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

DEFENDANTS' MEMORANDUM OF LAW IN SUPPORT OF MOTION *IN LIMINE* TO INVOKE ISSUE PRECLUSION AS TO FINDINGS FROM PRIOR LITIGATION

Defendants F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") respectfully submit this memorandum of law in support of their motion to invoke the doctrine of issue preclusion to prevent Amgen from arguing contrary to certain determinations made in prior litigation. These determinations are directly relevant to the claims in the instant litigation and have been fully and finally litigated by Amgen in prior proceedings. Thus, Amgen is precluded from litigating these issues again, and the jury should be advised of the prior holdings as to these issues.

I. Issue Preclusion Prevents Amgen From Introducing Testimony Contrary To What Has Already Been Litigated And Decided

Under the doctrine of issue preclusion (collateral estoppel), Amgen is prohibited from relitigating issues that have already been decided where the following factors are met: "(1) the issue is identical to one decided in the first action; (2) the issue was actually litigated in the first

action; (3) resolution of the issue was essential to a final judgment in the first action; and (4) the party against whom estoppel is invoked had a full and fair opportunity to litigate the issue in the first action." *Amgen, Inc. v. F. Hoffman-La Roche Ltd.*, ---F.Supp.2d---, 2007 WL 1893058 *2 (D. Mass. 2007) (citing *Innovad Inc. v. Microsoft Corp.*, 260 F.3d 1326, 1334 (Fed. Cir. 2001)).

There are at least two issues that have been finally decided in prior litigations and cannot be relitigated in this case: (1) that rEPO cannot be distinguished from uEPO on the basis of glycosylation; (2) that the common specification of the patents-in-suit does not support claims to analogs of EPO beyond the few disclosed in the patent specifications. For the convenience of the Court, Roche has attached hereto as Exhibit A a collection of judicial findings and holdings pertaining to each of these three issues, and attached as Exhibits B-E the judicial opinions from which the statements were derived (with the relevant statements marked according to the numbers assigned in Exhibit A). The requirements for issue preclusion apply to both of these issues for the reasons set forth below.[1]

Issue 1: Recombinant erythropoietin cannot be distinguished from urinary erythropoietin on the basis of glycosylation

A. <u>The Issue to be Precluded is Identical to the Issue in the Earlier Action</u>

Both this Court and the Federal Circuit Court of Appeals have issued findings on the very issue which Roche seeks to preclude Amgen from relitigating – that recombinant erythropoietin cannot be distinguished from urinary erythropoietin on the basis of glycosylation.

As support for the proposition that this issue has been litigated previously, Roche notes that this Court made special explicit findings on this issue, holding, for example, "<u>Dr. Lin's</u>

[1] While identity of issues is required for the invocation of issue preclusion, identity of parties is not; it is appropriate for Roche to seek issue preclusion of issues litigated in matters in which Amgen asserted its patents against other defendants. *Innovad Inc. v. Microsoft Corp.*, 260 F.3d 1326, 1334 (Fed. Cir. 2001).

disclosure [in the patents-in-suit] fails adequately to describe an EPO glycoprotein whose glycosylation differs from that of human urinary erythropoietin. . . . [T]he patent fails to convey to one of ordinary skill in the art as of 1984 that Dr. Lin invented an erythropoietin glycoprotein product having glycosylation which differs from that of human urinary erythropoietin.") (emphasis added); ***Amgen, Inc. v. Hoechst Marion Roussel, Inc.***, 126 F. Supp. 2d 69, 155 (D. Mass. 2001); ***see also id.*** at 165 ("Dr. Lin's specification falters, . . . because it fails to enable one of ordinary skill in the art to compare the glycosylation of the recombinant EPO product with that of human urinary erythropoietin."); ***id.*** at 156 ("Although the language [of the '933 patent] contemplates that a competitor concerned with infringing the '933 patent can empirically determine whether its product's glycosylation differs from the glycosylation of human urinary erythropoietin, a definitive comparison is rendered impossible by the fact that human urinary erythropoietin itself varies significantly.") (emphasis added); ***id.*** at 156 ("[B]ecause different urinary erythropoietin preparations vary in their glycosylation, and because neither the ['933] patent nor the prior art provides clear guidance as to which human urinary EPO standard ought be used, one of ordinary skill in the art would be unable to determine whether a particular erythropoietin has gylcosylation which differs from that of human urinary erythropoietin.) (emphasis added and citations to evidence omitted); ***id.*** at 155 ("[T]he glycosylation of human urinary erythropoietin is a standardless standard . . . [because] (1) the glycosylation of urinary erythropoietin has 'enormous heterogeneity'; (2) different purification techniques, several of which were known by one skilled in the art in 1984, result in differing glycosylated erythropoietin populations; (3) despite referring to at least two purification methods, the patent does not identify which human urinary erythropoietin preparation ought be used as a standard, nor would a skilled person know which urinary EPO preparation should be used; and (4)

different urinary erythropoietin samples have different glycosylation. As a result, making comparisons between the glycosylation of recombinant EPO and that of human urinary EPO is virtually impossible.") (emphasis added); *id.* at 129 ("Dr. Egrie's various SDS-PAGE experiments reveal that different uEPOs have varying glycosylation. … [T]he glycosylation of human urinary erythropoietin was in 1984, and continues to be, a moving target.").

As additional support for the proposition that this identical issue has been considered and litigated already, Roche notes that the Federal Circuit concurred with the district court's findings set forth above. The Federal Circuit stated, "By definition, one must know what the glycosylation of uEPO is with certainty before one can determine whether the claimed glycoprotein has a glycosylation different from that of uEPO. In its discussion characterizing recombinant glycoprotein products, the specification of the '933 patent does not direct those of ordinary skill in the art to a standard by which the appropriate comparison can be made." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1341 (Fed. Cir. 2003); *see also id.* at 1341 (explaining that the reference Miyake, et al., Purification of Human Erythropoietin, J. Bio. Chem. 252, 5558, 5562 (1977), "provides a method of purification," but does not suggest "uniformity of glycosylation of the human uEPO studied").

B. The Issue Sought to be Precluded Was Actually Litigated and Decided

The issue which Roche seeks to preclude Amgen from relitigating meets the requirement of having been "actually litigated" and "actually decided" in other proceedings, and indeed was the subject of extensive briefing and argument. In particular, with respect to the glycosylation issue, Amgen failed in attempting to defend claims 1 and 2 of the '933 patent against the argument that the claim term "having glycosylation which differs from that of human urinary erythropoietin" was indefinite. *See, e.g., Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d

1313, 1340-1341 (Fed. Cir. 2003). The Federal Circuit explicitly rejected Amgen's position, adopting this Court's alternative holding that claims 1, 2 and 9 of the '933 patent (if infringed) are invalid for indefiniteness. 126 F.Supp.2d at 165.

C. The Determination of the Issue Was Essential to the Judgment

The determination that recombinant erythropoietin cannot be distinguished from urinary erythropoietin on the basis of glycosylation was essential to the determination by the Federal Circuit that claims 1, 2 and 9 of the '933 patent are invalid under 35 U.S.C. § 112, for indefiniteness. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1342 (Fed. Cir. 2003).

D. Amgen Had a Full and Fair Opportunity to Litigate The Issue in Prior Actions

Amgen has had its day in court many times over. Since 1989, it has vigorously enforced its patents in this jurisdiction and in tribunals all over the world. As this Court recently noted in the claim construction context in the instant action, "Specifically, Amgen was a party in a previous case before this Court which construed many of the patent claims at issue here, and it had a full and fair chance to assert its arguments at that time. Thus, Amgen is barred from relitigating the claims that were the subject of that previous patent suit." *Amgen, Inc. v. F. Hoffman-La Roche Ltd.*, ---F.Supp.2d---, 2007 WL 1893058 (D. Mass. 2007).

The Court's determination on the glycosylation issue was finally adjudicated in the *Hoechst* case, as it was affirmed on appeal and is not affected by the other issues that are still subject to further proceedings on remand. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp.2d 69 (D. Mass. 2001).

Issue 2: The common specification of the patents-in-suit does not support claims to analogs of EPO beyond the few disclosed in the specification

A. The Issue to be Precluded is Identical to the Issue in the Earlier Action

In the litigation between Amgen and Chugai, it was decided that the common specification of the patents-in-suit does not support claims to erythropoietin analogs beyond the handful disclosed in the specification. The Federal Circuit addressed this issue with specificity, holding: "There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213-14 (Fed. Cir. 1991) (emphasis added); *see also id.* at 1214 (Fed. Cir. 1991) ("Considering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with attendant uncertainty as to what utility will be possessed by these analogs, . . . more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity. It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity."); *id.* at 1213 ("Details for preparing only a few EPO analog genes are disclosed" in the patents-in-suit).

The district court's analysis of the analog issue was consistent with the Federal Circuit's findings on appeal. Indeed, in 1989, the district court held, "After five years of experimentation, as of 1989 Amgen was still unable to specify which EPO analogs have the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *57 (D. Mass. 1989) (internal citations to evidence omitted); *see also id.* at *56 ("Dr. Elliott said that Amgen had not measured all of the biological properties of the

analogs he had made, and he did not know whether the analogs had the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake. Dr. Elliott did not know if any of the plasmids described in the [patents-in-suit] had this biological property.") (internal citations to evidence omitted).

B. The Issue Sought to be Precluded Was Actually Litigated and Decided

The analog issue was "actually litigated" and "actually decided" in other proceedings, as Amgen failed in attempting to defend the validity of claims 7, 8, 23-27, and 29 of the '008 patent against the argument that the claims were not enabled because they claimed every possible analog of EPO but disclosed only how to make EPO and a very few analogs. *See, e.g., Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991). As the Federal Circuit stated: " It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity. Under the circumstances . . . the generic DNA sequence claims are invalid under Section 112." *Id.* at 1214.

C. The Determination of the Issue Was Essential to the Judgment

As can be seen from the quotations above, the determination that the common specification of the patents-in-suit cannot support claims to analogs beyond the handful disclosed in the specification was essential to the conclusions of both the district court and the Federal Circuit that claims 7, 8, 23-27, and 29 of the '008 patent were invalid under 35 U.S.C. § 112, 1st ¶. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *57 (D. Mass. 1989); and *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1214 (Fed. Cir. 1991).

D. Amgen Had a Full and Fair Opportunity to Litigate The Issue in Prior Actions

The judgment in the dispute between Amgen and Chugai is final. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991); *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd*., 1989 WL 169006 (D. Mass. 1989). Accordingly, the Court correctly acknowledged in this case that, "Amgen was a party in a previous case before this Court which construed many of the patent claims at issue here, and it had a full and fair chance to assert its arguments at that time. Thus, Amgen is barred from relitigating the claims that were the subject of that previous patent suit." *Amgen, Inc. v. F. Hoffman-La Roche Ltd.*, ---F.Supp.2d---, 2007 WL 1893058 (D. Mass. 2007).

II. The Prior Determinations Should Be Provided To The Jury

In addition to precluding Amgen from disputing the above-referenced determinations on grounds of issue preclusion, the prior judicial determinations should be presented as such to the jury. The established points can be presented to the jury together with the stipulated facts, at the close of the testimony, or as part of the jury charge, in the Court's discretion.

As the U.S. Supreme Court explained in deciding similar issues in a civil antitrust suit that followed a criminal action:

> It is the task of the trial judge to make clear to the jury the issues that were determined against the defendant in the prior suit, and to limit to those issues the effect of that judgment as evidence in the present action. As to the manner in which such explanation should be made, no mechanical rule can be laid down to control the trial judge, who must take into account the circumstances of each case. He must be free to exercise 'a well-established range of judicial discretion.' He is not precluded from resorting to such portions of the record, including the pleadings and judgment, in the antecedent case as he may find necessary or appropriate to use in presenting to the jury a clear picture of the issues decided there and relevant to the case on trial.

Emich Motors Corp. v. General Motors Corp., 340 U.S. 558, 571 (1951) (internal citations omitted) (emphasis added).

CONCLUSION

For the foregoing reasons, Roche respectfully requests that the Court (1) preclude Amgen from introducing testimony, evidence or argument contrary to the statements listed in Exhibit A; (2) instruct the jury to disregard any such contrary testimony, evidence or argument; and (3) permit Roche to introduce as conclusive evidence the statements listed in Exhibit A.

Dated: August 16, 2007
Boston, Massachusetts

Respectfully submitted,

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