UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

**ROCHE'S OPPOSITION TO AMGEN'S MOTION *IN LIMINE* NO. 24 TO PRECLUDE EVIDENCE FOR OBVIOUSNESS THAT VIOLATES 35 U.S.C. § 103 PROHIBITION THAT "PATENTABILITY SHALL NOT BE NEGATIVED BY THE MANNER IN WHICH THE INVENTION WAS MADE" AND WHICH REFLECTS THE SUBJECTIVE BELIEFS OF THE INVENTOR**

## I. INTRODUCTION

Contrary to Amgen's assertions that the testimony Roche seeks to elicit is "legally irrelevant," evidence of Dr. Lin's expectations is clearly appropriate under controlling precedent. Roche intends to submit evidence and elicit testimony regarding Dr. Lin's expectation of success in carrying out and developing his "inventions," as this evidence is relevant to the state of the art and understanding what a person of ordinary skill in the art would have deemed obvious. In seeking to preclude Roche from presenting the full scope of its evidence on obviousness, Amgen's Motion *in Limine* ignores the law regarding the proper use of inventor testimony. This information, however, is highly relevant and will present the jury with a more complete version of the facts than what Amgen proposes. Amgen's motion should be denied.

## II. DR. LIN'S TESTIMONY IS HIGHLY RELEVANT TO OBVIOUSNESS

The Federal Circuit has repeatedly held that the "inventors' testimony [is] relevant to whether the inventions would have been obvious to a person of ordinary skill in the art." *Neupak, Inc. v. Ideal Mfg. and Sales Corp.*, 2002 WL 1363568, *4 (Fed. Cir. June 24, 2002); *see also In re QED Envtl Sys., Inc.*, 991 F.2d 809 (Fed. Cir. 1993) (trial testimony of inventors was "extremely relevant" to determining the "difference between what the inventors admit to be well known and the claimed subject matter" with respect to obviousness); *Leapfrog Enterprises, Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007) ("conclusion [of obviousness] is further reinforced by testimony from the sole inventor at trial"); *Frazier v. Layne Christensen Co.*, 2007 WL 1875909, *1 (Fed. Cir. June 29, 2007) (considering inventor testimony in obviousness determination); *Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 315-16 (Fed. Cir. 1985) (same); *Dystar Textilfarben GmbH & Co. v. C.H. Patrick Co.*, 464 F.3d 1356, 1361 (Fed. Cir. 2006) (same); *Freedman Seating Co. v. Am. Seating Co.*, 420 F.3d 1350, 1364 (Fed. Cir. 2005) (same); *LNP Eng'g Plastics, Inc. v. Miller Waste Mills, Inc.*, 275 F.3d 1347, 1358 (Fed. Cir. 2001) (same).

For example, in *Princeton Biochem, Inc. v. Beckman Coulter, Inc.*, 411 F.3d 1332 (Fed. Cir. 2005), "[i]n defining [the] problems" the invention was intended to address and the corresponding evaluation of obviousness, "the district court looked to [the inventor's] own testimony that the electrophoretic device needed to be compact and immobile." *Id.* at 1339. The Federal Circuit "agree[d]" with the district court and found its analysis to be "proper." *Id.*

Moreover, in *Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804 (Fed. Cir. 1989), the inventor claimed to have invented an effective therapeutic dose range for a drug combination taught in the prior art. "The evidence at trial showed that, though requiring time and care, the

experimentation needed to arrive at the claimed dosages was nothing more than routine." *Id.* at 809. The court further noted that:

> [i]t is to be expected that their co-administration would induce more sodium excretion than would either diuretic alone....Indeed, *the inventor named on both the '813 and '430 patents, so testified*....When further questioned on the point, the *inventor indicated* that his uncertainty inhered not in the fact that an increase was to be expected, but only in the magnitude of the increase.

*Id.* at 808-09 (emphasis added); *see also Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1371 (Fed. Cir. 2007), *reh'g denied*, 488 F.3d 1377 (Fed. Cir. 2007) (in determining success was not unexpected, inventor's "testimony reflects the fact that he believed that" new chemical entity would solve deficiency in prior art). In light of the Federal Circuit's holding in *Merck, Apotex*, and the several other Federal Circuit cases cited above, Amgen's argument with respect to "a 1991 Board of Patent Appeals decision" is entirely misplaced. As *Merck* makes clear, where Dr. Lin previously argued that certain steps of his developmental process "do[] not require the exercise of inventive skill," that testimony is a crucial factor to consider in assessing obviousness. *Merck*, 874 F.2d at 808-09; (D.I. 998 at 4). This not only serves as independent evidence supporting Roche's claim of obviousness, it corroborates Roche's additional evidence based on the scope and content of the prior art and it completely contradicts Amgen and Dr. Lin's current self-serving assertions that the patents-in-suit are non-obvious.

Roche's position, and the correct standards of law, have been recently explained in the Supreme Court's holding in *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741-42 (2007). The Court stated that in determining whether a particular invention is obvious in light of the prior art, the motivation of the inventor is one factor that must be considered. As the Court stated, "the problem motivating the patentee may be only one of many addressed by the patent's subject matter." *Id.* at 1742. While it is proper, even required, to look at a variety of factors in

determining the obviousness of an invention and the reasonable expectation of success that a person of ordinary skill in the art may have, the inventor's own motivation and expectation of success is one of those factors. *Id.* at 1742. Clarifying prior Federal Circuit jurisprudence, the Court emphasized that "a person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." *Id.* Because the person of ordinary skill in the art is a person who shows creativity, and does not just follow an instruction manual, the motivation and expectation of success of the inventor are important factors in determining the ultimate questions of reasonable expectation of success and motivation to combine elements in the prior art to determine obviousness of an invention. In short, although the expectation of success of the patentee is not the only evidence that goes to determining the obviousness of the claimed invention, it is always relevant and frequently the ***best*** evidence.

Amgen's argument that "isolating on individual steps performed during the inventive process to show obviousness violates the central obviousness inquiry [that] [o]bviousness must look at the claim as a whole and be compared to the prior art as a whole" also misses the point. (D.I. 998 at 4). Amgen's argument seeks to transform the obviousness inquiry into a modified question of anticipation. According to Amgen, a "claim as a whole" can only be rendered obvious if taught by the prior art, but this is not the test. One looks to, among other things, the level of skill in the art, the reasonable expectation of success, and the combination of prior art references. *Id.* As explained above, inventor testimony and evidence pertaining to the inventive process are relevant to this inquiry.

Moreover, Amgen itself put at issue the very testimony and evidence which it seeks to preclude in its opening statement to the jury. In its opening, Amgen informed the jury of Dr. Lin's state of mind, beliefs and expectations of success. Amgen told the jury that Dr. Lin

"dreamed" of making EPO, and that he "worked day and night" to achieve his dream of making recombinant EPO, despite repeatedly failing to succeed. Amgen told the jury in opening arguments that Dr. Lin was so unsure of his success in creating a biologically active protein that he allegedly devised three separate ways of expressing the protein: (1) bacterial expression; (2) yeast cell expression; and (3) mammalian expression. Amgen told the jury of Dr. Lin's expectations or lack thereof a mere hour after moving to have his testimony excluded. Although Amgen had no basis for its motion when filed, surely it has waived any objection it had by presenting these issues to the jury.

Finally, Amgen's experts repeatedly referred to the expectations, efforts and failures of Dr. Lin in their statements of expected testimony in an effort to defeat Roche's claim of obviousness, as detailed below:

| **Expert Report** | **Quotations** |
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| Rebuttal Expert Report of Harvey F. Lodish, Ph.D. (May 11, 2007) | • ¶117: "When Dr. Lin began his efforts to produce *in vivo* biologically active EPO using recombinant DNA techniques, *he faced a daunting array of difficult problems.* (emphasis added).<br>• ¶186: "It is apparent from Dr. Lin's patent application that *Dr. Lin's own research approach reflected the lack of an expectation of success* to achieve the claimed inventions." (emphasis added).<br>• ¶187: "*The fact that Lin did not claim such subsequent inventions in his earlier applications reflects the fact that such later inventions were not then obvious* to a highly skilled and motivated scientist, such as Lin, let alone to a lesser scientist of only ordinary skill in the art." (emphasis added).<br>• ¶214: "*[W]hen Dr. Lin was trying* to clone the human EPO gene, he had sufficient EPO protein to 'obtain the sequence information for any number of different portions of the amino acid sequence using known techniques for protein sequencing,' yet *it was difficult* to generate useful sets of |

| Expert Report | Quotations |
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| | degenerate probes." (emphasis modified). |
| Second Supplemental Expert Report of Harvey F. Lodish, Ph.D. (June 20, 2007) | • ¶12: *"Dr. Lin's experience illustrates the problems in the art at the time.* The amino acid sequence information that Dr. Lin had was incomplete and contained errors or uncertainties. Dr. Lin had to design and develop oligonucleotide probes based on that information. He then engaged in a difficult search that had a very low probability of success, complicated by erroneous sequence information." (emphasis added). |
| Rebuttal Expert Statement of Randolph Wall, Ph.D. (May 11, 2007) | • ¶26: "Even if accurate protein sequence information had been obtained, designing 'a suitable degenerate oligonucleotide probe' was not as simple as Dr. Lowe suggests. For example, *when Dr. Lin began his work to clone the EPO cDNA*, he had 'sequence information for different portions of the amino acid sequence [obtained] using known techniques for protein sequencing," yet even with these EPO peptide sequences, *he could not create useful sets of degenerate probes.*" (emphasis added). |
| Rebuttal Expert Statement of Stuart H. Orkin, M.D. (May 11, 2007) | • ¶73: "[E]ven if accurate protein sequence information had been obtained, designing a suitable degenerate oligonucleotide probe was not nearly as simple as they try to make it seem. For example, *when Dr. Lin was trying to clone the human EPO gene, he had sufficient EPO protein to obtain sequence information, yet it was difficult to generate useful sets of degenerate probes.*" (emphasis added). |
| Expert Report of Paul W. Kincade, Ph.D. (May 11, 2007) | • ¶45: "But studies often yield unexpected findings. Scientists often cannot determine ahead of time whether an experiment will be successful for the anticipated purpose, or perhaps for some other unconsidered purpose. *The case at hand is a good example. The scientists attempting to clone the EPO gene, including Dr. Lin, did not know what to expect from their experiments.*" (emphasis added). |
| Rebuttal Expert Statement of Eugene Goldwasser, Ph.D. (May 11, 2007) | • ¶57: "[I]t was [Dr. Lin's] *diligence, patience and creativity* that lead to the successful isolation of the gene encoding for human EPO....his persistence was extraordinary as was his ability to find creative solutions to difficult problems. To achieve his goal, Dr. Lin screened close to 2 million bacterial clones to find the two that were positive. *Dr. Lin faced tremendous obstacles* in cloning the EPO gene due to |

| Expert Report | Quotations |
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| | the magnitude of the job of looking for those positive clones among the millions of non-EPO clones." (emphasis added). |
| Expert Report of Arnold J. Berk, M.D. (May 10, 2007) | • ¶105: "Amgen simultaneously pursued multiple expression systems for the isolated EPO DNA. *Because he did not know* in advance which expression system would be useful in producing an *in vivo* biologically active recombinant EPO, *Dr. Lin pursued recombinant EPO expression in E. coli, yeast, and mammalian cells (both COS and CHO cells) simultaneously.*" (emphasis added). |

Accordingly, Amgen, its lawyers and its experts concede that Dr. Lin's efforts and actions are relevant to the obviousness inquiry. The law is clear that the inventor's expectation of success is a key factor to consider in determining whether the claimed invention would have been obvious to one skilled in the art, and such testimony should be permitted.

## III. DR. LIN'S TESTIMONY IS RELEVANT FOR ESTABLISHING DATE OF CONCEPTION AND REDUCTION TO PRACTICE

Roche should also be permitted to question Dr. Lin regarding his beliefs, thoughts and expectations as they pertain to his alleged conception and reduction to practice of the claimed "inventions." Amgen's asserted conception date for the patents-in-suit remains unclear at this point. For Roche to be able to properly put on its invalidity and inequitable conduct cases, it must be able to inquire as to Dr. Lin's beliefs, thoughts and expectations to determine when he realized he had an "invention" that worked. As the alleged date of conception remains a disputed issue, Dr. Lin's testimony is highly relevant. *See Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1169 (Fed. Cir. 2006) (while "inventor's testimony requires corroboration," it is nonetheless relevant to conception). Accordingly, Roche should be permitted to inquire on this issue.

Finally, Amgen's assertion that inventor testimony constitutes "acts of reduction to practice that occur after the invention (conception) to negative the invention (conception)" is completely unsupported by legal authority and nonsensical. Even if legally recognized (it is not), Amgen's position is internally inconsistent. Through its expert reports, Amgen has maintained that no one of skill in the art expected "in vivo biological activity" of its inventions until this was allegedly actually demonstrated. Hence, Amgen has advocated simultaneous conception and reduction to practice. As a result, acts of reduction to practice based on inventor testimony do not "negative" conception of the invention as Amgen argues in its motion, but actually define it.

## IV. CONCLUSION

In accordance with this memorandum, Roche respectfully submits that testimony and evidence from Dr. Lin regarding his expectation of success, his beliefs, thoughts and the work he did is relevant and important for consideration in determining the overall question of obviousness of the patents-in-suit. Accordingly, Amgen's motion should be denied in its entirety.

Dated: September 5, 2007
Boston, Massachusetts

Respectfully submitted,

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