EXHIBIT 12

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS
Civil Action No. 05-12237 WGY

AMGEN, INC.,) DEPOSITION OF:
) WILLIAM L. JORGENSEN,
) Ph.D.
Plaintiff,)
vs.)**HIGHLY CONFIDENTIAL**
)***RESTRICTED ACCESS***
F. HOFFMANN-LA ROCHE LTD., a) CONTAINS ROCHE
Swiss Company, ROCHE) CONFIDENTIAL BLA/IND
DIAGNOSTICS GmbH, a German) INFORMATION SUBJECT TO
Company, and HOFFMANN-LA) PROTECTIVE ORDER-LOCKED
ROCHE, INC., A New Jersey) ROOM ACCESS ONLY
Corporation,)
Defendants.)

TRANSCRIPT of the stenographic notes of the proceedings in the above-entitled matter, as taken by and before LISA FORLANO, RMR, CRR, CSR, CLNR, Notary Public, held at the offices of Duane, Morris, 1540 Broadway, New York, New York, on Friday, May 18, 2007, commencing at 9:02 a.m.

(This transcript contains Confidential BLA/IND Information. Please treat the entire transcript in accordance with the Amended Protective Order in this matter.)

Appearances:

DAY CASEBEER MADRID & BATCHELDER
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Also present: Nicholas Guzman, Videographer

Q Do you consider computer modeling an experiment?

A I don't use it in that way. Some people nowadays do.

Q So using experiments in a way that would exclude computer modeling for the moment, you haven't performed any experiments with any pegylated proteins, correct?

A Correct.

Q Prior to your involvement in this case, had you ever developed a computer model for the structure of EPO?

A No.

Q Prior to your involvement in this case, had you ever developed a computer model for the structure of any pegylated protein?

A No.

Q Is it fair to say, then, that the only modeling work that you've done with respect to EPO or pegylated protein is in connection with the work you did for your expert report?

MR. FLEMING: Objection. You have to allow me to --

THE WITNESS: Okay. Yes.

MR. FLEMING: Objection, vague to the

term pegylated protein, ambiguous. Go ahead.

BY MR. GALVIN:

Q Using the definition of experiments, excluding computer modeling for the moment, did you perform any experiments in connection with formulating your opinions for this case?

A No.

Q You did, however, do some computer modeling or simulation work in connection with your expert report, correct?

A Correct.

Q Did you ask Roche -- withdraw that.

Are you aware of any internal efforts by Roche to model, develop computer models for CERA?

A No.

Q You understand that Roche is one of the largest pharmaceutical companies in the world, correct?

A Yes.

Q And you know that Roche has experts like you who are experts in the field of computational chemistry, correct?

MR. FLEMING: Objection, assumes facts not in evidence.

THE WITNESS: I'm not sure if they would

know, with respect to this expert report. So I have taken EPO beta as a reagent and I have not read or reviewed a lot on the characterization of EPO beta.

Q You understand, although you may not know the specifics, that epoetin beta has a particular confirmation?

MR. FLEMING: Objection to form.

THE WITNESS: Proteins in general can have confirmation and it can -- proteins have primary, secondary and tertiary structure. The tertiary structure is sensitive to the environment, the conditions. So sometimes it can be more in a folded state, sometimes it can be in a less folded state, depending on the conditions.

BY MR. GALVIN:

Q Did you consider in forming your opinions whether the pegylation reaction caused the structural confirmation for the EPO polypeptide backbone to refold or reorganize as a result of pegylation?

MR. FLEMING: Objection, vague, mischaracterizes his opinion.

THE WITNESS: As I mention in my report, there is no reliable, accurate, experimental data on the structure of CERA.

BY MR. GALVIN:

Q Can the --

A The three-dimensional structure of CERA I meant there.

Q Can aspects of the three-dimensional structure of CERA be inferred as a result of its biological activity?

MR. FLEMING: Objection, beyond the scope of his report.

THE WITNESS: I, in my report, I address the binding issue and I also in my report provide my own model of the three-dimensional structure of CERA and we can discuss those. I feel that my model is consistent with the binding data.

BY MR. GALVIN:

Q In order to bind to the EPO-receptor CERA must have a particular confirmation, correct?

MR. FLEMING: Objection.

THE WITNESS: I would say no.

BY MR. GALVIN:

Q Does the -- does the fact that CERA binds to the EPO-receptor allow one to deduce anything about the structure of CERA?

MR. FLEMING: Objection, vague.

THE WITNESS: I think that's -- your

question is too vague. I think you have to rephrase it.

BY MR. GALVIN:

Q Does CERA specifically bind to the EPO-receptor?

MR. FLEMING: Objection, beyond the scope of his report.

THE WITNESS: The Lodish report and in Lodish where he refers to Roche documents, there's evidence that CERA binds to the EPO-receptor.

BY MR. GALVIN:

Q And are you aware of other molecules in the human body that bind and activate the EPO-receptor other than EPO?

MR. FLEMING: Objection, beyond the scope of his report.

THE WITNESS: That is again beyond the scope of my report. I stated in particular with regard to the binding data that there is data that, a form of EPO and CERA bind to the EPO-receptor.

BY MR. GALVIN:

Q Let me try it this way. Suppose you took the PEG starting reagent used to make CERA and you placed it in solution with the human EPO-receptor, would you -- would you expect to

observe specific binding of the PEG reagent to the EPO-receptor?

MR. FLEMING: Objection, incomplete hypothetical.

THE WITNESS: I have no data that I've seen discussing that. The PEG-EPO reagent is an activated reagent and it is a reactive molecule. There are a lot of things that could happen to it in an experiment such as the one you suggest. I don't think it would last very long.

BY MR. GALVIN:

Q Are you aware of any data or experiments which would establish that the structural confirmation of the epoetin beta starting material would be substantially different after the pegylation reaction?

MR. FLEMING: Objection to form.

THE WITNESS: You don't have a three-dimensional structure of CERA. CERA is a unique, much larger molecule than the EPO beta reagent. So all bets are off. I'd say, you know, in any -- I can't have a detailed discussion of the structural -- of the structure of CERA without -- in the absence of the experimental data, so --

BY MR. GALVIN:

atoms in the molecule are known.

Based upon your review, are you -- have you identified any errors in the identity, number and sequence of atoms in the CERA molecule depicted by Dr. Lodish or is it primarily an issue with respect to the structural confirmation of it that you criticize?

A The level of the model is so crude that I wouldn't be able to distinguish if there were errors.

Q The next sentence on page 53, what is not known about CERA, however, is its three-dimensional structure or confirmation, the overall shape of the molecule.

So isn't it the case, Dr. Jorgensen, that today no one really knows the three-dimensional structure of CERA, correct?

A Yes. I've stated that, that there is no more experimental structure that people would consider to be reliable for CERA.

Q And based upon the current data available, no model would have a degree of high reliability in terms of accurately depicting the molecule as it would exist in solution, correct?

MR. FLEMING: Objection.

THE WITNESS: No model is a, you know, pretty all encompassing term. I believe we could create a model that I would have faith in, that it was a reasonable depiction of CERA, you know, if I was given the time to do it.

BY MR. GALVIN:

Q And do you believe that the pictures that you generated for purposes of this report would satisfy that standard?

A No. I said that they're a starting point and I think that the -- in a short period of time, we gave it a good shot. There's nothing fundamentally wrong in what we did, but it is lacking in a number of areas I'm happy to discuss.

Q You don't know how long, if at all, Roche has been developing models for CERA, correct?

A No, we've talked about that before. I'm not aware that they have done anything in the way of modeling of CERA.

Q In attempting to model the structure of CERA, given the limits of our current knowledge, would you agree that an appropriate starting place would be to use data from the characterization of EPO?

MR. FLEMING: Objection.

THE WITNESS: I don't know what you mean data, what data and what characterization?

BY MR. GALVIN:

Q NMR or X-ray crystallography ordinance.

A In our own, you know, limited work on modeling CERA we did start with the NMR structure that is deposited in the Protein Data Bank. We do need to start with the structure. In the types of simulations we can do, however, we can do enough sampling to -- I can try to explain that, to let that system evolve so that the detail of the starting point for the more sophisticated calculations we do would not be critical.

Q Now, earlier you said that you tended to prefer X-ray crystallography over NMR. Why did you choose NMR as the basis for building the model of CERA?

A We chose the NMR structure because it's the only one that I saw in the Protein Data Bank for the uncomplexed, an uncomplexed EPO analog.

Q Now, if you were attempting to model the binding complex of CERA to the EPO-receptor, would you prefer then to use the X-ray crystallography data as opposed to the NMR data?

A Yes.

Q And you understand that one of the points that Dr. Lodish was trying to illustrate was binding of CERA to the EPO-receptor, correct?

MR. FLEMING: Objection to form.

THE WITNESS: I'm not sure what exactly he was trying to -- I mean I can give you my opinion of what he was trying to illustrate. There were graphics that showed an image of the complex as in the Syed paper.

BY MR. GALVIN:

Q And so depending on whether you're trying to illustrate or depict a complex EPO, an EPO-receptor or CERA, an EPO-receptor versus EPO or CERA in an unbound state, you might prefer the NMR data or the X-ray crystallography data as your starting point, correct?

MR. FLEMING: Objection.

THE WITNESS: The information that's available in the Protein Data Bank for this system is limited and we were interested in the uncomplexed EPO and it was a reasonable starting point for us to use the NMR structure. If we were to try to model the complex given what's in the Protein Data Bank, I would pick some structure of the complex. The complex is too big to do NMR, so we would have to use

some X-ray structure.

BY MR. GALVIN:

Q If you could turn to Paragraph 129. I'd like to, for you to just explain once you imported in the NMR structure for EPO, when you added the 600 ethylene oxy units around the EPO, did you predefine a shape by which the ethylene oxy units would be added?

A Can you expand on shape?

Q Sure. When you generated the image or the starting point for the modeling, did you randomly assign ethylene gylcols at any random position or did you define a sphere or some sort of shape and then populate that shape initially with ethylene gylcols before the simulation began?

MR. FLEMING: Objection.

THE WITNESS: We -- the work we did on this we did in about a day, two days. So we didn't put a lot of effort into it. We actually built the CERA model in a couple of ways. The one I felt easiest to describe here was something that I cooked up just for this where I took ethylene oxy units of CH2, CH2O and basically they were randomly placed in a volume surrounding the NMR structure of the EPO mutant. And then -- I don't know how much detail you

want to go in on this, but these units were then linked together and we attached them to the N-terminal, nitrogen of the EPO mutant.

BY MR. GALVIN:

Q Maybe it will be helpful at this point to look at Exhibit 2 of your deposition, which is Exhibit C. It's the other document we haven't looked at yet which has all your demonstratives.

A Uh-huh.

Q And fortunately, they're not exactly numbered, so we'll try to be clear when we talk about these to describe points. I'd like to turn to the picture of the model. Maybe we could turn to the picture of this model that you developed and this is the one with all the beads, but you can see the blue and green structures in the center. It's a large view, about halfway in.

A This one?

Q Yes. So what does the blue and green represent?

A On my tutorial part of my report, I mention that there were very many different ways of what we call rendering molecules, so at the base of any drawing like this graphic, there is a set of cartesian coordinates, XYZ coordinates. How you

then, you make the thing look in terms of balls and other pretty entities, the sizes of the balls is -- there are arbitrary decisions that are made. In the case -- this is a model of CERA that I feel pretty good about. To me the model makes sense. The blue part are helices and the CERA is a biopolymer and it has amino acid residues and one often represents amino acid residues in many different ways, but if there are helices, then you can show them in these helical ribbon forms. That's what the blue is.

Q And the blue and green is supposed to indicate the -- well, the blue and green is derived from the EPO NMR data in the Protein Data Bank that was reported by Cheetham, right?

MR. FLEMING: Objection, the term derived, vague.

THE WITNESS: Yeah, CERA is a biopolymer that contains some amino acid residue, so we have shown amino acid residues that appear to be in helices in the blue ribbons and the green are amino acid residues that are in less structure, in this sense a secondary structure which we call loops.

BY MR. GALVIN:

Q In the amino acid sequence that you are depicting and used for your model is a mutated form

of human EPO sequence?

A Yeah. We started, as I mentioned earlier, from the 1BUY coordinates that are deposited in the Protein Data Bank. And we were able to build a model of CERA, you know, with the aid of that. I don't, as I say here, I don't swear that this is. Well, you know, this is just my attempt to have an alternative to the models that were done by Dr. Lodish. I feel we could do a much better job on this, you know, letting it relax, adding water, adding counter ions. We may well do that.

Q Now, you don't depict in your model, you don't attempt to model the carbohydrate structure of CERA, correct?

MR. FLEMING: Objection, assumes facts not in evidence.

THE WITNESS: This was a model that I again didn't build just to illustrate that there was nothing special or legitimate about the Lodish model and that I could create a comparable or potentially more detailed model than Dr. Lodish provided.

BY MR. GALVIN:

Q But it doesn't -- your model doesn't show carbohydrate structures, correct?

A This model does not have any sugar residues.

Q Now, for lack of a better way of describing it, you've visualized and depicted the PEG surrendering the amino acid residues, correct?

MR. FLEMING: Objection, vague, mischaracterizes the term surrounding.

THE WITNESS: We didn't -- we didn't deliberately do anything here other than, you know, we started with a set up, which was in one version, which this figure and the other figure look the same. I added the ethylene oxzyene and then I -- they were annealed, if you will, random Monte Carlo statistical simulation to relax the ethylene oxy units and then we turned on some forces between them to build it into a contiguous chain of the ethylene oxy units.

BY MR. GALVIN:

Q Would you expect that for CERA to maintain in this spherical-like confirmation at all times or is this one snapshot in time?

A I really don't want you or anybody else to over interpret the significance of this picture. We haven't worked on it. This is not publishable, let me put it that way. I would never try to write this up and send it into a journal, you know. With

more work, we could get something published. This is a nice starting point. We would really need to run a simulation. Like I said, we had water, we had counter ions, we'd run it for a long time, a micro dynamic simulation and we would do a solid scientific state of the art simulation job, you know, on this system. And we would probably work on some other systems, too, you know, and try to get, you know, my curiosity is now peaked about molecules like CERA. But I think what you see here, and if you maybe squint a little is what I think is a reasonable picture as opposed to their cartoon, we'll even call it, compared to the Lodish picture, which I think is completely unreasonable and inconsistent with the facts.

Q Now, if you turn to the next page in Exhibit 2, which is another depiction of one of your structures and it's titled: "A Likely Ro50-3821 Structure (static)".

What's the difference between the two pictures we looked at? Is the first one a cutaway view?

A No, a good question. Just the rendering, what I call a rendering, we've now shown all atoms in what I call CPK colors, which is red

for oxygens, blue for nitrogens, gray for carbons. We haven't shown hydrogens in our model. We have the hydrogens in the coordinate file that we provided. You'll see there are hydrogens there as well. This is just now a rendering where all of the atoms are rendered as spheres and there are some size differences depending on the radii of the atoms. The little yellow dot is a sulfur and a cysteine ermathamine residue.

Q Now, looking at --

MR. FLEMING: Could you just hold that up to the camera so the jury can see what you're talking about? Thank you.

BY MR. GALVIN:

Q Looking at the caption here, A Likely Ro50-3821 Structure, what level of certainty do you have sitting here today that this is a likely structure?

A I feel it is a -- compared to the Lodish structure, I'm going to call it likely. For one thing, as you mentioned, we are -- CERA, we believe there is glycosylate. We don't have that. Ro50-3821 is CERA. So I mean there is some differences like that.

On the other hand, I do believe that

the general features here are consistent with my knowledge of what I expect with the result of a reaction or one pegylates a protein.

Q So if we go back to the other slide, the first slide we looked at which shows the ribbon structure.

A Uh-huh.

Q Does your depiction show the point of attachment between PEG, the polyethylene glycols and the amino acid residues?

MR. FLEMING: Objection, vague, objection to the term attachment.

THE WITNESS: To make this, as we talked, the pegylation reaction either uses a nitrogen of the lysine or nitrogen of the N-terminal residue of the protein reagent. In this case, we have used the N-terminus of the protein reagent to yield this illustration of potential product from a pegylation reaction.

BY MR. GALVIN:

Q And so in your depiction here, although just visually to a lay person you see these poly -- these little balls for the peg around, it's only actually bound and attached to the amino acid residues, the green and blue at one location in your

model?

MR. FLEMING: Objection.

THE WITNESS: There is a bond between the N-terminus of the protein reagent effectively and the PEG reagent. So this is again our shot at a very crude model of CERA without the sugars, not any sugars. There is a bond length, if you look at detail at our coordinates, you'll see that there is a bond.

BY MR. GALVIN:

Q Now --

A An amide bond.

Q Can CERA bind to the EPO-receptor and initiate signaling in this confirmation that you depict in your model?

MR. FLEMING: Objection.

THE WITNESS: I don't know what the structure is of CERA in solution. This is a cartoon and we need to work on it more and I don't know the structure of the complex of the EPO-receptor with CERA. So anything beyond that is conjecture.

BY MR. GALVIN:

Q Would your expectation be that when CERA binds to the EPO-receptor there are all of these ethylene gylcols between the amino acid

and we're back on the record.

BY MR. GALVIN:

Q Dr. Jorgensen, one of the questions going back a ways when I asked you about how you originally arrayed the ethylene gylcols when you were developing your model, you said you randomly filled the volume, what was the shape of that volume?

A A sphere.

Q And was this sphere centered around the center point of the EPO NMR structure that you started with?

A More or less.

Q And what was the basis for your assumption that the pegylation would be arrayed or at least that would be a reasonable place to begin your modeling from?

A Nothing in particular except it's a sort of standard feature we have in the software where we can add a solvent around a solute, what we call a solute and generally one puts that in a spherical shape or in a cubic shape.

Q And why wouldn't you start and center that sphere if you were going to use a sphere around the point where the amide bond would be between the

ethylene gylcols and the NMR and EPO structure?

MR. FLEMING: Objection to form.

BY MR. GALVIN:

Q In other words, haven't you biased it by assuming it would be equally distributed from the center of the molecule as opposed to centering it from a point of attachment?

MR. FLEMING: Objection to form.

THE WITNESS: All we've done here is created an image that's an alternative to the image that was provided in the Lodish report. What I said is, if we were given time, we would like to do a better job, let the system fully equilibrate and we could start, have different starting points and see where, if they equilibrate to a common point. So it's very preliminary and as I mentioned, I said to illustrate the point on page -- Paragraph 129, to illustrate the point that one can create alternative images for CERA, I provided the attached sample. That's really what we were doing here.

BY MR. GALVIN:

Q Another point that you mentioned before the break was that you hadn't received or reviewed data coordinate files relating to the model generated by Dr. Lodish. Is it your understanding

report, as I think I mentioned very early on felt to be redundant or irrelevant.

Q Can you turn to page 358.

MR. FLEMING: Of his report?

BY MR. GALVIN:

Q Of your report, Paragraph 136 of your report. And this is the section where you critique Dr. Lodish's depiction of the carbohydrate structure. Now, as you noted, Dr. Lodish acknowledged that the choices of how to actually make a depiction was uncertain. There was no experimental basis for drawing a structure. He identified that fact if his report, correct?

MR. FLEMING: Objection to form.

THE WITNESS: I say in Paragraph 135 says: Dr. Lodish himself recognized, however, the choice of carbohydrates is uncertain.

MR. FLEMING: Start over.

THE WITNESS: I'm quoting from Paragraph 135 of my report. As Dr. Lodish himself recognizes, however, the choice of carbohydrates is uncertain and the coordinates of these carbohydrate chains have not been obtained using currently available experimental techniques.

BY MR. GALVIN:

Q So the scientific truth here is that no one knows how to accurately represent a 3D representation of the attached carbohydrates of -- attached to either CERA or EPO based on our current state of knowledge, is that fair?

MR. FLEMING: Objection to form.

THE WITNESS: Yes. There's uncertainty about the carbohydrates.

BY MR. GALVIN:

Q But nevertheless, we know that the carbohydrates have a role and are present on the CERA molecule, correct?

MR. FLEMING: Objection, beyond the scope of his report.

THE WITNESS: Yes, I don't know that they have a role. I believe they're present.

BY MR. GALVIN:

Q You don't know whether they play -- they have a role in protecting the molecule from proteases?

A No, that's definitely outside of this. Any discussion of carbohydrates is really outside the scope of my report and I know there are carbohydrate experts that are involved in this.

Q But you don't consider yourself an

JURAT

I, WILLIAM L. JORGENSEN, Ph.D., the witness herein, the foregoing testimony of the pages of this deposition, do hereby certify it to be a true and correct transcript, subject to the corrections, if any, shown on the attached page.

_____

WILLIAM L. JORGENSEN, Ph.D.

Subscribed and Sworn to before me this _____ day of 2007.

_____

Notary Public