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 RESPONSE TO AMGEN'S BENCH MEMORANDUM TO PRECLUDE ROCHE FROM EXAMINING DR. TORCHILIN ON EVIDENCE REGARDING PATIENT CHOICE AND THE SAFETY AND DOSING BENEFITS OF MIRCERA IN CONTRAVENTION OF THE COURT'S PREVIOUS RULINGS

Amgen makes the spurious argument that a prior ruling on Amgen's motion relating to safety and efficacy issues precludes *all testimony relating to biological and pharmacological differences relevant to infringement.* On the contrary, Amgen's motion sought no such relief and indeed could not have as Amgen is currently offering testimony on these very issues. Amgen's motion was confined to safety and efficacy benefits rather than the functional differences regarding how MIRCERA operates in the body that are relevant to the issues of material change, doctrine of equivalents and the reverse doctrine of equivalents. Dr. Torchilin is poised to testify regarding the pharmacological and biological function of MIRCERA and Roche should be permitted to cross-examine Dr. Torchilin to rebut these arguments. In so doing, Roche will not address issues concerning safety, efficacy or the particular BLA filings that have been the subject of any previous ruling.

Pharmacological differences such as those relating to differences in half-life and dosing schedule are independent of the safety and efficacy issues Amgen invokes. In order to obtain FDA approval, Roche had to demonstrate, through clinical studies in the BLA, that MIRCERA's safety profile was comparable and non-inferior to those of the currently available ESAs. In terms of efficacy, Roche had to demonstrate non-inferiority irrespective of any dosing schedule; i.e., Roche had to prove to the FDA that MIRCERA was non-inferior in efficacy to the currently available ESAs regardless of whether MIRCERA was administered once a week, once every two weeks, or once every four weeks. Put simply, dosing schedule is wholly separate from the concept of efficacy.

The differences between MIRCERA and the currently available ESAs are differences at the heart of Roche's infringement case in chief. These biological and chemical differences are highly relevant to both 35 U.S.C. § 271(g) analysis[1] and analysis under the doctrine of equivalents[2] and reverse doctrine of equivalents and have nothing to do with any safety or efficacy discussion. The inherent biological and chemical differences between MIRCERA and the currently available ESAs cause MIRCERA to have a different half-life and dosing schedule than recombinant human EPO.

Amgen cannot claim that they would be at all prejudiced by an examination on the pharmacological differences between MIRCERA and the currently available ESAs. Roche has provided Amgen fulsome discovery on issues such as dosing schedule, including thousands of

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[1] *See Eli Lilly & Co., vs. American Cyanamid Co., et. al.*, 66 F. Supp. 2d 924, 928 (D. Ind. 1999) ("[U]nlike cefaclor, compound 6 cannot be taken orally. Oral activity is important because a drug that must be administered by injection requires a hospital visit or a doctor's appointment, but an oral antibiotic can be taken easily at home. This convenience not only makes oral antibiotics more desirable commercial products, but it lowers the costs associated with medical care. . . . There is little dispute that cefaclor has significantly different biological properties from compound 6. Because Opos' additional processing steps 'change the physical or chemical properties of the product in a manner which changes the basic utility of the product,' compound 6 has been materially changed.")

[2] *See Genentech, Inc. v. Wellcome Foundation Ltd.*, 29 F.3d 1555, 1568-1569 (Held that difference in half-life and affinity for binding meant results achieved were not substantially the same; judgment of infringement based on doctrine of equivalents reversed.)

pages from Roche's BLA and original data from Roche's clinical trials that contain extensive information on dosing. Thus, Roche should be fairly permitted to cross-examine Dr. Torchilin on the biological and pharmacological differences between MIRCERA and Amgen's claimed products.

Dated: October 15, 2007
Boston, Massachusetts

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

By its attorneys,

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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/ *Thomas F. Fleming*

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