doses administered weekly had an average half-life of 12 days. (Ex. 40 at AMGKAN02731815.) No half-life is reported for doses between 10 mg and 500 mg. (*Id.*) The Label also reports a mean half-life of 5.8 days (range of 1 to 32 days) for regimens using a loading dose of 4 mg/kg followed by a weekly maintenance dose of 2 mg/kg. (*Id.*)

5. Hellmann Patent

25. The Hellmann patent is directed to methods of treating cancer by administering anti-ErbB2 antibodies, including trastuzumab, with chemotherapeutic agents other than an anthracycline derivative. (Amgen Ex. 36, at 4:7-22.) The patent describes a clinical study in which trastuzumab was administered ***weekly*** with chemotherapy. (*Id.* at 30:61-31:32.) The Hellmann patent does not contain any discussion of extended dosing intervals for anti-Erb2 antibodies such as trastuzumab. It also lacks pharmacokinetic data of any kind. The ranges of possible trastuzumab doses that it volunteers is expansive: "about 1 μ/kg to 15 mg/kg (e.g. 0.1-20 mg/kg) of antibody is an initial candidate dosage for administration to the patient." (*Id.* at 28:24-28.) The lower end of the range differs from the upper end by many orders of magnitude; it is 15,000 times larger. (*See id.*) It also states that "a typical daily dosage might range from about 1 μg/kg to 100 mg/kg or more." *Id.* at 28:28-30.

B. Pharmacokinetic Factors A Skilled Artisan Would Consider In Designing Dosing Regimens For Trastuzumab In View of the Prior Art

26. A skilled person would consider many factors, including pharmacokinetics, when designing an alternative dosing regimen for trastuzumab.

1. A Skilled Artisan Would Seek to Maintain Therapeutically Effective Levels of Trastuzumab

27. For most drugs that are administered with repeat dosing—including trastuzumab—the goal is to achieve plasma concentration levels within a therapeutic window, *i.e.*, above a certain minimum or "trough" level where efficacy is maintained and below a ceiling or "peak" where unacceptable toxicity may occur. For a drug that has already been shown to be safe and effective at a particular dose amount and dose interval, a pharmacokineticist would generally seek to ensure that any alternative dose amount and interval would yield serum concentration data within the range previously known to be safe and clinically effective. Without an adequate understanding of the pharmacokinetics of a drug, it is impossible to make such a determination.

28. Serum drug concentration reaches a "peak" or maximum concentration shortly after administration. As the drug is eliminated from the body over time, it reaches a "trough" or minimum concentration just prior to the next dose. Dose amount and dose interval affect both peak and trough levels. For example, increasing the dose and extending the dose interval can result in significantly higher peak levels and significantly lower trough levels as compared to the same overall amount of drug given in lower doses more frequently. In fact, administering lower doses more frequently is a common method to minimize the variation between peak and trough levels.

29. At the priority date of the dosing patents in August 1999, a skilled artisan considering an alternative dosing regimen for trastuzumab would know that efficacy was associated with maintaining adequate steady-state trough serum levels, *i.e.*, maintaining a "therapeutic trough concentration." A skilled artisan would thus want to ensure that any alternative dosing regimen maintained therapeutic trough concentrations throughout the course

EXHIBIT 35

(Redacted in Full)

EXHIBIT 36

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC.; AMGEN MANUFACTURING, LIMITED; and AMGEN USA INC.	)	
Plaintiffs,	)	C.A. No.: 14-1317-SLR (CONSOLIDATED)
v.	)	[redacted]
SANOFI; SANOFI-AVENTIS U.S. LLC; AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC., and REGENERON PHARMACEUTICALS, INC.,	)	PUBLIC VERSION
Defendants.	)	

PLAINTIFFS' OPENING BRIEF IN SUPPORT OF MOTION FOR PERMANENT INJUNCTIVE RELIEF

[redacted]

1. Defendants Pursued Praluent® Despite Knowledge of the Infringement Risk and Then Launched At-Risk During the Pendency of This Litigation

Defendants were aware of the potential infringement risk when they chose to pursue Praluent® and should not now be permitted to avoid an injunction by relying on the harms suffered when this business decision did not pan out in their favor.[10]

As early as February 2009, Defendants knew of Amgen's published patent application and immediately identified multiple risks. Hr'g Tr. 187:18-188:7 (Papadopoulos designations). First, the PCT included the full specification of the patents-in-suit as well as both broad ***and*** specific claims that would have covered Defendants' REGN727, which Defendants knew and understood. *See* PTX 3888 at -232 (*see* claims 1, 7, 8, 9); *see* Hr'g Tr. 378:10-15 (Stahl cross). Second, by June 2009, Defendants had identified the risk of a "patent issue" if the "binding epitopes" between REGN727 and Amgen's antibodies were "similar." Hr'g Tr. 191:7-22 (Papadopoulos designations); PTX 3965. Defendants then confirmed that was the case when they discovered overlap in the epitopes between REGN727 and Amgen's antibodies. Hr'g Tr. 188:22-25, 192:20-194:2 (Papadopoulos designations); PTX 3972 at -755; PTX 3957; *see also* Hr'g Tr. 376:19-378:15 (Stahl cross); PTX 3880.

Defendants then performed x-ray crystallography studies for the express purpose of assessing whether Praluent® bound to the PCSK9 residues identified in Amgen's patent

[10] At the hearing, Defendants suggested that Amgen was re-arguing willfulness in support of its injunction position. Hr'g Tr. 38:20-24 (Maslowski opening). Not so. The Court need not reach issues of intent or objective or subjective reasonableness or belief. What the uncontested evidence showed was that Defendants took a calculated business risk, despite Amgen's patents, to press forward with their investment and, ultimately the launch of Praluent®. It does not matter whether they took that risk with a good faith belief that Amgen's patents were not valid. What matters is that they took the risk knowing that Amgen was seeking patent protection and that Amgen's patents might well be found to be valid and, in that event, Defendants' infringing product might be staring at an injunction. *See Acumed*, 551 F.3d at 1330.

application, which itself suggests that Defendants understood which residues would be important from a patent perspective, even without issued claims. Hr'g Tr. 199:12-203:9 (Engel designations); PTX 6077 at -792, PTX 6131 at -522-23; Hr'g Tr. 378:16-21 (Stahl direct). In fact, Dr. Engel's study of the PCSK9 residues at the PCSK9/LDLR interface as set forth in Amgen's patent application (*see* PTX 6131 at -522-23, "projection of binding residues onto PCSK9 sequence: REGN727 . . . , Amgen 31H4, 21B12 *and LDLR-EGFa as described in patent WO 2009/026558A1*" (emphasis added)), are the same exact set of residues that became claim 1 of the '165 patent, which come directly from Example 28 in the patent. In sum, *each* experiment performed by Defendants demonstrates that they understood all along the risk that patent claims would issue directed to the PCSK9 residues at the LDLR interface and/or to which 21B12 and 31H4 bound. Notwithstanding Defendants' knowledge of Amgen's pending patent portfolio, as well as their own experimental evidence of infringement, Defendants elected to continue their investment in Praluent®. *See, e.g.*, Hr'g Tr. 342:20-343:8, 357:9-12 (Edelberg cross); PTX 4051 at -878.

Thus, Defendants' suggestion at the hearing that they should not be held accountable for their choices because Amgen's published patent applications might never have issued or might have issued with different claims should not be credited. Indeed, one of the very purposes behind enacting the legislation that mandates publication of patent applications is to provide notice to potential infringers. *See* Hr'g Before the Subcomm. on Cts. and Intellectual Property, 104th Cong. 36 (1995) (statement of Bruce Lehman, Asst. Sec. of Commerce and Comm'r of Patents and Trademarks, Patent and Trademark Office, U.S. Dept. of Commerce).[11]

[11] Available at: https://archive.org/details/patentslegislati00unit.

[redacted]

Even if the Court were to countenance Defendants' hubris in moving forward in the face of Amgen's patent application, Defendants' actions after this lawsuit was filed in October 2014 are telling. Defendants intentionally accelerated their infringement by exercising a priority review voucher to speed up the FDA approval process and their commercial launch by four months. Hr'g Tr. 61:2-13 (Bradway direct); Hr'g Tr. 174:1-13, 175:16-176:13 (Broadhurst direct); PTX 4530, PTX 4758. Defendants chose to launch Praluent® at-risk despite the fact that the Court discussed, and then implemented, an accelerated trial date in lieu of preliminary injunction proceedings. *See* Compl., D.I. 1; Tr. of Feb. 24, 2015 Rule 16 Scheduling Conference 12:14-24, 16:25-17:4; Scheduling Order, D.I. 49. Upon the launch of Praluent®, Defendants knowingly exacerbated the harm to Amgen by "flooding" the market with free goods and by adopting highly aggressive negotiation tactics to secure exclusive agreements with various insurers, including one of the largest insurance companies in the country. JTX 195 at -758; Hr'g Tr. 315:7-15; 316:3-20 (Terifay cross); Hr'g Tr. 166:20-169:19 (Broadhurst direct); Hr'g Tr. 226:16-227:6 (Berndt direct); Hr'g Tr. 285:8-287:12 (Carey cross); JTX 266 at -954. The logical inference drawn from Defendants' actions is that they chose to develop at-risk and launch at-risk — in order to argue that Praluent® should not be enjoined. Defendants are now asking the Court to reward them for their risky business decisions and their infringement. But such a reward would undermine the very purpose of obtaining a patent.

Courts have held that where infringers launched at-risk, any damage caused by this at-risk activity weighs against the infringer in the balance of the hardships analysis. *See, e.g.*, *Merial Ltd. v. Cipla Ltd.*, 681 F.3d 1283, 1306 (Fed. Cir. 2012); *see also Robert Bosch LLC v. Pylon Mfg. Corp.*, 659 F.3d 1142, 1156 (Fed. Cir. 2011) (requiring a patentee to compete against its own patented invention places a substantial hardship on the patentee, weighing in favor of the

[redacted]

entry of an injunction); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383 (Fed. Cir. 2006) (affirming grant of preliminary injunction where generic drug manufacturer launched at-risk, stating that the balance of the hardships weighs in favor of the patentee where the infringer's hardships "were the result of its own calculated risk to launch its product pre-judgment"). The harms Defendants allege they will suffer simply do not outweigh the incalculable and irreparable harms inflicted upon Amgen due to Defendants' at-risk conduct.

2. Regeneron's Costs to Develop the Infringing Product Do Not Weigh in Defendants' Favor When Balancing the Hardships Because Those Costs Are Mitigated by Defendants' Collaboration Agreement

At the injunction hearing, Defendants signaled that they will claim harm because they spent time and money developing Praluent® and because Regeneron is a small biotech company. *See, e.g.*, Hr'g Tr. 481:3-6 (Oster direct). The decision to invest at-risk in development of Praluent® is addressed above. To the extent Defendants rely upon Regeneron being a "small" company, that argument fails. First, "[a] party cannot escape an injunction simply because it is smaller than the patentee or because its primary product is an infringing one." *Robert Bosch*, 659 F.3d at 1156; *see also Merial Ltd.*, 681 F.3d at 1306 (affirming entry of permanent injunction even where it would have a "crippling effect" on the infringer's business). Second, contrary to Defendants' assertion, Regeneron is by no means a small business and undoubtedly will continue due to its success as a pharmaceutical company, specifically with its Eylea® product, a self-proclaimed "best in class" drug for the treatment of macular degeneration, as well as other diseases of the eye. Trial Tr. 344:19-345:7 (Schleifer direct).

Third, if Praluent® is enjoined, Regeneron is shielded from significant harm due to its Collaboration Agreement with Sanofi. JTX 089 at §§ 9.1-9.12, Schedules 2 and 3; JTX 369 at §§ 4.1-4.10; Hr'g Tr. 237:22-238:22 (Berndt direct); Hr'g Tr. 312:10-18 (Terifay cross) (Sanofi

[redacted]

EXHIBIT 37

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMGEN INC.; AMGEN MANUFACTURING, LIMITED; and AMGEN USA INC.	)	
Plaintiffs,	)	C.A. No.: 14-1317-SLR (CONSOLIDATED)
v.	)	[redacted]
SANOFI; SANOFI-AVENTIS U.S. LLC; AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC., and REGENERON PHARMACEUTICALS, INC.,	)	PUBLIC VERSION
Defendants.	)	

PLAINTIFFS' OPENING BRIEF IN SUPPORT OF
MOTION FOR PERMANENT INJUNCTIVE RELIEF

[redacted]

in-suit are invalid. Defendants' infringement has continued unabated since judgment was entered against Defendants. Amgen now seeks a permanent injunction.

V. ARGUMENT

Analyzing the facts of this case under the well-known, four-factor test for an injunction as described by the Court in *eBay*, 547 U.S. at 394, leads to one conclusion: that entry of a permanent injunction is the only appropriate remedy.

A. AN INJUNCTION SHOULD ISSUE BECAUSE DEFENDANTS' CONTINUED INFRINGEMENT IS CAUSING AMGEN IRREPARABLE HARM

Defendants' infringement and direct competition in this two-supplier market is causing Amgen to suffer price erosion, reputational harm, lost sales, and lost market share. It also threatens to disrupt the very business model on which Amgen depends for the long-term, autonomous operation of its business. A permanent injunction is the only remedy to prevent such harm.

1. Defendants' Continued Infringement Is Causing Amgen to Suffer Price Erosion

Price erosion alone is sufficient to establish irreparable harm. *See Edwards Lifesciences AG v. CoreValve, Inc.*, No. CV 08-91, 2014 WL 1493187, at *6 (D. Del. Apr. 15, 2014) (citing *Celsis In Vitro, Inc. v. CellzDirect, Inc.*, 664 F.3d 922, 930 (Fed. Cir. 2012)). Amgen has experienced and will continue to experience significant price erosion. By launching Praluent® at-risk, Defendants have enabled insurers to pit the parties against each other to extract larger and larger rebates and other concessions as a condition to being included (even in a parity position) on national formularies, thereby eroding Amgen's net price for Repatha®.[3] *See* Ex. A (summary

[3] Defendants' economics expert Dr. Oster agrees that there is price erosion in this case, and she expects price erosion to continue into the future. Hr'g Tr. 492:4-10 (Oster cross).

[redacted]

Inc. v. Synthes (U.S.A.), 466 F. Supp. 2d 978, 984 (W.D. Tenn. 2006) (noting that dynamic market forces rendered damages award "speculative at best").

3. The Loss of Innovator Status and Reputational Harm that Defendants Have Caused Amgen Are Incalculable

Courts routinely recognize that certain types of harm, such as reputational harm and loss of innovator status, are unquantifiable and thus cannot be compensated with monetary damages. *See, e.g.*, *Douglas Dynamics*, 717 F.3d at 1344 ("Irreparable injury encompasses different types of losses that are often difficult to quantify, including lost sales and erosion in reputation and brand distinction."); *TruePosition*, 568 F. Supp. 2d at 531 (finding inadequate remedy at law where "[d]efendant has taken from plaintiff not only this important business, but the recognition of being a technology innovator and the first global supplier of the patented technology, and an unquantifiable amount of business opportunities flowing therefrom"); *Smith & Nephew*, 466 F. Supp. 2d at 983-85 (same).

Here, Amgen is suffering harm to its reputation, including loss of innovator and first-in-class status. Hr'g Tr. 69:12-70:1 (Bradway direct); Hr'g Tr. 235:6-15 (Berndt direct); Hr'g Tr. 150:23-151:13 (Ryan direct). Defendants' expert Dr. Oster, though she suggests that reputational harm can be quantified, never provides a way to calculate such harm. Hr'g Tr. 479:18-25 (Oster direct).[9] As Amgen's expert Dr. Berndt testified: "How do you quantify the foregone R&D opportunities, the lost reputation, the imposition on Amgen of a forced change in business model to rely instead [of] on patent protected products, on bringing products to market that will suddenly have fast followers[?] I don't know how you can quantify those damages with

[9] Indeed, the sum total of Dr. Oster's conclusory testimony on the subject is: "Q: Ok. And to the extent there even was reputational harm, could that be quantified? A: Yes." Hr'g Tr. 479:18-20 (Oster direct).

responsible for 100% of development costs up to the first successful Phase 3 clinical trial, after which Sanofi is responsible for 80%); *see also* Hr'g Tr. 489:23-490:6 (Oster cross). In the face of an injunction, Regeneron will not earn potential future revenue from the sale of Praluent® in the United States, but—because it will not earn revenue—it will not have to pay back the expense of development. Hr'g Tr. 238:6-22 (Berndt direct). By contrast, Sanofi, a large, diversified, global company (indeed, much larger than Amgen), really has no risk. Hr'g Tr. 238:23-239:6 (Berndt direct); Trial Tr. 359:13-360:6 (Edelberg direct). A permanent injunction would not force Sanofi to change its business model. Hr'g Tr. 238:23-239:6 (Berndt direct). There was no evidence to the contrary.

D. A PERMANENT INJUNCTION WILL SERVE THE PUBLIC INTEREST

The compelling public interest here is manifest: the assurance that there will be a continuous cycle of invention of new medicines to treat the diseases of today and tomorrow. Injunctive relief here will foster the incentives of the patent system to achieve this goal.

1. The Public Has a Strong Interest in a Robust Patent System that Maintains the Incentives for Pharmaceutical Innovation

Since Amgen was founded more than 35 years ago, it has been in the business of inventing, developing, manufacturing, and selling biopharmaceutical medicines to treat serious human illness, with 16 medicines currently on the market today. Trial Tr. 227:12-15 (Bradway direct). Amgen's ability to sustain this engine of innovation is built upon the right to exclude infringers from practicing their inventions for the period of time afforded by their patents. Hr'g Tr. 58:16-59:2 (Bradway direct); Hr'g Tr. 229:7-22 (Berndt direct). Without this patent right, Amgen would not have been able to protect its investment, generate adequate capital to re-invest in innovation-based R&D, or maintain the confidence of its investors. Hr'g Tr. 59:3-10, 61:14-

62:5 (Bradway direct). The same can be said of nearly every other innovation-based biotech and pharmaceutical company. Judge Young made this very point almost a decade ago:

> If the Court allowed [the defendant] to introduce [its infringing product] into the market, perhaps a few patients would benefit, and maybe Medicare would save a few dollars. These arguments, however, could be made for almost any infringing drug. Were courts to refuse injunctions on the basis of such speculation, then pharmaceutical patents would be worth far less than they are today because they would no longer include a right to exclude infringers from the market. The diminishing returns would disincentivize research and development for pathbreaking drugs by lowering the expected value of discovery. By contrast, granting injunctions encourages companies to devote their energies toward developing drugs that will satisfy unmet medical needs. *Were it possible to obtain market entry by making incremental improvements to existing drugs, it is doubtful that companies designed to generate discoveries could exist.*

Amgen, 581 F. Supp. 2d at 226-27 (emphasis added).

The patent laws are designed to reward inventors based on the profits the invention can command in the marketplace over the life of the patent "by offering a right of exclusion for a limited period as an incentive to inventors to risk the often enormous costs in terms of time, research, and development." *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1363 (Fed. Cir. 2008) (quoting *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974)); Hr'g Tr. 239:10-240:13 (Berndt direct). It is of no consequence that others may have independently arrived at the invention later. *See Radio Corp. of Am. v. Radio Eng'g Labs., Inc.*, 293 U.S. 1, 3 (1934) (J. Cardozo reinstating injunction where four different entities independently arrived at same or nearly the same discovery, stating, "The prize of an exclusive patent falls to the one who had the good fortune to be first."). Indeed, there is a "significant public interest in encouraging investment in drug development and protecting the exclusionary rights conveyed in valid pharmaceutical patents." *Sanofi-Synthelabo*, 470 F.3d at 1384 (internal quotation marks omitted).

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EXHIBIT 38

(Redacted in Full)