Amgen Inc. v. F. Hoffmann-LaRoche LTD et al Doc. 46

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, vs. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GMBH, AND HOFFMANN-LA ROCHE INC., Defendants	CIVIL ACTION No.: 05-CV-12237WGY

DECLARATION OF IRIS KINGMA-JOHNSON IN SUPPORT OF DEFENDANTS F. HOFFMANN-LAROCHE LTD, ROCHE DIAGNOSTICS GMBH, AND HOFFMANN-LAROCHE INC.'S MOTION TO DISMISS FOR LACK OF SUBJECT MATTER JURISDICTION AND FAILURE TO STATE A CLAIM FOR WHICH RELIEF MAY BE GRANTED

I, Iris Kingma-Johnson, M.D., Ph.D., hereby declare under penalty of perjury that:

1. I am a Medical Director at Roche Laboratories Inc. ("Roche Labs"), a wholly-owned subsidiary of defendant Hoffmann-La Roche Inc. ("Roche Inc.") (collectively, "Roche"), both of which have offices in Nutley, New Jersey. Roche is conducting clinical trials as part of the approval process for a new developmental anemia drug, CERA (Continuous Erythropoiesis Receptor Activator). I have been an employee at Roche Labs since 1999, and have been in my current position of Medical Director since January 2005. I am a board certified internist and nephrologist, with 18 years of clinical and research experience in the discipline of nephrology. Nephrology is the area of medicine involving diagnosis and treatment of diseases of the kidney. Among other medical and professional groups, I am a member of the American Society of Nephrology, and have over ten (10) years of pharmaceutical clinical trial experience. I submit

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this declaration in support of Roche Inc.'s Motion to Dismiss for Lack of Subject Matter Jurisdiction and Failure To State A Claim For Which Relief May Be Granted.

2. As Medical Director, I am knowledgeable about all clinical trials being conducted on CERA in the United States. I am also knowledgeable and familiar with clinical trials being done on CERA outside the United States by Roche Inc.'s affiliate, F. Hoffmann-LaRoche Ltd.

3. For planned clinical trials to be conducted in the United States, I am involved with the design of the clinical trials, including selection criteria for patients who will participate, and selection of the health care providers. I am also familiar with the medical literature pertaining to the use of Erythropoiesis Stimulating Agents ("ESAs") for the treatment of anemia of chronic kidney disease.

4. I am familiar with the requirements of the United States Food and Drug Administration ("FDA") for approval of new biologic drugs such as CERA. In order for a new drug or biologic to gain FDA approval for commercial sale and marketing in the United States, a sponsor of the drug must file an application to market the product ("NDA" or "BLA"). This application requires, among other things, analyzing and reporting the results of numerous clinical and preclinical trials. Hoffmann-LaRoche Inc. is the sponsor for the FDA approval process for CERA. An applicant, or drug sponsor, is the person or entity who assumes responsibility for the marketing of a new drug, including responsibility for compliance with applicable provisions of the Federal Food, Drug, and Cosmetic Act and related regulations.

5. In order to begin clinical trials involving administration of a developmental drug to humans necessary for compiling and filing a BLA, the drug's sponsor must file an "investigational new drug application" or "IND" for approval to administer the drug to humans. Once an IND is approved, clinical trials may begin.

6. As part of routine drug development there are three phases of clinical trials designated Phase 1, Phase 2 and Phase 3. These three phases are sequential, but they can overlap for significant periods of time. Phase 1 includes the initial introduction of an investigational new drug into humans, usually healthy volunteers. These studies are designed to determine the metabolic and pharmacologic actions of the drug in humans, to determine the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. Phase 2 includes the early controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug for a particular indication or indications in patients with the disease or condition. This phase of testing also helps determine the common short-term side effects and risks associated with the drug. Phase 2 studies are typically well-controlled, closely monitored, and conducted in a relatively small number of patients, usually involving several hundred people. If Phase 2 trials show sufficient effectiveness of the new drug, Phase 3 trials can begin. Occasionally, some Phase 2 trials continue as extension studies to gain further data, even while Phase 3 trials are under way. Phase 3 studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained in Phase 2, and are intended to gather additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug. Phase 3 studies also provide an adequate basis for extrapolating the results to the general population and transmitting that information in the physician labeling. Phase 3 studies usually include several hundred to several thousand people. Extension studies

may continue up until, and even after, drug approval. The results of all trials conducted up until the time the BLA is filed with the FDA must be included in the BLA submission.

7. I am familiar with the history and current state of development of CERA. Roche is currently conducting clinical trials to evaluate two separate uses of CERA - one set of trials involves the use of CERA to treat anemia of chronic kidney disease, including both dialyzed patients and patients not yet on dialysis, and the other set of trials involves the use of CERA to treat anemia in an oncology setting. The IND for use of CERA in patients with anemia of chronic kidney disease was filed in the United States on December 4, 2001, and the IND for use of CERA in an oncology setting was filed in the United States on March 17, 2003. The clinical trials for use of CERA in chronic kidney disease patients are further advanced, and a BLA for use of CERA to treat anemia of chronic kidney disease is expected to be filed significantly before a BLA for use of CERA in the oncology setting. Therefore, this declaration focuses on the clinical trials and BLA filing of the use of CERA in chronic kidney disease patients, since it will be filed first. A final disposition of the chronic kidney disease BLA will almost certainly precede a disposition on an oncology related BLA filed in the future.

8. Clinical testing for use of CERA to treat anemia of chronic kidney disease in humans began in Europe in June 2000. There were a total of thirteen (13) Phase 1 trials. Four (4) Phase 2 clinical trials for anemia of chronic kidney disease have been conducted, beginning in August 2001. Patients from three (3) of the four (4) Phase 2 trials for chronic kidney disease were able to continue CERA in extension studies to ascertain long-term maintenance of Hemoglobin (Hb) control and drug safety. The last of these Phase 2 extension studies is expected to continue until approximately November 2007.

9. The Phase 3 stage of clinical trials for treatment of anemia of chronic kidney disease contains six (6) registration Phase 3 clinical trials involving over 2400 patients. These Phase 3 trials began in March 2004. Four of these trials were completed in November 2005, with Roche announcing the completion of these trials on December 16, 2005. Analysis of these four (4) trials, as well as completion of the two (2) additional Phase 3 clinical trials occurred in March 2006. Even after sufficient results are obtained to file a BLA, at least one trial will continue to provide additional safety data four months after filing the BLA.

10. Although clinical trials may yield good results, even after a BLA for a particular treatment is filed, there is no assurance that the FDA will approve a new drug. Hence the approval date for CERA to treat anemia of chronic kidney disease cannot be determined with certainty. The FDA approval process takes a long time and has a certain degree of uncertainty. This uncertainty of the FDA approval process arises not only from its lengthy review process, but also from the FDA's inherent ability to require additional testing, and/or significant changes to the applicant's label, safety statements and manufacturing processes. These requirements and changes can occur at any time up until approval of the BLA, which can delay the approval process. Moreover, recent high profile drug safety issues have led to additional scrutiny on the FDA and the drug approval process. For example, recent reports of pure red cell aplasia (PRCA) and of severe anemia in certain patients taking ESAs, have resulted in changes to product information for some currently marketed ESAs and a recommendation to discontinue use of ESAs in patients who develop PRCA.[1] These findings have caused increased scrutiny of all ESAs.

[1] J&J, Amgen Caution on Anemia Drugs, A. Chang, TheStreet.com, Dec. 2, 2005, Suh Declaration Ex. 8.

11. Roche expects to file the BLA for approval of sales and marketing of CERA for treatment of anemia of chronic kidney disease in the United States later this month. Roche does not expect to file a BLA for approval of sales and marketing of CERA for treatment of anemia in oncology patients in the United States before some time in 2009.

Signed under the pains and penalties of perjury this 7th day of April, 2006.

/s/ Iris Kingma-Johnson
Dr. Iris Kingma-Johnson, M.D., Ph.D.

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 April 11, 2006.

/s/ Julia Huston

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