UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC.,

Plaintiff,

v.

F. HOFFMANN-LA ROCHE, LTD, ROCHE DIAGNOSTICS GMBH, and HOFFMANN-LA ROCHE INC.,

Defendants.

Civil Action No. 05 CV 12237 WGY

U.S. District Judge William G. Young

DEFENDANTS' OPPOSITION TO AMGEN'S MOTION *IN LIMINE* NO. 4 TO EXCLUDE GENENTECH'S PLA FILING [ROCHE TRIAL EXH. NO. 1072] BECAUSE IT IS NOT PRIOR ART

I. INTRODUCTION

Defendants F. Hoffmann-La Roche, Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively, "Roche") submit this memorandum in opposition to Amgen's motion *in limine* No. 4 to exclude Genentech's Product License Application filing (the "PLA"), Roche Trial Exhibit No. 1072. Amgen's motion to preclude Roche from introducing certain portions of Genentech's PLA is flawed in several respects. First, Amgen incorrectly presumes that in order to be relevant to Roche's obviousness contentions the PLA must qualify as prior art. As discussed below, regardless of whether the PLA is prior art, it is highly relevant in rebutting Amgen's arguments regarding the supposed lack of enablement of two prior art patent references relied on by Roche as demonstrating the obviousness of Amgen's asserted claims. Second, the PLA in fact qualifies as prior art evidence under 35 U.S.C. § 102(g) by demonstrating actual reduction to practice of an invention predating the December 1983 filing date of Amgen's patents.

II. ARGUMENT

Genentech Inc.'s U.S. Patent No. 4,766,075 (the "'075 patent"), filed on April 7, 1983, and its counterpart European patent application EP 0 093 619 (the "'619 EP application"), published November 9, 1983, disclose the prior art use of Chinese Hamster Ovary ("CHO") cells to make a biologically active, human tissue type plasminogen activator ("tPA") glycoprotein, as well as the therapeutic use of the CHO cell produced tPA product.[1] Both the '075 patent and the

[1] Based on the same specification, the PTO allowed claims directed to the therapeutic use of the CHO cell tPA product, which issued in a divisional of the '075 patent, substantiating that Genentech's specification disclosed and enabled an *in vivo* biologically active tPA product made in CHO cells. *See* U.S. Patent No. 6,274,335 (claiming priority to May 5, 1982).

EP '619 application claim a priority date of May 5, 1982.[2] Roche relies on these documents as evidence that by 1983 one of skill in the art would and could use CHO cells to produce an *in vivo* biologically active "obligate" glycoprotein (such as the CHO cell produced EPO protein claimed in Amgen's patents) with a reasonable expectation of success and, thus, the asserted claims would have been obvious.[3]

Prior art that demonstrates obviousness under 35 U.S.C. § 103 is the art enumerated in 35 U.S.C. § 102. *Bose Corp. v. JBL, Inc.*, 112 F. Supp. 2d 138, 152 (D. Mass. 2000), *aff'd*, 274 F.3d 1354 (Fed. Cir. 2001). An issued U.S. patent, such as the '075 patent, constitutes prior art as of its filing date under § 102(e)(2) and the EP '619 application qualifies as prior art to the patents-in-suit under §§ 102(a) It is also black-letter law that allowed patents are presumed valid. *Union Carbide Chems. & Plastics Tech. Corp. v. Shell Oil Co.*, 308 F.3d 1167, 1186 (Fed. Cir. 2002). Furthermore, "a presumption arises that both the *claimed and unclaimed disclosures* in a prior art patent are enabled." *Amgen Inc. v. Hoechst Marion Roussel, Inc*., 314 F.3d 1313, 1355 (Fed. Cir. 2003) (emphasis added). A party challenging a patent's enablement bears the burden of proving that a patent's specification fails to teach the invention. *Union Carbide*, 308 F.3d at 1186. Here, however, Amgen is unable to rebut the presumption of enablement: the

---

[2] The '075 patent and the EP '619 application share a common specification.

[3] For example, Roche will show at trial that the utility of using CHO cells to express a functional recombinant human glycoprotein was demonstrated by the use of DHFR-CHO cells to express human tissue type plasminogen activator (tPA), as described in the '075 patent and the EP '619 application. Further, evidence will show that as demonstrated by the Genentech PLA, production of recombinant human tPA using CHO cells resulted in a glycosylated protein biologically indistinguishable from human tPA derived from human melanoma cells. In fact, the Genentech process steps for producing recombinant human tPA in DHFR CHO cells was no different than the methodology described in the later filed asserted Lin patents for producing recombinant human EPO in DHFR CHO host cells.

FDA approved recombinant t-PA covered by the '075 patent (and described by the EP '619 application) in 1987. *See* [FDA press release]

In an attempt to challenge Roche's use of the Genentech references as prior art, Amgen apparently intends to argue that the references fail to enable an *in vivo* biologically active human glycoprotein produced in CHO cells. However, the Genentech PLA plainly rebuts Amgen's erroneous argument. The PLA describes clinical trials conducted with a tPA product produced in CHO cells according to the teaching of the'075 patent and confirms the therapeutic use and effectiveness of that product. (*See* Roche Trial Ex. 1072, ROCHE-GEN 00005-00010; 00032-00034). Thus, Roche intends to rely on the PLA to demonstrate that Genentech's '075 patent discloses and enables use of CHO cells to produce an *in vivo* biologically active "obligate" human glycoprotein.[4] Relevant case law makes plain that a party may properly rely on later publications to prove enablement of an earlier disclosure. *See, e.g., Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1335 (Fed. Cir. 2003) ("numerous post-filing publications demonstrated the extent of the enabling disclosure"); *Hormone Research Found., Inc. v. Genentech, Inc.*, 904 F.2d 1558, 1568 (Fed. Cir. 1990) (later publications suggested that claimed method for solid phase peptide synthesis may have been enabled).

Moreover, the PLA itself qualifies as evidence of prior invention under § 102(g), something Amgen's motion ignores entirely. The PLA describes clinical trials reflecting the actual practice of Genentech's prior invention of the use of CHO cells to produce an *in vivo* biologically active "obligate" glycoprotein. That the PLA was not public until later is irrelevant

[4] Amgen continues to argue the non-obviousness of the subject matter claimed in the Lin patents in part on grounds that there was no prior art demonstrating that CHO cells could be used to make an "obligate" human glycoprotein, that is, a human protein requiring glycosylation for its *in vivo* biological activity. Amgen admitted during prosecution, however, that human tPA was an "obligate" glycoprotein.

to its status as prior art. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 107 (D. Mass. 2001) (finding later publications qualified as prior art because work began prior to Lin's invention date). Furthermore, Amgen provides no evidence that Genentech abandoned, suppressed, and concealed its invention, such that it would not constitute prior art under § 102(g).[5] In fact, the invention undeniably was public as of November 9, 1983 in Genentech's EP '619 application, and data from clinical trials with Genentech's tPA were published by 1985. *See The Thrombolysis in Myocardial Infarction (TIMI) Trial*, 312 New Eng. J. Med. 932-36 (1985) (ROCHE-GNE 00428-00432). Thus, there is no basis to argue concealment.

Amgen urges the Court to preclude Roche's reliance on the PLA as it purportedly describes only a "later arising invention." However, this argument is based entirely on Amgen's erroneous presumption that the PLA has no relevance to and misrepresents the state of the art in 1983. The therapeutic use of CHO tPA was not a "later arising invention." It was disclosed both in the '075 patent, and in the EP '619 application. In fact, Genentech's clinical trials predate any evidence of the use of CHO cells by Amgen, which was included only in Amgen's application filed on September 28, 1984. *See* U.S. Serial No. 06/655,841. In addition, as explained above, even if the PLA reflected a "later arising invention" -- which it does not -- the PLA is still admissible evidence of enablement of the '075 patent and the EP '619 application.

The PLA, which describes the actual use of the invention disclosed in Genentech's '075 patent and '619 EP application, is, therefore, highly probative as to the state of the art in 1983, as well as the enablement of the '075 patent and its '619 counterpart application. If there is any risk

[5] After a patent challenger demonstrates the existence of a prior invention by clear and convincing evidence, "the burden of production shifts to the patentee to produce evidence sufficient to create a genuine issue of material fact as to whether the prior inventor has suppressed or concealed the invention." *Apotex USA, Inc. v. Merck & Co.*, 254 F.3d 1031, 1037 (Fed. Cir. 2001).

of prejudice here, that risk is to Roche, which would be denied a full and fair opportunity to address Amgen's contentions about that prior art if Amgen were to succeed in excluding evidence of the Genentech PLA.

III. CONCLUSION

For the foregoing reasons, the Court should deny Amgen's motion *in limine* No. 4 to exclude any reference to the Genentech PLA.

Dated: September 1, 2007
Boston, Massachusetts

Respectfully submitted,

F. HOFFMANN-LA ROCHE, LTD,
ROCHE DIAGNOSTICS GMBH, and
HOFFMANN-LA ROCHE INC.

By their attorneys,

/s/ *Thomas F. Fleming*

Leora Ben-Ami (*pro hac vice*)
Patricia A. Carson (*pro hac vice*)
Thomas F. Fleming (*pro hac vice*)
Howard S. Suh (*pro hac vice*)
KAYE SCHOLER LLP
425 Park Avenue
New York, NY 10022
Tel: (212) 836-8000

Lee Carl Bromberg (BBO# 058480)
Timothy M. Murphy (BBO# 551926)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO# 663853)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel: (617) 443-9292

CERTIFICATE OF SERVICE

I hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non-registered participants on the above date.

/s/ Thomas F. Fleming
Thomas F. Fleming