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-12237WGY

ROCHE'S OFFER OF PROOF REGARDING EVIDENCE THAT WAS EXCLUDED AT THE VALIDITY PHASE OF THE TRIAL

Defendants F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH and Hoffmann-Law Roche Inc. (collectively "Roche") respectfully submit this Offer of Proof of evidence pertinent to its claim that the asserted claims of the patents-in-suit are invalid. The evidence that is subject of this offer is as follows[1]:

1. Exhibit NCF -- Dr. Eschbach Article

The Court sustained Amgen's objection to admitting Exhibit NCF, a publication by Joseph W. Eschbach (Nephrology 4: 279-87, 1998), into evidence. Had this evidence been admitted, Dr. Spinowitz would have testified that Dr. Eschbach had administered a pharmaceutical composition comprising human erythropoietin to a patient. Dr. Spinowitz would have offered the opinion that reticulocyte and iron uptake responses in this patient were consistent with the presence of a therapeutically effective amount of human erythropoietin

[1] In addition, Roche would have presented additional evidence to the jury regarding its claim that Amgen's patents are invalid for obviousness-type double patenting, which evidence will now be presented to the Court instead. Roche maintains that evidence related to obviousness-type double patenting should be presented to the jury.

according to the Court's claim construction. Dr. Spinowitz would have further been able to testify that this patient exhibited similar responses (demonstrated by the side-by-side presentation in Figure 7 of Exh. NCF) when she was administered recombinant human erythropoietin in the context of Amgen's phase I clinical trial for Epogen. Dr. Spinowitz would have then been able to offer his opinion that Dr. Eschbach and Amgen (who ultimately approved the design of the Epogen phase I study) understood how to determine whether a response to human erythropoietin administration had occurred. This testimony, provided in Dr. Spinowitz's expert reports dated April 6, 2007 at paragraphs 71-74, May 1, 2007 at paragraphs 24, 32 and 34 and August 6,. 2007 at paragraphs 66-71 is relevant to Roche's obviousness defenses for the '422 and '933 pharmaceutical composition claims, as this evidence demonstrates the understanding of one of ordinary skill in the art (i.e., Dr. Eschbach).

2. Exhibit VI -- Article

The Court sustained Amgen's objection to admitting Exhibit VI, a publication from *Biochemica et Biophysica Acta*, 670, 176-180 (1981) into evidence. Had this evidence been admitted, Dr. Lowe would have explained how it supports his opinion that with sufficient purified EPO protein in 1983-1984, one of skill in the art could have determined the amino acid sequence of the protein and synthesized the gene encoding EPO using routine techniques. This testimony would have been consistent with Dr. Lowe's Third Supplemental Expert Report dated June 13, 2007 at paragraph 31 and is relevant to Roche's obviousness defenses.

3. Exhibit OUX -- Genentech PLA (in its entirety)

The Court allowed only pages 3009, 3050, 3054 and 3059 from Exhibit OUX and sustained Amgen's objection to admitting Exhibits PNT and PXY. Had this evidence been admitted, Dr. Lowe would have testified that these exhibits supported his opinion that the PLA is

prior art evidence under 35 U.S.C. § 102(g) demonstrating actual reduction to practice of an invention predating the November 30, 1984 effective filing date of Amgen's Lin patents and refute Amgen's contentions that Trial Ex. 2029 and 2030 are not enabling. The PLA demonstrates that Trial Ex. 2029 and 2030 disclose and enable use of CHO cells to produce an *in vivo* biologically active "obligate" human glycoprotein. 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 and 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. All of this is prior to Lin's effective filing date of Nov. 30, 1984. This testimony, provided in Dr. Lowe's Expert Reports dated April 6, 2007 at paragraphs 126 and 134 and dated May 1, 2007 at paragraphs 6-14 is relevant to Roche's obviousness defense.

4. Exhibit QDZ (Amgen IND in its entirety); Exhibit PUY; Exhibit WGY

The Court allowed only four pages (as admitted Trial Ex. 2054) from Exhibit QDZ and otherwise sustained Amgen's objection to admitting these exhibits.[2] Had this evidence been admitted, Dr. Spinowitz would have testified that this evidence supports the fact that Amgen was in possession of the data from the Baron Goldwasser clinical trial. The fact that Amgen possessed the data from the clinical trial is relevant to Roche's claim that the patents are invalid under 35 U.S.C. § 102(f) as derived from another's invention. Specifically, "to prove derivation under § 102(f), the party asserting invalidity must prove both prior conception of the invention by another **and communication of the conception to the patentee**." *Eaton Corp. v. Rockwell Int'l Corp.*, 323 F.3d 1332, 1344 (Fed. Cir. 2003) (emphasis added). Exhibit QDZ is critical to

[2] In the alternative Roche requests that the Court deem it to be a stipulated admission that Amgen was aware of the data from the Baron Goldwasser clinical trial. (Trial Tr. at p. 799)

demonstrating that Baron-Goldwasser conception of a pharmaceutical composition was in fact communicated to Amgen. Moreover, the possession of the data by Amgen is also relevant to Roche's claim that the patents are invalid under 35 U.S.C. § 102(g), which invalidates a patent if the claimed invention was made by another inventor who had not abandoned, suppressed, or concealed it." The receipt by Amgen of the data of the Baron Goldwasser clinical trials would tend to show that the Baron Goldwasser invention was not suppressed, concealed or abandoned. Dr. Spinowitz would have testified consistent with his August 13, 2007 Reply Expert Report at paragraphs 43-45, 58.

5. Testimony on Safety Issues on Amgen Products

The Court precluded Roche from questioning Dr. Spinowitz on the issue of his awareness of safety issues regarding Amgen's EPO products. Amgen had opened the door to safety issues by questioning Dr. Spinowitz on his opinions about whether Amgen's products met a long-felt need, and by questioning Dr. Spinowitz on whether it is safe to give plasma to patients. Both lines of questioning sought to impress upon the jury that Amgen's products are safe. If permitted, Dr. Spinowitz would have testified as safety issues that have arisen with respect to Amgen's products based on his first-hand knowledge from running clinical trials and other sources.

Dated: September 14, 2007

Boston, Massachusetts

Respectfully submitted,

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

By their Attorneys,

/s/ Nicole A. Rizzo
Lee Carl Bromberg (BBO# 058480)
Robert L. Kann (BBO# 258025)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO# 663853)
Kregg T. Brooks (BBO# 667348)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel. (617) 443-9292
nrizzo@bromsun.com

Leora Ben-Ami (*pro hac vice*)
Patricia A. Carson (*pro hac vice*)
Thomas F. Fleming (*pro hac vice*)
Howard S. Suh (*pro hac vice*)
Peter Fratangelo (BBO# 639775)
Vladimir Drozdoff (*pro hac vice*)
KAYE SCHOLER LLP
425 Park Avenue
New York, New York 10022
Tel. (212) 836-8000

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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). Pursuant to agreement of counsel dated September 9, 2007, paper copies will not be sent to those indicated as non registered participants.

/s/ Nicole A. Rizzo
Nicole A. Rizzo

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