EXHIBIT 1

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

Civil Action
No. 05-12237-WGY

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AMGEN, INC.,

Plaintiff,

v. MARKMAN HEARING

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

Defendants.

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BEFORE: The Honorable William G. Young,
District Judge

APPEARANCES:

DUANE MORRIS LLP (By Michael R. Gottfried, Esq.), 470 Atlantic Avenue, Suite 500, Boston, Massachusetts 02210
- and -
DAY CASEBEER MADRID & BATCHELDER, LLP (By Lloyd R. Day, Jr., Esq., Linda A. Sasaki-Baxley, Esq. and Jonathan Loeb, Ph.D.) 20300 Stevens Creek Boulevard, Suite 400, Cupertino, California 95014
- and -
McDERMOTT WILL & EMERY (By William G. Gaede, III, Esq.), 3150 Porter Drive, Palo Alto, California 94304
- and -
WENDY A. WHITEFORD, ESQ., Of Counsel, Amgen, Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1789, on behalf of the Plaintiff

1 Courthouse Way
Boston, Massachusetts

April 17, 2007

call it that, by saying they continued to try to get bigger and bigger and bigger and they got so big that they claimed something they didn't invent. Or that --

THE COURT: What do you mean they got bigger and bigger and bigger?

MS. BEN-AMI: In other words, the original claim of the '008 is the DNA sequence. And they knew what the DNA sequence was and they claimed it. Right? Then they go ahead and they say we're claiming human EPO. That they had not sequenced. So they didn't know what that was. Other than its three-dimensional total package of structure.

And that's what I'm saying to your Honor. I want to be clear about this. I'm not saying you must define human EPO as being limited to the 166 amino acids. I'm not saying that. Quite frankly --

THE COURT: And that's not true in the real world.

MS. BEN-AMI: I'm not saying that. I think that the patent is ambiguous because they did not know. But what I'm saying is, if you're going to do an analysis that says it's a specific amino acid sequence then it has to be 166.

The alternative approach, which I think takes into account somewhat more of your views on seminal patent, how do you deal with it, is to say human EPO must be everything that is human EPO. It must be the amino acid sequence, it must be the secondary structure, it must be the tertiary

structure, it must have the three-dimensional structure, it must be human EPO.

What Amgen's construction is -- and I can go through this in more detail, because that was the next part of my presentation -- what Amgen's construction is it's only the specific amino acid sequence of 1 to 165.

THE COURT: I follow you.

MS. BEN-AMI: No glycosylation, no secondary formulation, no tertiary structure, no three-dimensional conformation. And what I'm saying is it can't be 1 to 165 alone. If it's going to be human EPO, it means human EPO, then it's got to be all human EPO. Where --

THE COURT: Well, I don't know that your proposed instruction -- construction is helpful here. I have to explain this to a jury. And I take that very seriously. If you want this construed -- and, you know, I'm not going to be tautological. Human EPO is human EPO. That doesn't mean anything, to a jury. And at one time it didn't mean anything to me.

MS. BEN-AMI: Well, your Honor, our construction says it has to have all the structure of human EPO, which is, and we can continue going through, I will show you that the patent tells you what these various structures are.

THE COURT: Well, now, not, not in your first slide here. It doesn't say all the structure.

MS. BEN-AMI: It says the structure. It says the structure that would be produced in mammalian cells as of the invention date.

THE COURT: Well, I --

MS. BEN-AMI: It's not the amino acid sequence, it's the structure of human EPO.

THE COURT: Well, suppose we were to take Amgen's then and say a protein having the structure of human EPO such as the amino acid. Just have the same such as.

MS. BEN-AMI: So it no longer says amino acid sequence. It says --

THE COURT: Well, I'm just talking here.

MS. BEN-AMI: I understand in theory.

THE COURT: So what do you think about that?

MS. BEN-AMI: If it had all the structure of the human EPO.

THE COURT: Well, I'm not saying all. A protein having the structure of human EPO, such as the amino acid sequence of EPO isolated from human urine.

MS. BEN-AMI: No, I don't think that's right, your Honor. Because such as is now saying if you only have the amino acid sequence that's out.

THE COURT: That's an embodiment-- that's an aspect of it.

MS. BEN-AMI: That's including them rather than

such as, your Honor.

THE COURT: Well, it is including them. You would be happy, though, if I simply said human erythropoietin was a protein having the structure of human EPO.

MS. BEN-AMI: Yes, the total structure of human EPO.

THE COURT: Well, the structure. All right.

MS. BEN-AMI: I think, your Honor, when it says such as the amino acid sequence, that's saying if you just have the amino acid sequence that's not, and I don't believe that's correct.

THE COURT: Grammatically you may be, you may be right there.

All right, let's hear from Mr. Day and we'll be back to you.

Mr. Day, she made some headway here. What -- how do you feel about a protein having, human erythropoietin is a protein having the structure -- maybe we should call it DNA structure, if that means anything -- having the structure of human erythropoietin.

MR. DAY: That would be an erroneous construction, your Honor.

THE COURT: Okay. I'll hear you.

MR. DAY: And your Honor was right to go to Phillips. And the reason you're right to go to Phillips is

because the process of claim construction is a highly structured analysis. It's not a walk through the forest. It begins with a very structured set of principles that have been repeatedly laid out by the Federal Circuit to guide a Court through the difficult question of figuring out what does a claim mean. And the Court well appreciates the mantra. Judge Michel laid it out very clearly in Medtronic. You start with the claims. You look at the other claims in the patent. You look at the specification. You look at the prosecution history. You don't begin where Ms. Ben-Ami began with an expert report that hasn't even been submitted to the Court.

THE COURT: Well, try -- what do you say about my reading of Phillips? Do you think that's right?

MR. DAY: Pardon me?

THE COURT: What do you say about my reading of Phillips? Do you think that's right?

MR. DAY: Yes, I do think that's right. I think that Phillips, if I understand your point correctly, I think Phillips says that in the case of a seminal patent where you have a pioneering patent, which is what these patents are --

THE COURT: Well, she may give you '008.

MR. DAY: She will disagree.

THE COURT: But the others in her view you're just getting bigger and bigger.

MR. DAY: That's correct. She will, she will disagree. It has been many, many years since this invention was made and nobody has yet found another way to do what Lin did. So, in the case of a pioneering patent, then in a pioneering patent claims are ordinarily entitled to a broader scope. Amgen's claims are both broad and they are narrow. They are not uniformly broad. The impulse to claim broad is not unchecked. There is also a reason to claim narrowly, and Amgen claims narrowly as well.

THE COURT: To, to avoid anticipation.

MR. DAY: Not to avoid anticipation. By claiming narrowly, you can delimit what it is that an accused embodiment must have in order to infringe. If you claim a lot then the accused embodiment has to have all of those things. And that, of course, is what's going on here. Roche is trying to blow this claim out to include more and more things in the meaning of human EPO in order to argue we don't have this, we don't have that, we don't have that.

So you can claim both broadly and you can claim narrowly. So the question is in the context of this claim, '422, claim 1, where you have to look at the entire claim language, in the context of this claim what does the claim term human erythropoietin mean. That's the issue for the Court.

I have some binders, too, that I would like to hand

up to the Court, if I may. Could you give them some to opposing counsel.

Okay. And these are simply the slides that I will be talking about.

The first thing that I want to illustrate for the Court is the difference in the claim construction that Roche proposes and Amgen proposes.

Amgen's construction is a protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine.

Now, the question for the Court in considering that, is that consistent with the other claim language, is that consistent with the specification, is that consistent with the prosecution history, as to what that term human erythropoietin means in the context of the entire claim, '422, claim 1.

Roche's construction differs. And I've highlighted on the right what is importantly different about Roche's construction. First of all, they say it's not a protein. They say it's a glycoprotein. That means that it must have glycosylation. It has the amino acid sequence of erythropoietin isolated from human urine. So they agree with us about the amino acid sequence. This argument you just heard from Ms. Ben-Ami, which was not in their papers, was made for the first time this morning on oral argument,

is predicated on an expert report not before the Court, is inconsistent with what they acknowledge. This --

THE COURT: Well, we're trying to get at the best construction.

MR. DAY: I understand.

THE COURT: You do have, you do have a problem with that position 166. I mean, her argument does resonate.

MR. DAY: No, we don't have a problem with that.

THE COURT: All right, tell me why.

MR. DAY: And the reason we don't have -- because these are -- this is human erythropoietin purified from mammalian cells grown in culture. And the cells cleave off the 166 amino acids. And Lin produced and made and had in his possession an EPO that was produced by mammalian cells grown in culture. So he possessed a 165 species of human erythropoietin when he filed his application.

THE COURT: But he didn't know it.

MR. DAY: Oh, did he, did he know it?

THE COURT: Well --

MR. DAY: He possessed it.

THE COURT: Well, let's just go back.

MR. DAY: But, no, your Honor, this is an important point.

THE COURT: Go ahead.

MR. DAY: You asked a very good question and it's

an important point. But it's irrelevant. It's irrelevant whether he knew it. What is relevant is whether he possessed it and he taught others how to get the same thing. That it was later discovered to be 165 and not 166, not what he had deduced it to be, is irrelevant.

THE COURT: Well, I understand that's your position.

MR. DAY: Okay. The second thing is, that Roche seeks to add to this claim is having the structure that would be produced in mammalian cells as of the invention date.

Now, let me ask you to turn the page and I'll illustrate for you what the difference is first of all between these two constructions.

On the left you have a picture of Amgen's construction. Amgen construes human erythropoietin as referring to the amino acid sequence of human erythropoietin as isolated from urine. Roche construes human erythropoietin as referring not only to the amino acid sequence but also to all of the glycosylation that's attached to that sequence by the cells. And they say there is one structure. They call it the structure. And so there's only one such structure.

Now, what's wrong with Roche's construction? Why is it inconsistent with the other claims, with the

specification, with the prosecution history?

Okay, the first thing is they would require that the human erythropoietin be glycosylated. That, that structure is not provided by the term human erythropoietin as the Court will see. That structure is provided by the fact that it's produced in mammalian cells. And that's why the source limitation in this claim is so important. As Roche's own expert, Dr. Kadesh, in the declaration that Roche submitted in support of their claim construction, describes in detail glycosylation is a cell by cell dependent function. The cell determines what glycosylation goes on a protein. The glycosylation that will be put on a protein varies by cell species. Different species of cells will glycosylate proteins differently. That's all laid out very clearly by Dr. Kadesh. This was well understood by those of ordinary skill in the art. It's the fact that the protein is produced in a mammalian cell that gives it certain types of glycosylation. A certain structure beyond the amino acid sequence.

Roche then says it must have the identical glycosylation as originally attached by the cell. So, in other words, there can't be any post-expression changes in the molecule. That's the other thing they're trying to do. They're trying to narrow the scope of this claim so that human erythropoietin, that amino acid sequence, which is

then glycosylated by the cell, can't be modified in any way, has to be exactly as produced by the cell.

And then what they're trying to do, then what they say is that it must be produced in cells that were available as of 1983. In other words, any mammalian cell that was adapted for growth in culture after 1983 couldn't be used. Couldn't be used to make this product. And if it was, if it was it wouldn't infringe according to that.

And then they say that there has to be no alteration in the secreted glycoprotein due to post-expression modification. It's a point I made earlier.

Now, what's wrong with all that? Why is all of that not correct as a matter of law and as a matter of claim construction? Claim construction. Construing what this claim means.

Well, the first thing is that their construction would be inconsistent with Lin's other claims. When Lin claimed a human erythropoietin that was a glycoprotein he said so expressly. Take a look at '933, claim 4 where he refers to human erythropoietin glycoprotein. Roche's construction would render the word glycoprotein irrelevant. And for that reason it is erroneous as a matter of law. Every word in a claim must be given meaning. Where related claims from a single application use the same terms they should be given consistent meanings. The use of human

erythropoietin glycoprotein shows that when Lin is referring to human erythropoietin he is saying nothing about whether it's glycosylated or not.

The second thing is that Lin's specification makes clear that the polypeptides of the invention may or may not be glycosylated. There's no necessary requirement. The only thing that requires in '422, claim 1 the human erythropoietin to be glycosylated is the fact that it is produced in mammalian cells and purified from mammalian cells grown in culture. And that step, that source from which the EPO's obtained imparts a structure in addition to the amino acid sequence of human erythropoietin.

The last thing in the specification that is critical to understand is that when Lin took his DNA, he did not express it only in mammalian cells. As described in Examples 11 and 12 of the patent he also expressed it in E.coli. E.coli does not glycosylate. There is no glycosylation on human erythropoietin. And yet Lin still describes that as human erythropoietin. The human erythropoietin that Lin is talking about in his patent is the amino acid sequence that is produced by the DNA that encodes human erythropoietin. And when that DNA is placed into a mammalian cell and the cells are produced in mammalian cell culture, the cells cleave off the 166 and they may or may not glycosylate the cell, the protein.

This was all brought out in the prosecution history specifically with reference to the amendment of an allowance of '422, claim 1. In Exhibit 8 of Amgen's original claim submission, claim brief, we attached the prosecution history for this claim. And in that prosecution history Amgen explained what human erythropoietin means. It defined the term. Human erythropoietin is understood to include any polypeptide having amino acid sequence of EPO isolated from human urine and may be produced in human cells or other mammalian cells.

And so, what does that necessarily mean? That language means that human EPO includes any, any polypeptide having the amino acid sequence of EPO. If a polypeptide has the amino acid sequence of EPO it is by definition human erythropoietin as the claim term reads.

Having is open-ended. It's a tern of art in patent law, which means an open-ended construct. It's not limited. And so it doesn't exclude additional elements. There's no reference to glycosylation in the prosecution history, let alone any specific glycosylation, any statement that it must have the structure. And there's no limitation on the mammalian cells that can be used to produce it.

THE COURT: All right, I think I have it.

Brief rebuttal, Ms. Ben-Ami.

MS. BEN-AMI: Well, I have an extensive rebuttal.

THE COURT: Well, you may but --

MS. BEN-AMI: I won't go through everything, but I think there's a lot of points here and I think I really do need to discuss this a little bit more.

THE COURT: While you're getting set let me talk to the clerks.

MS. BEN-AMI: Okay.

(Pause in proceedings.)

THE COURT: Go ahead.

MS. BEN-AMI: Your Honor, when I say extensive it might still be brief. But I would like to start with this.

If you look at your screen, your Honor, this is what Amgen told you human EPO meant in the Markman hearing in the TKT case. Now, I'm not collaterally estopped and we can argue about what the meaning is in terms of claim construction. But Amgen was here before your Honor defining human EPO as a glycoprotein having a specific sequence of amino acids -- it doesn't say they're 1 through 165 -- and the ability to stimulate formation of red blood cells.

So Mr. Day is now telling you that human EPO isn't a glycoprotein. And if you want me to go through every slide here where the specification says it's a glycoprotein, and the testimony of Dr. Lodish and Dr. Goldwasser and everyone else, I can. But it's in your binder going through slide 21, slide 22. We can just go to slide 21 as

representative.

This is Dr. Lodish's tutorial. EPO is a glycoprotein. Human EPO in the body is a glycoprotein. It's a glycoprotein. The way they got over obviousness was to say what's unique about this molecule is that it's an obligate, is a term they phrase, glycoprotein. And your Honor can look at all the slides so that we don't spend as time. But it is throughout the specification and throughout the prosecution history.

THE COURT: But suppose I, suppose I adopted that and said, but modified their definition and called it a glycoprotein, and then everything else the same, having the amino acid sequence. That doesn't get you anywhere.

MS. BEN-AMI: Well, I don't know if it gets me anywhere or not --

THE COURT: No, but you --

MS. BEN-AMI: -- but it's not what I think is right. I think it has to have the structure of human EPO.

THE COURT: All right, I understand.

MS. BEN-AMI: That's part of the structure. But it's not all of the structure.

THE COURT: All right. All right.

MS. BEN-AMI: Mr. Day really went through many of these points. But he said something that I think is incorrect here about the E.coli. I think that is earlier

on. Can you -- he said, you know, they showed that with E.coli you wouldn't get glycosylation.

It's 153. Can I have that, please?

We must be very careful when we have a patent that is trying to trying to claim analogs and derivatives. And your Honor will remember that the Federal Circuit said they couldn't claim analogs, many years ago; that they didn't have sufficient description for analogs.

So we can't look at a specification that says I'm claiming EPO, I'm claiming analogs of EPO, I'm claiming parts of EPO, I'm claiming everything in the world, and then say all that means human EPO.

But let's look at this part of the prosecution -- of the specification where it says about making this E.coli product. It doesn't call it human EPO. It's called des Ala EPO.

THE COURT: Excuse me.

MS. BEN-AMI: That's all right.

THE COURT: Go ahead, Ms. Ben-Ami.

MS. BEN-AMI: I'm sorry, your Honor.

THE COURT: All right. But --

MS. BEN-AMI: This, this is important. Because when they talk about the E.coli product they're saying that E.coli product has not only 166 but it has an additional, an additional at the front.

THE COURT: What is this I'm reading from now?

MS. BEN-AMI: This is the specification of the patent at column 33. Mr. Day just said to you, well, your Honor, it talks about making EPO in E.coli and they're not glycosylated. But what I'm saying when they talk about that E.coli, they're saying it's not human EPO. Because what they say is the expression product is -- I'll write it on the back here, your Honor -- the expression product of the specification at that point is Met -- I'm sorry -- Met-166. And then they say by processing the Met comes off so you're left with 166. And if it's not just the Met that comes off, amino acid 1 comes off as well. So now you have 165. But it's not the same 165 as human EPO. Because human EPO is 2 through 166. I mean, this EPO, I'm sorry, is 2 through 166. Human EPO --

THE COURT: Is 1 through 165.

MS. BEN-AMI: -- is 1 through 165.

THE COURT: Right.

MS. BEN-AMI: So now we have something that they're calling a variant, a des, whatever it says, right, product. And they're saying it's 167 or 166, or if it's 165, it's a different 165 than Amgen says EPO is.

THE COURT: Right.

MS. BEN-AMI: Human or otherwise.

THE COURT: Let me ask Mr. Day a question.

What if we modified yours, I'm still working with Amgen's, but called it a glycoprotein. Is that a problem? Isn't that -- that's the, that's the most accurate and we're going to hear a lot about glycosylation. So it would seem to me that that would be both accurate and fair.

MR. DAY: Your Honor, I think it would be -- I don't think it's a problem. I think it would be an erroneous claim construction. And I think it would be erroneous for the reasons I cited. Because the claims differentiation -- and your Honor may have noticed when, when Ms. Ben-Ami flashed that specification up, she didn't point to the fact that it denominates the EPO as hEPO. H stands for human.

THE COURT: Well, no, she said it was a different --

MR. DAY: No. No. H, little h stands for human. Amgen identified the EPO that's being produced in this E.coli as human EPO, and then it made a number of alterations to the amino acid sequence. It made a number of analogs to that human sequence and said, well, we take this out, we put this in, we take this out, we put this in. These are all the changes from the human EPO. It would be wrong as a matter of claim construction, your Honor, because you would be reading out of the definition of human EPO human EPO produced in E.coli cells. It would be wrong as a

matter of claim construction because you would be construing human EPO in a way that renders human erythropoietin glycoproteins redundant and unnecessary. So as a matter of claim construction you would be making a mistake. That's Amgen's position.

THE COURT: Thank you.

Here's what we're going to do. At this stage and for these purposes we're going to adopt Amgen's proposed construction. I'll reflect on whether I'll add the glycoprotein before the word, substitute it for protein.

Turning now to purified from mammalian cells grown in culture. Now, Roche's proposed construction comes straight out of this Court's own analysis of this subject. And why ought I not stick with it? I've analyzed this and I see -- so I'll hear from you, Mr. Day. What's the matter with that?

MR. DAY: Okay. First of all, I don't think Roche's construction comes right out of the Court's construction. I will certainly grant you that the first part of their construction is a verbatim recitation and Amgen offered an alternative, if this is to be a jury trial, Amgen offered an alternative statement of that which I think says the same thing.

The difference between the parties in claim construction here is what I have highlighted. And that is

Roche's contention that the limitation cannot define the structure of the claim product. And let me --

THE COURT: Well, I'm not, I'm not proposing that. What I'm proposing is the Court's language.

MR. DAY: That's fine.

THE COURT: Purified from mammalian cells grown in culture means obtained in substantially homogenous form from mammalian cells, using the word "from" in the sense that it originates in mammalian cells, without limitation to, without limitation to it only taking it directly out of the interior of the cells which have been grown in the in vitro culture.

MR. DAY: And that's fine. And we merely offered an alternative --

THE COURT: All right.

MR. DAY: -- clarifying statement to that.

THE COURT: Then we'll stick with my language for now. But that's without prejudice to revisiting it if I think I can explain it to the jury better.

Then, next, a non-naturally occurring glycoprotein product of the expression, et cetera. Now, here it seems that Amgen's proposal makes the most sense. And of course we're bound by the Federal Circuit. Non-naturally occurring means not occurring in nature, but that makes perfect sense and we'll follow it. And that's, that's in the Amgen

proposal.

What's the matter with that, Ms. Ben-Ami? They're a glycoprotein product not occurring in nature that is expressed in a mammalian cell from a DNA sequence that does not originate in the genome of the host and comprises a DNA sequence encoding human erythropoietin.

MS. BEN-AMI: Well, first of all, your Honor, I think non-naturally occurring is a separate element. And so I do think that's important.

THE COURT: Well, non-naturally occurring, aren't we bound by the Federal Circuit? It means not occurring in nature.

MS. BEN-AMI: I agree with that, but that's a separate element than glycoprotein product of the expression of a mammalian cell. That's all I'm saying. In other words, you'd have to break down the claim. And I think non-naturally occurring is one element. Glycoprotein product of the expression of mammalian host cell, et cetera, is a different product. Element. That's my first fundamental difference.

THE COURT: Well, all right. But in trying to explain it to the jury I say, I come to this and I say, now, non-naturally occurring, what that means is it does not occur in nature. Now --

MS. BEN-AMI: That means --