IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMGEN, INC., Plaintiff, v. F. HOFFMANN-LA ROCHE Ltd, a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN-LA ROCHE INC., a New Jersey Corporation, Defendants.	Civil Action No. 05-12237 WGY U.S. District Judge Young

ADDITION TO BENCH MEMORANDUM REGARDING
RELEVANCE AND ADMISSIBILITY OF GENENTECH'S PLA

Roche respectfully submits this addition to the bench memorandum provided to the Court on Friday, Sept. 7, 2007 relating to the relevance and admissibility of Genentech's Product License Application ("PLA") for its human tissue plasminogen activator ("tPA"). For the Court's convenience, a copy Roche's Bench Memorandum is attached as Ex. A.

Roche wishes to point out that Mr. Day during his cross of Dr. Lowe on Sept. 7 went into an area that directly shows the relevance of the Genentech PLA. Mr. Day asked questions to give the impression that the product produced pursuant to the disclosures in the '075 patent and '619 EP application were not enabled. For example, Mr. Day asked Dr. Lowe whether the Genentech patent has any description of glycosylation of the product produced in CHO cells or that the product as active in vivo.[1] By calling into question the enablement and disclosure of the

[1] Q: Is the answer yes or no? Is there any description in the Genentech patent of any glycosylation of the CHO cell produced product?

(continued...)

Genentech patent and counterpart European application, Mr. Day has proven the relevance of the Genentech PLA - it rebuts this claim that these earlier filed references were not enabled. Now that there is no question that Amgen makes this claim and has left the jury with this impression, Roche should be allowed to use the PLA to rebut this false impression of non-enablement.

Roche also believes it will be helpful to the Court to provide a description of selections of the PLA relevant to show enablement and actual reduction to practice of the inventions claimed in admitted exhibits 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, as explained in Roche's Bench Memorandum. Also attached, as Exhibit B, is a timeline showing the relevant dates, including the filing of Lin's patents, filing of the '075 patent and '619 EP application, and the dates established by the PLA.

The PLA describes clinical trials conducted with a tPA product produced in CHO cells according to the teaching of the '075 patent and the '619 EP application, and confirms the therapeutic use and effectiveness of that product. The PLA demonstrates that Genentech's '075 patent and '619 EP application disclose and enable use of CHO cells to produce an *in vivo*

A: No.

Q: Is there any demonstration, any experiment or data presented in the Genentech patent disclosure to show that the product produced from CHO cells was active in vivo; yes or no?

A: So you want a yes or no answer?

Q: Yes.

A: No, there isn't.

Trial Transcript, 9/7/07 at 389:9-19.

biologically active "obligate" human glycoprotein.[2] For example, the PLA reports that "recombinant DNA clones containing Human Tissue-type Plasminogen Activator (t-PA) cDNA sequences were prepared and identified as described in Penneca et al."[3] Pennica et al. was published in the journal Nature in 1983.[4] The Master Working Cell Bank of CHO cells expressing the gene for human tPA was prepared by Jan. 19, 1984.[5] The PLA also demonstrates that the therapeutic product containing the recombinant tPA made in these CHO cells was administered to patients in a clinical trial containing 56 patients at least as early as February 17, 1984.[6] Another clinical trial involving recombinant human tPA from Genentech was conducted beginning in September 1984 by the National Heart, Lung and Blood Institute in cooperation with Genentech as part of the Thrombolysis in Myocardial Infarction (TIMI) research program.[7] All of this is prior to Lin's effective filing date of Nov. 30, 1984. The results of the TIMI clinical trial, showing the effectiveness and biological activity of Genentech's tPA, prepared according to the disclosures of the '075 patent and '619 EP application, were reported in the

[2] 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.

[3] Trial Ex. OUX at ROCHE-GNE 03050.

[4] Trial Ex. OUX at ROCHE-GNE 03054.

[5] Trial Ex. OUX at ROCHE-GNE 03059.

[6] Genentech Clinical Study 83-007 "A Controlled Randomized Phase I Trial of Recombinant Tissue-type Plasminogen Activator (rt-PA) in Acute Myocardial Infarction." Trial Ex. PNT at ROCHE-GNE 01450-51; 01545.

[7] Trial Ex. PXY at Roche-GNE 00387.

New England Journal of Medicine on April 4, 1985.[8] Genentech's PLA was submitted to the FDA on April 24, 1986.[9] As the cited materials demonstrate, Genentech's PLA is relevant to rebut Amgen's claim and presentation to the jury that the '075 patent and '619 EP application are not enabled, and also to show actual reduction to practice for § 102(g) purposes of the inventions claimed in the '075 patent and '619 EP application.

[8] Trial Ex. PXY, ROCHE-GNE 00427-00432.

[9] Trial Ex. OUX at ROCHE-GNE 03009.

Dated: September 10, 2007

Respectfully submitted,

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

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CERTIFICATE OF SERVICE

I certify that, on the above date, 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.

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