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Transcript of Alain Munafo, Ph.D.

Date: June 7, 2024
Case: TWI Pharmaceuticals, Inc. -v- Merck Serono SA (PTAB)

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EXHIBIT 1045, TWi
IPR2023-00049, -00050

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TWI PHARMACEUTICALS, INC.

Petitioner,

v.

MERCK SERONO SA

Patent Owner.

IPR2023-00049 (Patent 7,713,947 B2)

IPR2023-00050 (Patent 8,377,903 B2)

PROTECTIVE ORDER MATERIAL

Deposition of

ALAIN MUNAFO, Ph.D.

Conducted Virtually

Friday, June 7, 2024

1:06 p.m. CEST

Job No.: 541019

Pages: 1 - 179

Reported by: Cassidy Western, RPR

Deposition of ALAIN MUNAFO, Ph.D., conducted virtually.

Pursuant to notice, before Cassidy Western, RPR, Notary Public in and for the Commonwealth of Pennsylvania.

A P P E A R A N C E S

ON BEHALF OF THE PETITIONER, TWI PHARMACEUTICALS, INC.:

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ON BEHALF OF ALAIN MUNAFO, PH.D., AND THE PATENT OWNER:

ASHER S. McGUFFIN, ESQUIRE
VINITA FERRERA, ESQUIRE
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60 State Street
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ALSO PRESENT:

Gabriel Martin, A/V Technician
Dr. Matthias Dotzauer
Willem de Weerd

C O N T E N T S

E X H I B I T S

(Not attached to transcript.)

ALAIN MUNAFO, Ph.D.,
of lawful age, being first duly sworn or affirmed to testify to the truth, the whole truth, and nothing but the truth, was examined and testified as follows:

EXAMINATION BY COUNSEL FOR THE PETITIONER, TWI PHARMACEUTICALS, INC.

BY MR. SEGREST:

Q Good morning, Doctor. My name's Philip Segrest, and I'm representing the party TWi Pharmaceuticals in this case. I'm going to be asking you some questions this morning.

My first question, how do I pronounce your last name, please?

A Good morning, Counsel. My last name is Munafo, M-u-n-a-f-o. Munafo.

Q Munafo. Munafo. Am I saying that correctly?

A That's -- that's good enough. Thank you.

Q Thank you, Doctor.

Would you --

A I -- I would like just -- just before starting, I would like to comment on one thing. English is not at all my mother language. You can see -- you can hear it from my accent. But also in this case, I'm going to ask you to speak slowly and intelligently so that I can make sure that I understand what you are saying and be able to address your question as -- as I should.

So please be -- be conscious that I need you to speak slowly and make sure that I understand. Thank you.

Q And if you have any questions about your understanding, will you ask me for clarification?

A I will.

Q So if you don't ask me for clarification, I'll assume that you understood my question. Does that make sense?

A I will -- I may have to, you know, iterate some question later on while I'm trying to make up my mind that I do understand clearly what you are asking for.

Q Now, Dr. Munafo, you understand that

you're here today in connection with a declaration that you submitted in a case that is brought by TWi. Right?

A Yes, I do.

Q And you were previously deposed in another case involving these same patents that was brought by a company called Hopewell. Right?

A I had a deposition a couple of months ago now in -- when -- in relation with an IPR by -- with -- by Hopewell, yes.

Q Okay. And that was about March 27th that you had that deposition?

A Sitting here today, I do not recall the exact date, but it was a couple of months ago.

Q And just in terms of ground rules, we'll be operating the same today. I'll ask questions, I'll try to speak clearly and distinctly so that you can understand. You'll need to give a verbal response on the record so the court reporter can write it down. There is a video recording being made for backup, but the official record is the written, stenographic record that the court

reporter provides. So it's very important to give verbal answers, not just nod or shake your head.

Your counsel may object to some questions, but unless you are given an instruction not to answer, you'll need to go ahead and answer. And there will be a ruling on any objections later.

Do you have any questions about the process this morning?

A No, I don't have any question at this moment.

Q And where are you physically located for your testimony this morning?

A So we are sitting here in a conference room in a hotel in Divonne-les-Bains, which is in France.

Q And you say "we are sitting here." Who else is present with you?

A I am here together with Willem de Weerd, who introduced himself --

Q And who is that?

A He introduced himself a moment ago. He

is working and representing Merck Serono and RS Trading.

Q And I understand you have some copies of exhibits there with you. Is that correct?

A This is correct.

Q What papers do you have with you?

A I have in front of me my declaration with respect to TWi, Petitioner. I have the so-called '947 patent. I have the so-called '903 patent. I have what we refer to as Bodor patent, last three digit being '100 -- '101. I have the product development and license agreement by and between IVAX and RS Trading. I have the meeting minutes of -- the minutes of the meeting hold in August 2003 in Amsterdam, named Oral Cladribine for MS Project. And I have the cladribine briefing documents for review that's together with the cover email, the cover email having a date of December 17, 2003.

And this is all I have with me.

Q In preparing your declaration, did you review any documents that are not cited in your

declaration?

MR. McGUFFIN: I'm going to object to privilege.

Dr. Munafo, to the extent you reviewed anything by yourself, you can answer, but don't reveal the contents of communications with counsel.

THE WITNESS: So yes, I did.

BY MR. SEGREST:

Q And what documents did you review that are not cited in your declaration?

MR. McGUFFIN: I'm going to give the same objection, the same instruction. You can talk about anything you reviewed separately, but you should not talk about what we -- what you discussed with counsel.

MR. SEGREST: And I'll note for the record that the witness is required to provide whatever facts were sent by counsel. You can't shield that as privileged. I'm not asking him what you provided him, I'm not asking what he provided himself. I'm asking him what he reviewed

and he's required to answer that.

MR. McGUFFIN: So, Mr. Segrest, he is definitely required to talk about the facts, but asking specifically what documents he has looked at could reveal communications with counsel. And I'm just cautioning him not to reveal any communications with counsel.

MR. SEGREST: But he has to say what documents he's looked at without saying where he got them from.

MR. McGUFFIN: I don't necessarily agree. I think anything that he reviewed himself without counsel and anything that is cited in his declaration, he can talk about. But I'm going to instruct him not to reveal the contents of communication with counsel.

BY MR. SEGREST:

Q You can answer the question, Doctor.

A I have reviewed a few documents, but sitting here today, I'm not able to -- to give you an exhaustive list.

Q Do you remember looking at any documents

that are not cited in your declaration?

MR. McGUFFIN: I'm going to give the same objection, the same instruction. Just don't talk about the contents of communications with counsel.

THE WITNESS: I have seen a few documents, but sitting here today, I would not be able to list exhaustively what I have seen or reviewed.

BY MR. SEGREST:

Q So even if you can't give a complete list, do you remember what any of those documents are?

MR. McGUFFIN: Same objection, same instruction.

THE WITNESS: Sitting here today, I would not be able to name precisely these document. I would feel more at ease if you present a document and ask me whether I have reviewed or seen it before.

BY MR. SEGREST:

Q Yes. Doctor, I'm asking you about

things that were not cited in your declaration. So I can't tell you what you didn't say.

Can you remember anything about those documents that you did review that you chose not to cite in your declaration?

MR. McGUFFIN: Same objection, same instruction.

THE WITNESS: Sitting here today, and given the time lapse since I wrote this declaration, I'm unsure of what I had seen by then or after then. And I cannot give you -- cannot be more specifically than that in total honesty and being -- having sworn that I can tell the truth and only the truth.

BY MR. SEGREST:

Q Other than your deposition for the Hopewell IPRs, have you given any other testimony about these patents? Given any other depositions about these patents?

A I am going to ask you to repeat the first part at least of your question to make sure that I understand completely.

Q Yes. Other than your deposition in the Hopewell IPRs, which we mentioned before, have you given any other depositions about the '947 and '903 patents?

A So yes, I have.

Q And when was that?

A Sitting here today, I am not able to state the exact date, but this was within the last few month.

Q And was that a deposition for a lawsuit in federal district court in the United States?

MR. McGUFFIN: Object to form.

THE WITNESS: Could you please repeat your question?

BY MR. SEGREST:

Q Was that a deposition for a lawsuit pending in federal district court in the United States?

MR. McGUFFIN: Object to form.

THE WITNESS: I'm not an expert in legal terms, so I'm not sure how to address your question precisely. Yet I have deposed in

relation with this case. And, again, excuse for my naivete and lack of knowledge of legal terms, but the terms "district court" was indeed mentioned.

BY MR. SEGREST:

Q Let's turn to your declaration, which is Exhibit 2053.

THE TECHNICIAN: Would you like that on the screen, Counsel?

MR. SEGREST: I think the witness has a copy of this. It may be useful to display a copy so that we can make sure we're on the same page .

And let's go to page -- page number 25 at the bottom, but I think it's going to be the 26th page of the PDF. You're on the 27th page of the PDF. That's page 25 at the bottom, 26th page. Has paragraph 56 on it.

(MUNAFO Exhibit 2053 was marked for identification.)

Q So, Dr. Munafo, are you at the page that has the number 25 of your declaration?

A Yes, I see that.

Q Is that your signature?
A Yes. This is -- this is my signature.
Q And where were you physically when you signed this declaration?
MR. McGUFFIN: Object to scope.
THE WITNESS: I was at home.
BY MR. SEGREST:
Q And where is home?
MR. McGUFFIN: Object to scope.
THE WITNESS: I live in Switzerland. Do you need the exact address?
BY MR. SEGREST:
Q No. So you were in Switzerland when you signed this declaration. Is that correct?
MR. McGUFFIN: Object to scope.
THE WITNESS: Yes, this is correct.
BY MR. SEGREST:
Q And just to be clear, you were outside the United States when you signed this declaration. Correct?
MR. McGUFFIN: Objection; asked and answered. Object to scope.

THE WITNESS: I was in Switzerland.
BY MR. SEGREST:
Q Now, I'll direct you to paragraph 56, the last paragraph of your declaration.
Do you see the first line there has a statement that "all statements made herein of my knowledge are true"?
A Yes, I do.
Q And then in the next line, you see another clause and it says that "statements made on information and belief are believed to be true."
Do you see that?
MR. McGUFFIN: Object to form.
THE WITNESS: I see the second line reads, indeed, "and that all statements made on information and belief are believed to be true."
And there's a continuation on that, yes, I do.
BY MR. SEGREST:
Q Yes. So those statements made on information and belief are not based on your

personal knowledge. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: Sitting here today, I am not able to make a difference between information that I have, belief that I have, and knowledge that I have.

BY MR. SEGREST:

Q Let's go to paragraph 54 of your declaration that begins on page 23.

Do you see this paragraph begins with the phrase, "to the best of my knowledge"?

A I see on page 23 the paragraph 54 starting, "to the best of my knowledge," yes.

Q And the rest of this paragraph describes work at IVAX. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: You are talking about the rest of the whole paragraph 54?

BY MR. SEGREST:

Q Let's say the rest of that -- this sentence. The rest of that first sentence is about what IVAX did not design or develop. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: This whole sentence reads, to make sure that I'm with you:

"To the best of my knowledge, IVAX did not design or develop any regimen for treating MS using cladribine, let alone the regimen of administering 10-milligram of oral cladribine tablets per day for five to seven days per month for two months followed by a 10-month cladribine-free period that I and my team at Serono designed and communicated to IVAX before February 2004."

BY MR. SEGREST:

Q All right. You did not work at IVAX. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: I did not work at IVAX, this is correct.

BY MR. SEGREST:

Q Now, you have information on which you based a belief that this statement is true, but you don't have personal knowledge of what IVAX did

and didn't develop. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: I do not have knowledge of what IVAX was doing, but given the principle of the collaboration, given what we shared at meetings where IVAX was present, given the agreed-upon distribution of responsibilities, and given all what I understand and recall sitting here today, it is my conviction that we at Serono developed a dosing regimen, and that is mentioned in this sentence. And that it was not developed by IVAX.

BY MR. SEGREST:

Q You were in charge of a team of people that were working at Serono. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: This is a vague question. I would like you to clarify what you mean with -- whether this is in relationship with cladribine, whether this is altogether my work at Serono, and at what time you refer to.

BY MR. SEGREST:

Q In your work at Serono between 2001 and 2004, when it was developing a cladribine product, you had a team that you worked with. Right?

A Between the period 2001 to 2004, I was part of a team at Serono. A project team at Serono that was working on developing oral cladribine for the treatment of multiple sclerosis.

Q Let me direct you to paragraph 18 of your declaration on page 7.

That team at Serono included many people other than the named inventors on the '947 and '903 patents, didn't it?

MR. McGUFFIN: Object to form.

THE WITNESS: The team at Serono included experts and colleagues from various expertise within Serono. And yes, it was larger than the three co-inventors of the '947 and '903 patent.

BY MR. SEGREST:

Q Let me direct you to Exhibit 2049.

(MUNAFO Exhibit 2049 was marked for identification.)

THE WITNESS: Can you let me know what this is exhibit?

BY MR. SEGREST:

Q I think you referred to it as the briefing document, and it's got a cover email. It's the one displayed on the screen.

A I have it, yes, thank you.

Q And looking at this very first page, which I think you've described as a cover email, it has addresses for the sender, from, the addressees, to, and the CC list for additional recipients. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: This cover memo does, indeed -- was initiated from Isabelle Emery and lists a whole series of people either as addressees or in CC, correct.

BY MR. SEGREST:

Q And Isabelle Emery was one of the people on your team at Serono that you referenced in

paragraph 18 of your declaration. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: Sitting here today, I cannot be sure of -- of the exact composition of the team as it fluctuated to some extent along the -- along the time. So being part of the team is related to an exact time period. But, again, sitting here today, I'm not able to address formally your question.

BY MR. SEGREST:

Q Well, at the time of this email which has a date of December 17th, 2003, 11:23:17 a.m., was Isabelle Emery on your team?

MR. McGUFFIN: Object to form.

THE WITNESS: This is more than 20 years ago, and sitting here today, I'm not able to say exactly at what time Isabelle Emery or what month Isabelle Emery was on the project team or not.

BY MR. SEGREST:

Q So is it your belief that this email was distributed from and to people other than those who were on that specific product team?

MR. McGUFFIN: Object to form.

THE WITNESS: If I re- -- rephrase your question to make sure I understand it correctly, you are asking if all the addressees here, all the people listed in the "to" or "CC" were part of the Serono project team?

BY MR. SEGREST:

Q Okay. Let me ask a different question.

Looking at the email addresses, you can see that some of them are listing Serono as the organization for that person. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: In the list of people in the "to," there -- and in the "CC," there are several people listed with a Serono address.

BY MR. SEGREST:

Q Okay. And there are others like Yogesh Dandiker in the recipient list who were at different organizations. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: Yogesh Dandiker is listed with a IVAX address.

BY MR. SEGREST:

Q Okay. Would this email have been sent to people at Serono who were not on the team that you describe in your declaration?

MR. McGUFFIN: Object to form, foundation.

THE WITNESS: This email was distributed to the people listed in "to" and "CC." I am not able to say here whether this has been distributed to other people or seen by other people.

BY MR. SEGREST:

Q Are there people on the "to" and "CC" list in the Serono organization that were not on your team in December of 2003?

MR. McGUFFIN: Object to form.

THE WITNESS: If I understand your question, whether in the list of "to" and "CC" people, there are people from Serono that are not on the project team, I am not able, sitting here today, to reply definitely because I do not recall, as of today, who was on the team by that date of December 2003.

BY MR. SEGREST:

Q So looking at the -- starting with the "to" list of addressees, was Gordon Francis on the team that you referred to?

A Inasmuch as I recall sitting here today, Gordon Francis was involved in this -- in many discussions that we had with this development program. But, again, sitting here today, I do not recall whether he was formally on the team or not.

Q Was Maria Lopez-Bresnahan on the team that you testified about?

A Sitting here today I had -- I know that Maria Lopez-Bresnahan has been working extensively on this project, and I have collaborated with her, but I am not able to say whether she was formally part of the team or not.

Q Was Samir Shah on this team that you testified about?

A Samir Shah was working on the cladribine oral for treatment of MS, but sitting here today, I'm not able to state whether he was formally on the team at the date of December 2003.

Q Was Alain Micaleff on the team that you testified about?

A Alain Micaleff has contributed and worked on the project of development of oral cladribine for the treatment of MS, but sitting here today, I am not able to recall whether he was formally on the product team as of the date of December 2003.

Q Would your answer that you don't recall if the person was on the product team at that time be the same for the other email recipients listed with a Serono email address?

MR. McGUFFIN: Object to form.

THE WITNESS: Sitting here today more than 20 years later, I do not recall, remember, who was formally on the product team by that date.

BY MR. SEGREST:

Q And sitting here today, if you don't remember who was on the team, you also don't personally remember who made exactly what contributions on the team. Right?

MR. McGUFFIN: Object to form.

Objection; mischaracterizes testimony. Objection; argumentative.

THE WITNESS: I'm sorry. I'm going to ask my advise -- my counsel to repeat his objection.

BY MR. SEGREST:

Q His objection should not affect your answer, sir.

A I -- I just want to make sure that I understand everything that is said during this deposition please.

MR. McGUFFIN: Yeah, Mr. Segrest is right. You should answer. My objections are just to note my objections on the record.

THE WITNESS: Okay. So excuse me for this diversion. Could you please repeat your question?

BY MR. SEGREST:

Q Sure. And I'm trying to read it from the realtime.

And sitting here today, if you don't remember who was on the team, you also don't

personally remember who made exactly what contributions to the team. Right?

MR. McGUFFIN: Same objections.

THE WITNESS: Sitting here today, I have a good recollection of contribution I had with several colleague at Serono. But I cannot list exhaustively all the contribution that all colleagues have had on this project.

BY MR. SEGREST:

Q Let's turn to the Exhibit 1001.

Dr. Munafo, the Exhibit 1001 is the '947 patent. Do you have that in front of you now?

A I have the -- a reprint of the '947 patent in front of me, yes. And I can see it on screen.

(MUNAFO Exhibit 1001 was marked for identification.)

Q And you're listed as the third-named inventor on this patent. Right?

A The inventors are four, Giampiero De Luca, Arnaud Ythier, myself, and Maria Lopez-Bresnahan. I'm not aware whether the number

is relative or not.

Q And the first name on that list, Giampiero De Luca, he's the chief intellectual property counsel at Serono. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: Sitting here today and more than 20 years later, I do not recall his title at the company at that time.

BY MR. SEGREST:

Q Let's go back to your declaration, Exhibit 2053. Go to paragraph 21 of your declaration.

A Yes.

Q And here you testify that Dr. De Luca was Serono's chief intellectual property counsel. Did you not have a recollection of what his position was when you gave this testimony?

MR. McGUFFIN: Object to form.

THE WITNESS: My memory had been -- my recollection has been refreshed by the time I wrote this -- this declaration. And now that I read what I wrote, I can positively answer your

previous question that, indeed, at that time Giampiero De Luca was Serono's chief intellectual property counsel.

BY MR. SEGREST:

Q And at the time you wrote your declaration, what refreshed your recollection about Dr. De Luca's title at Serono?

MR. McGUFFIN: I'm just going to caution you not to reveal the contents of communication with counsel. If you recall a particular document that refreshed your recollection, you can identify it.

MR. SEGREST: And I'm going to state our position that's an improper instruction because refreshed recollection can't be privileged. But we'll address that in the motions that are -- we'll be filing.

MR. McGUFFIN: I think my instruction was pretty clear. Just don't reveal the contents of communication with counsel. But if you recall any document that refreshed your recollection, you can identify it.

THE WITNESS: Beside discussion with my counsel, I do not recall of any document that helped me refresh my memory.

BY MR. SEGREST:

Q So was that fact about what Dr. De Luca's position was something that was communicated to you by counsel?

MR. McGUFFIN: Object; privileged.

I'm going to instruct you not to reveal the contents of any communication with counsel. Again, if you -- if you recall any document that refreshed your recollection, you can identify it.

THE WITNESS: Sitting here today, I do not recall any other document.

BY MR. SEGREST:

Q We can go back to Exhibit 1001 now, the '947 patent. And we'll go to the second page of this document, page 2 of 13. And I'm looking at the column on the left under the heading "Other Publications."

At the bottom of that column on the left, do you see a publication of Rice from 2000?

A I see a publication authored by G. Rice, et al., named Cladribine and progressive MS clinical and MRI outcomes of a multicenter controlled trial in "Neurology," March 2000, page 1145 to 1155, Volume 54. Yes.

Q Let's go to Column 2 of the patent, Line 45.

A So the page -- are you referring, sorry, for the page -- page number, number 3?

Q It is page 3 of 13. And I'm referring to Column 2, Line 45 and continuing from there.

A Yeah, I see this line.

Q And does this part of the specification of your patent cite that Rice 2000 article?

A This sentence, Line 43 to 45, reads:

"In addition, placebo controlled phase III study was conducted in patients with primary progressive or secondary progressive multiple sclerosis, Rice, et al., 2000, 'Neurology' 54, 5, 1145 to 1155."

Q And that's that Rice 2000 article that was listed in the other publications we looked at.

Right?

A This -- this is the way we refer to a publication. And yes, I understand it to be the one we mentioned in the other publications on page 2.

Q And then does the rest of that paragraph indicate that in the Rice 2000 study, both patient groups received a cladribine dose of 0.07 milligrams per kilogram per day repeated for either two months or six months?

MR. McGUFFIN: Object to form.

THE WITNESS: I'd like to read the exact sentence. It says:

"In this study both patient groups received cladribine by subcutaneous injection at a dose of 0.07-milligram per kilogram per day. The treatment was repeated for either two months or six months."

BY MR. SEGREST:

Q And looking at the last sentence of the next paragraph, which is Lines 56 through 58, this again cites Rice 2000. Right?

MR. McGUFFIN: Object to form.
THE WITNESS: The last sentence reads:
"Phase II study results were positive on the significant reduction of MRI-measured brain lesions, in parentheses, Rice, et al., 2000, above, close parentheses."
BY MR. SEGREST:
Q Let's go to Exhibit 1008 please.
(MUNAFO Exhibit 1008 was marked for identification.)
MR. McGUFFIN: Object to scope. I don't believe this was cited in Dr. Munafo's declaration. Was it?
MR. SEGREST: It may not have been.
THE WITNESS: I don't think --
BY MR. SEGREST:
Q And, Doctor, I think you may not have a copy of this in front of you, but do you see the one that's displayed on the screen there?
A I see a -- the top of a page 1 of what appears to be a publication by George P.A. Rice and others. Name, "Cladribine and Progressive MS,

Clinical and MRI Outcomes of a Multicenter Controlled Trial." And after the end of the abstract, it says that this is published or appears to be published in "Neurology" 2000, Volume 54 page 1145 to 1155.

MR. McGUFFIN: I'm going to renew my objection to scope.

BY MR. SEGREST:

Q And this is the article cited in the specification of your patent. Right?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: I have not seen the whole paper. I'm just here on the top of the first page. But the reference seems to correspond to the reference we quote in the patent '947.

MR. SEGREST: Can you show us the full first page? Just the first page is fine.

Q And you can see this is marked as Exhibit 1008. Right?

A I do not see this on the screen.

Q Do you see the bottom right hand of the

screen, it says EX1008?

A No, I do not see the bottom of the screen.

Now I see it. I see there that it says "Petitioner TWi Pharms, Inc. EX1008, page 1 of 11."

MR. SEGREST: If the technician could put the full first page on the screen again for me please.

Q Dr. Munafo, on your screen, what's the lowest line in this document that you can see on your screen?

A It's very small and I'm not sure I can read it properly, but it seems to be partial line received June 10 I think with a date I'm not sure I can read and accepted in final form, November 1 with a date that is too small to be read fully.

Q Okay. So that'll give us an idea for the technician of how much we need to zoom in for you to be able to see a full page. Thank you.

I want to look now up in the abstract, about the fifth line.

Do you see the line in the abstract that the first characters on the left are "0.07"?

A I see this starting -- a line starting by this, but I'm going to ask you to allow me just a minute to put this in context and read quickly the abstract.

Q Okay.

A Okay. I have read the -- the article abstract and I'm ready to take your question regarding the line starting with 0.07-milligram per kilo per day.

Q Right. So is this describing two cladribine arms of the Rice 2000 study, one with a total dose of 0.7 milligrams per kilogram and another with a total dose of 2.1 milligrams per kilogram?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: This is describing a study with apparently three arms: One of a placebo, and two arms with a dose of 0.7-milligram per kilo and 2.1-milligram per kilo, respectively.

BY MR. SEGREST:

Q And does it indicate that it achieves the 0.7 milligrams per kilo and the 2.1 milligrams per kilo by dosing for either two or six cycles, respectively?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: Other than interpreting what it says, I'm going to read it again.

It says that the patient "were randomly assigned to receive placebo or cladribine 0.07-milligram per kilo per day for five consecutive days every four weeks for either two or six cycles."

BY MR. SEGREST:

Q Every four weeks would be every 28 days. Right?

A I would have to go through the detail of the methodology in the paper to confirm whether in this study, they considered a week of seven days or some variance of it.

Q Let's turn to the second page of the

document. In the right-hand column, the paragraph at the top of the page, this is the second full sentence, which begins with the words "patients were assigned."

Do you see that sentence, Doctor?

A I only see the second column to a part of the word by "subcutaneou-" (ph.) And then I have the screen with the video that hides -- okay.

MR. McGUFFIN: And I'll renew my objection to scope.

BY MR. SEGREST:

Q And do you now see the sentence that begins with the words "patients were assigned"?

MR. McGUFFIN: Objection to scope.

THE WITNESS: Are you referring to the -- make sure I am with you -- to the sentence on the sixth line of the column to the right?

BY MR. SEGREST:

Q Yes.

A Okay. So I read this sentence to make sure.

"Patients were assigned to one of three

parallel treatment groups, in parentheses, cladribine, 2.1mg per kilo, cladribine, 0.7mg per kilo or placebo according to a computer-generated randomization schedule stratified by baseline disease severity and site."

Q Okay. Let's go to the last paragraph on this column.

Do you see this paragraph with the heading "study medications and dosage"?

MR. McGUFFIN: Object to scope.

THE WITNESS: I can read a part of the paragraph to the bottom of the page, which is named in italics "study medications and dosage."

BY MR. SEGREST:

Q And does the second sentence indicate that the total dose of 2.1 milligrams per kilo was achieved by administering --

A Sorry. Can you point me again exactly to where you want me to look at?

Q Yeah. I'm looking at the sentence that begins "patients received six courses of cladribine."

Do you see that sentence?

MR. McGUFFIN: Object to scope.

THE WITNESS: I will read it for the sake of making sure we are on the same one.

"Patients received six courses of cladribine 0.07mg per kg per day SC for five consecutive days, in parentheses, total dose 2.1mg per kg, close parentheses, followed by two courses of placebo or two courses of cladribine 0.07mg per kg per day SC for five consecutive days, parentheses, total dose, 0.7mg per kg, close parentheses, followed by six courses of placebo or eight courses of placebo SC for five consecutive days."

Q Okay. And does that indicate that the total 2.1mg per kilo was achieved by patients receiving six courses of cladribine of 0.07mg per kilogram per day for five consecutive days?

MR. McGUFFIN: Object to form, scope and foundation.

THE WITNESS: It reads what it reads, that the author claimed that patient received six

courses of cladribine 0.07 manages per kilo per day for five consecutive days subcutaneously with a total dose being 2.1mgs per kilo. This is, indeed, the author's claim.

BY MR. SEGREST:

Q Okay. And 0.07 times 5 times 6 is 2.1. Right?

MR. McGUFFIN: Object to scope.

THE WITNESS: I'm not able to do the arithmetic by my head like this in such an important instance.

BY MR. SEGREST:

Q Okay. Does it also indicate that the total dose of 0.7mg per kilogram was administered as two courses of cladribine 0.07 milligrams per kilogram per day for five consecutive days?

MR. McGUFFIN: Object to form, scope, foundation.

THE WITNESS: The sentence says, "and the author claimed that the patient received two courses of -- in the -- in the second group, the patient received two courses of cladribine 0.07mgs

per day SC for five consecutive dose -- five consecutive days, in parentheses, total dose being 0.7mgs per kgs."

BY MR. SEGREST:

Q And 0.07 times 5 times 2 is 0.7. Right?

MR. McGUFFIN: Object to scope.

THE WITNESS: Arithmetically, 0.07 times 5 times 2 equals 0.7. 0.07 times 5 times 2 equals 0.7.

BY MR. SEGREST:

Q And then one of those five-day cycles of 0.07 milligrams per kilograms per day, a patient would receive 0.35 milligrams of cladribine. Right?

MR. McGUFFIN: Object to form, scope, foundation.

THE WITNESS: Arithmetically, 0.07 times 5 is indeed equal to 0.35. Understanding everything here for the arithmetic. For the rest of the sentence, I'm not sure I got it totally.

BY MR. SEGREST:

Q Let's look at page 9. Scratch that.

We can set that one aside and go to Exhibit 2050 now.

MR. McGUFFIN: Yes.

(MUNAFO Exhibit 2050 was marked for identification.)

BY MR. SEGREST:

Q I think you referred to these as the August meeting notes.

MR. McGUFFIN: Mr. Segrest, if you're switching documents, would this be a good time for a short break?

MR. SEGREST: Yeah, we can do that. Five minutes? 10 minutes?

MR. McGUFFIN: Five would be enough for us.

Dr. Munafo, do you think five is enough?

THE WITNESS: Yeah, I think eight minutes so I have time to go to the restroom.

MR. SEGREST: Let's say 10 to make it easy.

THE WITNESS: Okay. Thank you.

MR. McGUFFIN: See you back here at

8:20 Eastern.

(Whereupon, there was a recess in the proceedings.)

BY MR. SEGREST:

Q Doctor, I want to direct you now to Exhibit 2050, which I think you had referred to as the "meeting minutes."

A I see on screen the document that I have in front of me, yes. Thank you.

Q And does this document purport to be minutes of a meeting held August 27th, 2003 in Amsterdam?

MR. McGUFFIN: Object to form.

THE WITNESS: The front page here is named "Oral Cladribine for MS Project, meeting on 27 August 2003, Amsterdam." And the bottom says that these are draft minutes.

BY MR. SEGREST:

Q Were you one of the Serono participants in this meeting?

A In the meeting of August 2003, 27, in Amsterdam, I am indeed listed as a participant.

Q And so are you basing your testimony on seeing yourself listed as a participant in this document? Is that how you know that you were a participant in this meeting?

A No. I'm just confirming that I'm listed as a participant, and I have no reason to believe that that is in any way not representing the truth.

Q But you're testifying about what's printed on the document. You don't have any present recollection of this meeting. Right?

MR. McGUFFIN: Object to form. Objection; mischaracterizes testimony.

THE WITNESS: You are speaking a little fast. Can I ask you to please repeat your question?

BY MR. SEGREST:

Q Yes. My question was, but you're testifying about what's printed on the document. And you don't have any present recollection of this meeting. Right?

MR. McGUFFIN: Object to form.

Objection; mischaracterizes testimony.

THE WITNESS: This is not what I was saying. I was just confirming that I am listed as a participant. I did not say that I do not recall being present at that meeting.

BY MR. SEGREST:

Q Do you have a present recollection of the meeting?

A Sitting here today and more than 20 years later, I have a partial recollection of that meeting.

Q Looking at the document again, [redacted]

MR. McGUFFIN: Object to form. Objection; asked and answered.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: To make sure I understand completely your question, could you point me to the paragraph you are -- you would be referring to here?

BY MR. SEGREST:

Q Well, first, I'm asking about your recollection of this -- what was happening at this time. And if we need to, I can point you to something later, but I want to get your answer about your recollection.

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

[redacted]

BY MR. SEGREST:

Q Well, now let me direct you to page 4 of this document, and we'll look at the paragraph beginning at the top of the page there. [redacted]

A I'm with you on the top of the page number 4 of the draft minutes.

Q [redacted]

MR. McGUFFIN: Object to form. Objection; mischaracterizes document.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q Does that refresh your recollection that at the time of this meeting in August 2003, [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q Well, as you sit here today, do you remember that yourself? Or are you just relying on what the document says?

A As I said, [redacted]

Q And that sentence also indicates that [redacted]

[redacted] Right?

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q And Yogesh is Yogesh Dandiker from IVAX. Right?

A This is my understanding.

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: IVAX, according to the license agreement, was in charge of developing a formulation for oral administration of cladribine. They have investigated various formulations and strengths. [redacted]

BY MR. SEGREST:

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: I do not agree with this statement. [redacted]

BY MR. SEGREST:

Q What's your understanding of the difference between referring to strength and referring to dose?

A The strength is, in my understanding, relates to the amount of active ingredient in a

certain pharmaceutical form, while the dose is what is administered or to be administered to a patient in that case.

Q On that same page 4 of the document, scroll down to about halfway down the page, and you can look on the paper there.

Do you see a heading, "Expert Panel and Phase III Design"?

A I see what is on screen and I have it in front of me.

Q [redacted]

[redacted]

MR. McGUFFIN: Object to form; foundation.

THE WITNESS: [redacted]

[redacted]

BY MR. SEGREST:

Q [redacted]

[redacted]

A Sitting here today, I remember having participated to that meeting, but the exact -- I would not be able to give an exhaustive list of everything that has been discussed.

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q And do you agree that that sentence is accurate, that that's what happened at that expert panel?

A To the best of my recollection, sitting here today, more than 20 years later, I have no reason to believe that this is not reflecting what has indeed happened.

Q But sitting here today, more than 20 years later, [redacted]

[redacted]

MR. McGUFFIN: Object to form; calls for an opinion.

THE WITNESS: Sitting here today, more than 20 years later, [redacted]

BY MR. SEGREST:

Q Could there be --

A But (indiscernible) were discussed.

Sorry.

Q I didn't mean to interrupt you, sir.

A (Indiscernible) --

Q Could there have been other things that

were discussed that you don't recall currently?

MR. McGUFFIN: Sorry. I want to be clear. It sounded like you accidentally cut off Dr. Munafo again.

Did you have more to say, Dr. Munafo, or were you done?

THE WITNESS: I would have to go back to what I was saying before to -- to say definitely whether I was done or not because my attention was captured by the next question of the counsel.

BY MR. SEGREST:

Q Why don't I go ahead and ask you the next question again.

So sitting here today, more than 20 years later, could there have been other things discussed at that expert panel [redacted]

MR. McGUFFIN: Object to form; calls for speculation.

THE WITNESS: I have difficulty to answer a question if I recall what I do not

recall. Maybe you can rephrase your question.
BY MR. SEGREST:
Q [redacted]
A Yes, this is correct.
Q Those [redacted] experts are not Serono employees. Right?
MR. McGUFFIN: Object to form, foundation.
THE WITNESS: To the best of my recollection sitting here today, they were experts and not employee by Serono.
BY MR. SEGREST:
Q And sitting here today, do you agree that you can't recall everything that was discussed at that expert panel?
MR. McGUFFIN: Object to form.
THE WITNESS: Sitting here today, I recall several point that were discussed. [redacted]

[redacted]

But it is true that more than 20 years later, I cannot swear that I remember everything that has been discussed or not discussed.

BY MR. SEGREST:

Q And after that paragraph, [redacted]

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: On page 4 of these minutes under the paragraph [redacted]

[redacted]

BY MR. SEGREST:

Q And that first primary phase III study suggestions has a row with the heading "Arms." Right?

A I can see this -- this row, yes.

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

The dose that are mentioned here as 0.7mgs per kilo and 2.1mgs per kilo were targets -- were to be considered as target exposure that we wanted to have for the patient in the two -- in the two arms.

BY MR. SEGREST:

Q Right. And you wanted the cumulative dose in each of those arms to approximate those

target exposures. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: When you say "you wanted," I'd like to clarify that these are -- this is a summary of the presentation made in that meeting. And when you say "you," I should specify that this is not necessarily me that you refer to. Is this correct?

BY MR. SEGREST:

Q Yes, that's correct. I'm asking you what was intended in this description of the arms? Was it intended that the cumulative dose approximating 0.7 milligrams per kilogram would be the target exposure in one arm?

MR. McGUFFIN: Object to form.

THE WITNESS: In one arm, the target exposure would accumulate to 0.7mgs per kilo as 0.35mgs per kilo times 5 days times 2 months.

BY MR. SEGREST:

Q But it says approximating 0.7 milligrams per kilo. Right?

A It reads what it reads. I can read

it -- I can read approximating as well.

Q Okay. And it also -- in the other arm or in the other cladribine arm, it says cumulative dose again is approximating 2.1mgs per kilo. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: Sitting here today, I do not -- I'm not able to recall what -- what's the meaning and intent between -- behind the word "approximating" here. But it reads what it reads.

BY MR. SEGREST:

Q And 0.7mgs per kilo and 2.1mgs per kilo, those are the total doses in each of those arms, respectively, that are being approximated. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: I am not sure what your use of the word that had been approximated. What I'm reading here is that this cumulative dose approximating 0.7mgs per kilo and 2.1mgs per kilo were the two active treatment arms in addition to the placebo arm.

BY MR. SEGREST:

Q And in each of those active treatment arms, it wants to -- it says that it's going to approximate those total doses. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: Again, the use of the term "approximating" here, I am not able to recall, sitting here today, what was the intent or meaning of "it." But I'm not reading it in exact same wording as you are using in your last sentence. I'm reading it as really it reads here, that the cumulative dose approximating 0.7mgs per kilo and 2.1mgs per kilo were the two active treatment arms doses.

BY MR. SEGREST:

Q And a total dose of 0.7mgs per kilo is the same total dose as in one of the arms of that Rice 2000 study we looked at, isn't it?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: Would you specify what you mean with same dose here?

BY MR. SEGREST:

Q Well, one of the arms of the Rice 2000 study we looked at was 0.7mgs per kilo achieved by two cycles of five days administration. Right?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: I -- in what you call the Rice paper, there was indeed a mention of -- of such a dose and such doses in the study that they report.

BY MR. SEGREST:

Q And the other cladribine arm in the Rice 2000 paper was a total dose of 2.1mgs per kilo achieved by six cycles of five days. Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: In the Rice -- what you call the Rice paper in "Neurology" 2000, there was indeed an arm in the study that they report communicating that dose of 2.1mgs per kilo cumulative.

BY MR. SEGREST:

Q [redacted]

MR. McGUFFIN: Object to form; mischaracterizes testimony.

THE WITNESS: [redacted] Is it my understanding of your question?

BY MR. SEGREST:

Q [redacted] Right?

MR. McGUFFIN: Object to form; mischaracterizes testimony.

THE WITNESS: The process of designing the clinical trial and its dosing regimen and the process of -- and this -- this part was Serono responsibility. And the process of developing a formulation for oral cladribine, which was the responsibility of IVAX, were two process that were developed in parallel with a strong

superimposition of the timetable.

So IVAX was, at that time, developing cladribine oral formulation in various strengths, formulations and -- and, yes, strengths and formulations and even pharmaceutical form, while we at Serono were developing a clinical trial and development plan.

BY MR. SEGREST:

Q Was --

A There is --

Q I'm sorry. I didn't mean to interrupt.

A There is a superimposition of the two processes, but I do not recall, sitting here today, that there has been -- that there was the intention to use all formulation developed by IVAX, but rather to select one to go into a clinical trial and clinical development.

Q [redacted]

A Yes. I'm with you. [redacted]

[redacted]

Q [redacted]

[redacted]

[redacted]

A It reads what you just said, yes.

Q Right. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: In -- yes, my understanding is that we -- [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

BY MR. SEGREST:

Q Okay. Let's go back to page 4 and the arms again.

MR. SEGREST: Okay. So we're under suggestions for primary phase III study, and the third item on there says "Arms." Can you get us to that?

THE WITNESS: Yes, I'm with you.

BY MR. SEGREST:

Q Okay. Now, the parentheses after 0.7mgs per kilo says, ".35mgs per kilo multiplied by five days multiplied by two months." Right?

A Right.

Q So there are two multiplication symbols in that parenthetical. Right?

A There is mention of times 5 days times 2 month.

Q Okay. And after the 2.1mgs per kilo, there's a parentheses that says, ".35mgs per kilo multiplied by five days multiplied by six months." Right?

A I can read it.
Q And that's correct. Right?
A Yeah, I can read what you said.
Q Okay.
MR. McGUFFIN: Object to form.
BY MR. SEGREST:
Q And, again, there's two multiplication symbols in that second parenthetical. Right?
A This parentheses says, ".35mgs per kilo times 5 days times 6 months."
Q Okay. So looking back at the first parenthetical, though, if you multiple .35 times 5 times 2, that would be 3.5mgs per kilo. Right? Not 0.7mgs per kilo?
A .35 times 10 is 3.5. I think there is a -- a mistake in this, the way it has been written here.
Q Okay. And for the second one, if you multiple .35 times 5 times 6, that would be 10.5mgs per kilo, not 2.1mgs per kilo. Right?
A I think that as in the first parentheses, there have been a mistake in the way

the sign times -- the sign "X" has been used.

Q [redacted]

A This sentence reports the exposure and so the -- the dose as you put it, and not the strengths.

Q [redacted]

A I'm asking you to please repeat your question. There is a bit of background noise here.

THE WITNESS: Can we close the window --

BY MR. SEGREST:

Q Yes. [redacted] Right?

A This line on the paragraph mention the dose, not the strengths.

Q Okay. [redacted]

[redacted]

A This line on the arms report the dose, not the strengths.

Q Right. [redacted]

[redacted]

[redacted]

A Same response. The line on the arms mention the dose, not the strengths.

Q So we've been looking at this language under the heading "Expert Panel and Phase III Design." Was the section before that which begins on page 3 under the heading "Formulation progress and patent issues"?

A So you are on page 3 of the draft minutes?

Q Yes.

A Okay.

Q I just want to make the record clear about what part we're looking at. This is "Formulation progress and patent issues." Right?

A I can read this title bold, yes.

Q Okay. And this is the part that has the

language I was asking you about earlier about the [redacted]
Right? It's on the next -- I'm not sure what's on the screen now. I was on page -- yeah, [redacted]
[redacted] Right?

MR. McGUFFIN: Object to form.

THE WITNESS: On the next page, there are mention of -- [redacted]

Is this what you are referring to?

Q Yes.

A Thank you.

Q And then below that, you see a list of

[redacted]

A Yes.

Q Now, the last [redacted]

[redacted]

A [redacted]

[redacted]

Q Okay. [redacted]

[redacted]

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

[redacted]

That's what it reads.

BY MR. SEGREST:

Q And that language about [redacted]

[redacted] Right?

A Yeah. [redacted]

Q [redacted]

[redacted]

A Sitting here today, I do not know.

Q Let's go back to the cover of the document.

Do you see a blue stamp on this first page that says "Serono International SA Corporate IP Department"?

A I see a stamp with Serono International SA with a date of 09 October 2003, and in small, "Corporate IP Dept".

Q Do you know if there was somebody in the corporate IP department [redacted]

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: Sitting here today, no, I do not know.

MR. McGUFFIN: I'm about to move onto a

new document if y'all want to take another short break now.

THE WITNESS: Yes, please. I would appreciate.

(Whereupon, there was a recess in the proceedings.)

BY MR. SEGREST:

Q So I want to turn now to Exhibit 2049, which we looked at briefly earlier, which is what you called the briefing document, I believe.

MR. McGUFFIN: I don't think we looked at that earlier, Counsel.

Oh, no. We did look at the first page. Sorry.

BY MR. SEGREST:

Q Dr. Munafo, do you have that document?

A I have -- the document that is on screen now, I have in front of me. Just to confirm, the bottom says Merck 2049. Is that correct?

Q That's correct. Thank you.

A Yes. Then I have it in front of me.

Q Now, is this document from

December 2003?

A The date on the front page is 17 of December, 2003.

Q Do you remember this document being from December 2003?

A Sorry. Sitting here today, I do not remember when I saw this document for the first time, but I have seen it, and my memory has been refreshed on it.

Q So in December 2003, clinical studies on pharmacokinetics and bioavailability of the contemplated oral dosage forms were still underway. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: When you -- when you refer to studies on bioavailability and the rest of your sentence, could you please be more specific to which one you are referring to?

BY MR. SEGREST:

Q I'll direct you to page 9 of 59 on this document. And just for clarification, in the top center, you'll see an indication of page 9 of 59.

There may be other page numbers at the bottom, but I'm referring to those page numbers at the top.

And you see the fifth paragraph that starts with the words "Serono partnered with IVAX"?

A I see a paragraph starting like this.

Q And then in the second sentence, do you see where it says that "two clinical studies to study the pharmacokinetics and bioavailability of three tablet and capsule oral formulations of cladribine are currently being conducted in MS patients"?

A I see -- I can read what you just read, yes.

Q Okay. That's what I'm referring to when I ask you: In December of 2003, do you recall that studies on the pharmacokinetics and bioavailability of the contemplated oral dosage forms were still being conducted?

MR. McGUFFIN: Object to form.

THE WITNESS: Sitting here today, that long after, I recall that these studies were

conducted by IVAX. I do not have the precise timetable of these two studies in mind. But the sentence reads that they are currently being conducted, referring to December 2003.

BY MR. SEGREST:

Q And you agree that the -- the oral formulation of cladribine to be used in the proposed phase III study in MS patients would be selected based on the results of those trials?

MR. McGUFFIN: Object to form.

THE WITNESS: These trials were designed to inform on the characteristics of the -- of various formulation and pharmaceutical form that IVAX was developing. And provided that one would meet -- that -- that -- no. Sorry. I strike this.

[redacted]

BY MR. SEGREST:

Q The formulations that were being studied included at least three different tablets in the capsule oral formulation. Right?

A That sentence reads -- refer to three tablet and capsule oral formulations of cladribine.

Q Let's turn to the next page. This is page 10 of 59. And I'm looking at the first full paragraph on that page, the paragraph that starts with [redacted]

A The whole sentence reads: [redacted]

Q Let's turn to page 13 of 59.

Now, Doctor, [redacted]

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: This page on screen, page 13 of 59, is [redacted] the composition of various tablets in a capsule.

BY MR. SEGREST:

Q [redacted] Right?

A [redacted]

Q [redacted] Right?

A [redacted]

[redacted]

Q Right. [redacted]

[redacted]

[redacted] Right?

A [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Q Let's turn to page 17 of 59. I'm looking at the bottom of the page on this one.

[redacted]

[redacted]

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

[redacted]

[redacted]

BY MR. SEGREST:

Q [redacted]

[redacted]

[redacted] Right?

MR. McGUFFIN: Objection; relevance.

THE WITNESS: Last paragraph on page 17 of 59 starts by mentioning [redacted] Yes, it mentions this.

BY MR. SEGREST:

Q And it refers [redacted] Right?

A [redacted]

Q And you read the question mark that's in parentheses. [redacted]

A Can you repeat your question?

Q Yes. [redacted]

[redacted]

A Sitting here today, I do not know. I do not recall why this was included, and I'm not the author of this section at least.

Q [redacted]

A I see that on the screen, not on my print. But I see that on the screen.

Q That's not on your printed version?

A On the printed version, it is only in black-and-white, so there is something in gray, but I cannot tell you whether it is yellow or not.

Q [redacted]

A I -- sitting here today, I can only comment that this was a document sent for review, and the various reviewers are listed on the second page of the cover letter. So it would be an

assumption, but I assume -- and, again, it is a speculation. I insist on that. And I assume that these are -- would mean that this was a point to be reviewed.

Q Let's turn to page 25 of 59.

A I'm with you.

Q [redacted]

[redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

[redacted]

BY MR. SEGREST:

Q Right. [redacted]

[redacted] Right?

A I would not say that this is a description because a description of a study is much more complete and comprehensive that what is mentioned here. This is a mention of other

trials.

Q Okay. [redacted]

[redacted] Right?

MR. McGUFFIN: Object to form.

THE WITNESS: Sentence -- you're speaking fast, so I'm reading the sentence to make sure we are on the same -- on the same page.

[redacted]

BY MR. SEGREST:

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: The first sentence of the next paragraph reads:

[redacted]

BY MR. SEGREST:

Q [redacted] Right?

MR. McGUFFIN: Object to form.

THE WITNESS: This is part of the sentence.

[redacted]

[redacted]

BY MR. SEGREST:

Q [redacted]

[redacted] Right?

MR. McGUFFIN: Object to form; scope, foundation, mischaracterizes testimony.

THE WITNESS: When you say -- you ask about was it the same regimen?

BY MR. SEGREST:

Q Yes.

A I am -- I am not sure the Rice paper refers to both studies. [redacted]

Q Right. And Rice 2000 also was 0.07mgs

per kilo per day. Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: I -- is it possible to quickly go back to the Rice paper --

BY MR. SEGREST:

Q Sure.

A -- to make sure that this is exactly it?

Q This is Exhibit 1008. It's the one that you don't have there. And I think we can go to the abstract again.

THE TECHNICIAN: Which page is that, Counsel? Sorry.

MR. SEGREST: The first page. The abstract.

Q And the fourth line, you see this is also 0.07mgs per kilo per day?

A So here, to be precise, there is reference of 0.07mgs per kilo per day for five consecutive day every four weeks for either two or six cycle, [redacted]

[redacted]

Q Right. [redacted] Rice 2000 also refers to administering this 0.07 milligrams per kilogram per day for five days in each cycle. Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: [redacted] the document of the so-called Rice publication mention 0.07mgs per kilo per day for five consecutive days every four weeks for either two or six cycles followed by placebo.

BY MR. SEGREST:

Q And both Rice 2000 [redacted] Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: [redacted]

[redacted]And Rice arrives to a total dose of 0.7mgs per kgs or 2.1mgs per kilo, respectively.

BY MR. SEGREST:

Q Right. [redacted] Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: The -- in the Rice paper, there is the word "respectively," which is used to demonstrate to -- to clarify that 0.7mgs per kg or 2.1mgs per kg refer to two cycle for the first one and six cycle for the second one. [redacted]

[redacted]

BY MR. SEGREST:

Q Let's turn to page 35 of 59.

[redacted]

A I'm with you.

Q Okay. And there are three groups in that study. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q [redacted]

Right?

MR. McGUFFIN: Objection; form, scope,

foundation.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q [redacted]

A [redacted]

Q Let me repeat the question for you.

A Yes, please.

Q [redacted]

[redacted] Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q Right. [redacted]

[redacted] Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: [redacted]

[redacted] Could you go back to the Rice paper? Because if it is -- they mention four weeks or 28 days. I don't remember.

Four weeks. So in Rice, it is four weeks. [redacted]

MR. McGUFFIN: I just want to note for the record that halfway through that answer, the tech switched to Exhibit 1008. And I want to note for the record now we're looking at 2059. Excuse me, 2049.

BY MR. SEGREST:

Q [redacted]

[redacted] Right?

MR. McGUFFIN: Object to form; scope, foundation, calls for an opinion.

THE WITNESS: The same response to what I just gave on the previous statement.

BY MR. SEGREST:

Q The next page, [redacted] Do you see that?

A [redacted] Yes.

Q [redacted] Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: When you say "also," can you refer -- can you specify to what your "also" refers to please?

BY MR. SEGREST:

Q [redacted]

Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: [redacted] Sorry. Forget about. [redacted]

BY MR. SEGREST:

Q Let's turn to page 47 of 59.

Now, is this where the draft begins to address the phase III clinical trials that Serono was considering?

MR. McGUFFIN: Object to form.

THE WITNESS: The draft document that we have in front of us here does have a Table 5.1-1 that is labeled -- named Synopsis of the Proposed

Phase III Design [sic].
BY MR. SEGREST:
Q And the last row on the page for that Table 5.1-1, do you see that row has the title of "Study Design"?
A Yes, I see that.
Q Okay. And does it indicate that the treatment groups have two doses, high and low, approximating cumulative doses of 2.1mgs per kilo and 0.7mgs per kilo?
A I can read this -- this sentence for the treatment groups.
Q And that's the same cumulative dose that we saw in those other studies we looked at, MS-001, Scripps-B, and Rice 2000. Right?
A Numerically, the numbers of 0.7mgs per kg and 2.1mgs per kg as we saw in the previous page on the screen. So just numerically, yes, now I read that this is high and low approximating cumulative doses of 2.1 and --
MR. McGUFFIN: And I want to note objection --

THE WITNESS: -- 0.7.

MR. McGUFFIN: Sorry. I didn't mean to cut you off. I just was noting objections to form, scope, foundation.

BY MR. SEGREST:

Q And this entry in the table continues on the next page, page 48 of 59. Do you see the heading "Duration of treatment"?

A I read that.

Q And does this indicate for the duration of treatment that there are three phases?

MR. McGUFFIN: Object to form.

THE WITNESS: Definition of "phase" being vague, I will just read what is written here.

Duration of treatment, first phase, dash, six cycles, in parentheses, high/low/placebo, period. Second phase, slash, re-treatment, dash, six cycles, parentheses, low/low/placebo, period. Third phase, slash, re-treatment, dash, six cycles, low/low/low.

BY MR. SEGREST:

Q So that lists three phases. Right?

A Yes. I just said definition of "phase" is vague. But three -- there are three phases as described here that are mentioned in this duration of treatment.

Q And it also describes three arms in each of those three phases. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: The cycles are mentioned as being six cycle, and a parentheses high/low/placebo for the first phase. Low/low/placebo for the second phase. And low/low/low for the third phase.

BY MR. SEGREST:

Q So all three phases say that it's six cycles. Right? That's the same for all three phases?

MR. McGUFFIN: Object to form.

THE WITNESS: Six cycles are mentioned for each phase with a definition of a cycle being five-day course of treatment during a 28-day

period.
BY MR. SEGREST:
Q Okay. And in the first phase, the six cycles have a high arm, a low arm, and a placebo arm. Right?
MR. McGUFFIN: Object to form.
THE WITNESS: This is what it -- it reads.
BY MR. SEGREST:
Q And then in the second phase, the first arm changes from high to low, the second arm is still low, and the third arm is still placebo. Right?
MR. McGUFFIN: Object to form.
THE WITNESS: This is what it -- it reads. But I would like to comment here and put in context that when we have six cycle mentioned here, and I take the example of first phase, my recollection is that this was six cycles of active drug for the high, it was two cycles of active drug and four cycles of placebo for the low, and six cycle of placebo for the placebo.

BY MR. SEGREST:

Q It doesn't say that here, does it?

A It may not say it here, but it is my recollection.

Q And then for the third arm, the third phase --

A Sorry. Sorry. Sorry. I was not finished. I was not finished.

It doesn't say here, but this is my recollection. And on page 49 on the blinding, it says -- so "assignment to treatment groups" row, "blinding" in the parentheses, it does say that low-dose patient receive placebo to fill out a high-dose cycle.

So it may not be said on page 48 under duration of treatment, but this is clearly designed -- clearly described on page 49 on the blinding.

Q Okay. Now --

A And it is --

Q You need to answer my questions instead of volunteering other information. We're going to

get to that --

MR. McGUFFIN: Mr. Segrest, he was --

BY MR. SEGREST:

Q -- discussion of blinding.

A No. I was finishing my answer.

MR. McGUFFIN: Mr. Segrest, he was answering your question. You interrupted him.

MR. SEGREST: With respect, Asher, he was not. He had answered my question and then said, "I want to make an additional comment," which is not appropriate on cross-examination.

MR. McGUFFIN: Mr. Segrest, just because he paused and you may or may not have liked what he said does not mean he was done answering. I think the record is extremely clear that he wanted to add context and felt it was important to understand his answer, and I don't appreciate you trying to cut my witness off.

MR. SEGREST: I don't appreciate --

MR. McGUFFIN: And I would ask --

MR. SEGREST: -- your witness trying to say I want to add an additional comment that's not

responsive to the question. We can move on. We are going to talk about all of that.

MR. McGUFFIN: Excuse me. That was clearly responsive. And it is the witness's right to give as clear an answer as he wants to. I don't appreciate you interrupting him when he paused. And if you want to ask another question now, you're free to do so.

BY MR. SEGREST:

Q So this description "duration of treatment," it doesn't say anything here about using placebos during the low cycle. Right?

MR. McGUFFIN: Objection.

THE WITNESS: The section on duration of treatment is part of a synopsis that is almost four pages long and has to be seen in the entirety. And I'm not willing to extract a single word when, in fact, it is described elsewhere in complement to -- and it has to be seen in its totality.

BY MR. SEGREST:

Q So, again, my question is there's

nothing in this duration of treatment portion that we're looking at that talks about administering a placebo during the low-dose cycle, is there?

MR. McGUFFIN: Objection; asked and answered.

THE WITNESS: There is nothing in that row, but it is clearly mentioned in another row of the same table on the synopsis of the proposed phase III study.

BY MR. SEGREST:

Q Let's turn to page 49 of 59.

Do you see the row labeled "Study Treatment"?

A Yes, I'm with you.

Q And do you see the line that says "strength"?

A Yes, I'm with you.

Q And it gives three different strengths, right? 0, 3 and 10 milligrams. Right?

A At the time of this draft for proposed phase III study, the various strengths or the strengths to be used had not been defined yet, and

there are indeed on this line reporting strengths the possibility of 0 and 10-milligram of active treatment dose -- strength. Sorry.

Q It doesn't say 0, 3, or 10 milligrams. It says 0, 3, and 10 milligrams, doesn't it?

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q Do you think that you didn't know if you were going to use a 0 or a 3 or a 10? Is that your testimony today?

MR. McGUFFIN: Object to form.

THE WITNESS: So 0 is placebo. Whether we were going to use 3 and/or 10-milligram, to the best of my recollection at the time of that and

sitting here today, I do not recall that the decision had been taken.

BY MR. SEGREST:

Q [redacted] Right?

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q [redacted] the next line says it's going to have a 0-milligram, a 3-milligram, and a 10-milligram strength, doesn't it?

MR. McGUFFIN: Object to form; mischaracterizes document.

THE WITNESS: The 0-milligram is referring to the placebo, and then the 3 and the

10 milligrams are two strengths that IVAX was investigating at that time and of which decision had not been taken which one to pursue for clinical development and clinical trial.

BY MR. SEGREST:

Q But this lists two different strengths that are going to be used in addition to the placebo in a clinical trial which corresponds to a high and low-dose in the two arms, doesn't it?

MR. McGUFFIN: Object to form; mischaracterizes testimony and document.

And I think this has been asked and answered, Philip.

MR. SEGREST: I don't think this one has.

THE WITNESS: According to my reading of this -- of this, and, again, I'm -- I have attempted through this discussion to differentiate dose and strength, which in my understanding of your question, you put together.

So can you perhaps repeat your question?

BY MR. SEGREST:

Q 0 milligrams is the placebo. Right?

A I understand it this way.

Q And 3 milligrams would be a lower dosage strength than 10 milligrams. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: The strength is 3-milligram for the 3-milligram, 10-milligram for the 10-milligram. That arithmetically 3 is less than 10, I agree.

BY MR. SEGREST:

Q And 3 milligrams administered in five days for six cycles would be a lower cumulative dose than 10 milligrams administered in five days for six cycles. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: My understanding and recollection of the design we proposed there was that as described in the "duration of treatment" as well as in the "blinding" section, the low-dose and the high-dose were differentiated by the number of cycle, not by the strengths of the

medication.
BY MR. SEGREST:
Q And that does not answer my question.
My question was, 3 milligrams dosage strength administered in five days for six cycles would be a lower cumulative dose than 10 milligrams dosage strength administered in five days for six cycles. Right?
MR. McGUFFIN: Object to form; scope, relevance.
You're right he didn't answer your question. But I think your question seems irrelevant in view of his answer.
MR. SEGREST: Well, objection's noted, but let's not make longer speaking objections.
Q You can answer my question now.
A Arithmetically, you want to make a calculation, and your calculation is correct in terms of, again, arithmetic. But not in terms of the definition that we had for low and high dose in that synopsis.
Q So the -- where are -- are you -- back

up.

There's nothing supporting your definition of low and high dose in the portion of the synopsis labeled "Study Design." Right?

MR. McGUFFIN: Object to form; asked and answered.

THE WITNESS: I need you to please repeat your question. You were speaking a little bit --

BY MR. SEGREST:

Q Yeah. There's --

A -- fast.

Q -- nothing supporting your definition of low and high dose in the portion of the synopsis that is the study design, is there?

MR. McGUFFIN: Object to form; asked and answered.

THE WITNESS: I have addressed my position on that earlier, that synopsis has to look -- to be looked in its totality. This is four pages here, and even if it is not mentioned in the row on "Study Design," it is mentioned in

the row on assignment to treatment group under blinding.

BY MR. SEGREST:

Q Well, let's look at that row, "assignment to treatment group." The first line there is assignment of subject ID numbers. Right?

A First line is assignment of subject ID numbers, central randomization.

Q And central randomization, assignment of subject ID numbers has nothing to do with the treatment regimen. Right?

MR. McGUFFIN: Object to form; scope, relevance.

THE WITNESS: I cannot agree to this statement. Randomization to a ID number links directly to -- to the treatment groups. So I cannot agree with what you were saying.

BY MR. SEGREST:

Q But it doesn't affect the definition of the treatment regimens for each arm, does it?

MR. McGUFFIN: Object to form.

THE WITNESS: Randomization is a

procedure of assignment of the study ID number and does not have -- and refers to the patient group in this sense. The treatment group.

As you will see from the second bullet that randomization should ensure equal distribution to all treatment groups.

BY MR. SEGREST:

Q And isn't blinding how the study prevents the subjects from knowing to which treatment group they are assigned?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: Blinding is an element of relevance to ensure that neither the patient know the treating physician, as in this case it is double blinding, would know which treatment the patient was assigned to.

BY MR. SEGREST:

Q And the blinding process as described of filling out high-dose cycles is in part how blinding was achieved in studies like Rice 2000. Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: This synopsis, the design of the clinical trial, the dosing regimen, was a comprehensive process encompassing knowledge and expertise from within the company from information that was obtained either publicly or confidentially of knowledge about the disease, knowledge about the clinical trial in multiple sclerosis, about its feasibility, about potential recruitments, about -- knowledge about the pharmacokinetics, the pharmacodynamics, the course of the disease, relationship between endpoints.

And the list is not exhaustive, but it does include information that was gathered, as I said, either from publication or confidentially. And to this sense, the -- the dose -- dosing regimen that you mention and keep referring to in the Rice paper were part of this -- I would not accept to say the word "relying on," but part of the elements that we considered in designing the dosing -- the study in its totality is reflected

into the four pages that you have here on the synopsis of the phase III design -- on the proposed phase III design.

BY MR. SEGREST:

Q The Rice 2000 study indicated that each arm included eight cycles. Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: What you call the Rice paper 2000 mention indeed doses, total doses, and principle of cycles. And it -- as I said, this was part of the elements, among many others, that we have used in designing this trial and the dosing regimen.

BY MR. SEGREST:

Q And in Rice 2000, and in Scripps-B, and in MS-001, all of those, it said that it achieved the 2.1 milligrams per kilo total dose by administering the dose for six cycles of the active dose. Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: It says that the dose -- the total dose was achieved by giving cladribine parenterally for the duration and repetition of cycles. This is true. Yet as I said, this is only one of the elements, given that confidential and publicly available information were all looked together to develop our proposal.

BY MR. SEGREST:

Q And in Rice 2000 and in Scripps-B, it expressly says that the lower cumulative dose comes from two cycles of administering the active ingredient. Right?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: I would have to go back to the exact text of Rice and Scripps study. But the principle of achieving the total dose by administering the dose for a certain duration repeated 28 days or one month later, depending where it comes from, is what could be read in the reference you mentioned.

BY MR. SEGREST:

Q And --

A But -- but this is not the only element that we took into consideration when designing this dosing regimen for our proposed development and clinical study.

Q And neither Rice 2000 nor Scripps-B, nor MS-001 included three different strengths for their dosage, did they?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: Sitting here today, I do not recall the detail of the strengths that were used in Rice, Scripps studies, given the formulation that they had used.

BY MR. SEGREST:

Q Okay. In this four-page synopsis, Table 5.1-1, there is nowhere that says the low dosage arm is two months of active ingredient, is there?

MR. McGUFFIN: Object to form; asked and answered.

THE WITNESS: I disagree. In page 49 of 59, "assignment to treatment group, blinding, parentheses, low-dose patient received placebo to fill out high-dose cycle."

So it is clearly said.

BY MR. SEGREST:

Q Where does it say "two months" in what you just read to me?

MR. McGUFFIN: Object to form.

BY MR. SEGREST:

Q I mean, we can have the tech give you control of the screen if you want to highlight where it says "two months."

A It is my reading and understanding and recollection that when we say -- we said in this synopsis, which, again, has to be seen in its totality, that we define six cycle high/low/placebo, second phase of six cycle, low/low/placebo. And then we say in the blinding that low-dose patients receive placebo to fill out high-dose cycles.

And then it says in the treatment

regimen, three phases -- next row, three phases, five-day consecutive dosing within 28-day cycles for six-cycle phase. That this is indeed exactly what we had proposed and -- and designed thereafter in -- in -- in our development plan and clinical study.

So, again, I have to look into this in its totality and not just one line by one line to say that I confirm that this is what we had proposed and shared with -- within the company at meetings where IVAX representatives were present.

Q Okay. Looking at the synopsis as a whole -- I don't think you answered my question -- where does this synopsis say that a low dose is two months administering the active ingredient? Point me to the words "two months."

MR. McGUFFIN: Objection; form, asked and answered.

MR. SEGREST: It's been asked. It hasn't been answered.

THE WITNESS: I don't see how I can answer your question better than what I just did,

so I will -- I will not repeat my -- my exact answer. But I repeat the principle of it.

It is my recollection that in the synopsis that we have in front of us that was shared with IVAX that we planned to send to the health authority, we have here it's written, but it has been discussed orally at meetings, the principle of this is that low treatment were to receive two cycles followed by -- of treatment of active medication followed by four cycles of placebo, while the high-dose patient were to receive six cycle of active treatment and the placebo were to receive six cycles of placebo.

This is what we have described by the five-day consecutive dosing within 28-day cycles for six cycles, what we have described in saying that the low-dose patient receive placebo to fill out high-dose cycles, and when we describe the -- the six-cycle phase in the duration of treatment that I have read already several times.

BY MR. SEGREST:

Q Right. And none of that that you have

read includes the words "two months," does it?

MR. McGUFFIN: Objection; form, asked and answered.

THE WITNESS: I think, with all due respect, that I have already answered this question twice.

BY MR. SEGREST:

Q Well, the words "two months" do not appear in this synopsis, do they?

MR. McGUFFIN: Object to form.

Mr. Segrest, I think the document speaks for itself. I think the --

MR. SEGREST: Don't make a speaking objection.

THE WITNESS: Although the words "two months" may not appear in the synopsis as written in this briefing document, it has been shown to the project team and to the Joint Development Committee and that the principle by which we wanted to differentiate the low-dose and the high-dose was that the low-dose were to get two successive months of treatment followed by four

months of placebo, while the high-dose were to receive six cycles of active treatment.

BY MR. SEGREST:

Q Now, two months of active treatment followed by four months of placebo is the same as those other studies we've looked at. Right? Rice 2000, Scripps-B?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: The word "same" is -- if the word "same" is referring to the arithmetic, I -- I would not object. But the regimen that we have designed here included much more than just consideration of the Rice paper.

BY MR. SEGREST:

Q Sure. I mean, there's more to it. But two months of active ingredient and four months of placebo is not a part that you invented. Right? That was something that was already disclosed in Rice, in Scripps, and in other references?

MR. McGUFFIN: Objection; form, scope, foundation, calls for an opinion and a legal

conclusion.

THE WITNESS: The invention on the dosing regimen is -- is described in the -- in our patents, and includes all the aspects that -- that are mentioned there, including the dose, the duration, the frequency, and the repetition of -- on the second year. All of this is part of the invention altogether, and I cannot comment on Rice elements, but only on the totality.

This was a process that required a lot of experience, expertise, integration of knowledge from -- from our understanding of the course of the disease, our understanding of the patient suffering from MS, our understanding of the pharmacokinetic, of the pharmacodynamic, of the intermediate endpoints, and ultimately, of the clinical endpoints as well and integrating information that we got both from publicly-available sources like the publication you keep mentioning, but also from confidential information that we received. And all of this contributed to the invention, and not a factor in

isolation.
BY MR. SEGREST:
Q Looking at your declaration in Exhibit 2053. Do paragraphs 39 through 49 of your declaration concern this Exhibit 2049 that we've been looking at?
MR. McGUFFIN: Object to form.
THE WITNESS: So I'm with you on my declaration, page 17, with the header starting B, December 2003 Briefing Document.
BY MR. SEGREST:
Q Do any of these paragraphs, 39 through 49, discuss the 3-milligram dosage strength that's described in the briefing document, Exhibit 2049?
A Sorry. I think I misunderstood -- misunderstand what you just said. Are you talking that it refers to the 3-milligram?
Q Yes. Is there any testimony in paragraphs 39 through 49 about the 3-milligram dosage strength that's recited in the briefing document, Exhibit 2049?
MR. McGUFFIN: Object to form.

THE WITNESS: I -- I can -- I can read again these numerous pages that you referred to. But I am requiring you to confirm that you strictly want me to comment on referring to 3-milligram strengths?

BY MR. SEGREST:

Q Yes. I don't know of anything in this section that refers to the 3-milligram strengths, do you?

MR. McGUFFIN: Object to form.

THE WITNESS: So in my declaration, paragraph 39 to 49, I do not mention the 3-milligram strengths.

MR. SEGREST: Okay. We can take another short break if y'all want to.

MR. McGUFFIN: That works well for us. Five minutes?

MR. SEGREST: Sure.

(Whereupon, there was a recess in the proceedings.)

BY MR. SEGREST:

Q Dr. Munafo, let's look back at your

declaration again. That's Exhibit 2053.

And does paragraph 6 of your declaration refer to the Bodor PCT application?

A Yes.

Q And is the Bodor PCT application WO 2004/087101?

A When I -- I'm referring to the Bodor application, it has indeed 2004/0871002A2 as an application number.

Q You said 1002 with A2 as the number. I believe it does say WO 2004/87101 for the Bodor PCT?

A Yes. And then it has a label A2 which I -- this is why I said A2 at the end.

But yes, it is '101.

Q And looking at paragraph 7, does this paragraph quote some language from Bodor that appears in both another disclosure document and you say the Bodor PCT contains the same language?

MR. McGUFFIN: Object to form.

THE WITNESS: Can you please repeat your question? I've lost --

BY MR. SEGREST:

Q Yeah. Sorry. You see the block quote in paragraph 7 of your declaration?

A Yes.

Q And in the sentence after that, you say the Bodor PCT contains that same language that's in your block quote?

MR. McGUFFIN: Object to form.

THE WITNESS: I am in the paragraph 7 says Bodor 328 includes the following disclosure of a regimen for treating multiple sclerosis using cladribine.

Is that what you're referring to?

BY MR. SEGREST:

Q No, sir. I was asking about actually the Bodor PCT which you mention in the sentence after the block quote.

Doesn't that sentence after the block quote say "the Bodor PCT contains the same language"?

A Can you point this on the screen? It will help me, because I'm not with you.

Q So the -- after the --
A After that.
Q -- block quote, do you see the sentence, "The Bodor PCT contains the same language"?
A Yes, I see that sentence.
Q Okay. And in the Bodor PCT, it cites page 23, lines 15 through 20. Right?
A This is what it reads here, so I would have to go back to the -- to the initial document.
Q Okay. Let's go to Exhibit 1001, the '947 patent.
I'll direct you to Column 6, Line 24. In Column 6, Line 24, do you see the citation to WO 2004/87101?
A I'm sorry. I'm not used to this numbering. So I need to go very slowly. And if you want to highlight something very specific, you need to let me know. Because as I said I'm -- first, you start to speak a bit fast again, and then I'm not used to this numbering. So.
Q Yes, sir. So I'm on Column 6.
A Yes.

Q Are you at Column 6?

And the line numbers are down the middle of the page there. So I'm looking at Line 24 of Column 6.

A Yes.

Q And do you see the citation to WO 0 -- I'm sorry -- WO 2004/087101?

A I do.

Q And that is the Bodor PCT application from paragraphs 6 and 7 of your declaration. Right?

A Yes, it is.

Q So you and your co-inventors were aware of the Bodor PCT application when you filed this application. Right?

A Sorry. You went fast at the beginning of your sentence. I'm sorry. I'm --

Q I'll try to speak more clearly.

A Thank you.

Q You and your co-inventors were aware of the Bodor PCT application when you filed the application for this patent. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: I -- sitting here today, I cannot speak for my co-inventors. [redacted]

BY MR. SEGREST:

Q But you cited to it here in your patent application. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: This -- I'm sorry to -- just I have to inform you that we have a technician entering into the room, so I hold my response by just a few seconds.

Okay. Technician is -- is away now.

So I can see that in our patent application, the so-called Bodor patent is mentioned, but I did not write every single paragraph of our patent. And I particularly did not write this section here.

BY MR. SEGREST:

Q I'm going to direct you to Column 12,

Line 9.

Sorry. And at Column 12, Line 9 of Exhibit 101 --

A Yes.

Q Or 1001, the '947 patent. Here again you cite the Bodor patent. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: In Line 9 of Column 12 of our -- of the '947, I can indeed see the number of WO 2004/087101.

BY MR. SEGREST:

Q And in Column 14, Line 44, you again cite to the Bodor PCT application. Right?

A On Line 44 on --

Q Column 14?

A Column 14?

Q Column 14. Yes, sir.

A Sorry? What did you say?

Q Column 14, Line 44, you again cite to the Bodor PCT application. Right?

A This is what I was about to reply. On Line 44 of Column 14 of the '947, indeed we

mention again the Bodor application.

MR. McGUFFIN: And just object to form.

BY MR. SEGREST:

Q And in that same -- and in that same column down at Line 62, this is in a little bit smaller script, it's right below Table 2. But you again cite to the Bodor PCT application. Right?

A When you say "you," do you mean me personally or do you mean it is cited in this application? Because I did not write that part.

MR. McGUFFIN: Object to form.

BY MR. SEGREST:

Q I mean you and your co-inventors. You read the application that was filed. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q But somebody who wrote this patent clearly had seen it. Right?

MR. McGUFFIN: Object to form.
BY MR. SEGREST:
Q Because they cite to it?
A I cannot speak for the other author. [redacted]
[redacted]
Q And you understand that as one of the inventors, you're responsible for reading your specification and you submit an oath that refers to that. Right?
A I'm sorry. You speak --
MR. McGUFFIN: Object to form.
THE WITNESS: -- too fast again.
BY MR. SEGREST:
Q Sure. You understand that as one of the named inventors, you're responsible for the specification of your patent, and you submit an oath including a statement that you're -- you've read it?
MR. McGUFFIN: Object to form.
THE WITNESS: I understand that this patent has been written by colleagues and co-inventors at Serono. I cannot comment, sitting

here today, on who wrote which section and who reviewed what application. I can only comment that I did not by that time.

BY MR. SEGREST:

Q Let's open up Exhibit 1003.

(MUNAFO Exhibit 1003 was marked for identification.)

MR. McGUFFIN: Object to scope. I don't believe Exhibit 1003 is cited in Dr. Munafo's declaration.

BY MR. SEGREST:

Q Dr. Munafo, do you see on the cover that this document is a file wrapper and contents of application for Patent Number 7,713,947?

A I -- I'm not familiar with this kind of document, not at all. So I am seeing an application number, patent number, issue date.

So what is your question?

Q Well, that patent number on the cover is for the '947 patent. Right? It's for the patent that's Exhibit 1001?

A The patent number that is here on the

front page corresponds to the -- our U.S. Patent '947, yes.

Q Okay. And let's turn to page 16 of 822 in the document.

MR. McGUFFIN: Object to scope.

BY MR. SEGREST:

Q And Dr. Munafo, do you see that on this information disclosure statement by applicant, citation F1, down under the foreign patent documents, is the Bodor PCT application. Right?

A I'm --

MR. McGUFFIN: Object to scope.

THE WITNESS: Not with you. Information disclosure and statement by applicant. I see a write up which says "complete if known." Then there is another box which is U.S. Patent documents, which is essentially empty. And foreign patent document? This is what you refer to?

BY MR. SEGREST:

Q Yes, sir.

A So yes, I see -- I see that there is

reference to the '101 patent.

Q Let's go to page 385 out of 822.

MR. McGUFFIN: Object to scope.

THE WITNESS: I'm sorry. I need clarification. What -- what is the document that we look at? Because I only saw the -- the first page and I don't know what it is in here, and I have seen pages out of -- out of the blue. I don't know what -- what is this document. Can you clarify for me please?

BY MR. SEGREST:

Q So let's go back to the cover page. So you see that sentence there:

"This is to certify that annexed is a true copy from the records of this office of the file wrapper and contents of," and then it gives the application number, filing date, patent number, and issue date?

A I can see this, but, as I said, I'm not at all familiar with -- with this kind of document.

Q Yes, sir.

A So this is -- I saw that there are several hundred pages long. That is correct?

Q That's correct. So what this document is is a certified copy from the Patent Office of the whole history of the correspondence between the applicants, including you, your legal representative, and the Patent Office, that led to the issue in this patent.

And, like I said, there's hundreds of pages, there's lots of stuff in it. I've just got a few parts that I'm going to ask you about.

A Thank you for the clarification.

Q So I think I directed us to page 385 of 822.

Now, have you seen this kind of document before?

A You mean about this -- this -- this --

Q This page.

A -- this very long document here --

Q I mean this page.

A -- or this page? This page?

Q This kind of correspondence from the

Patent Office?

MR. McGUFFIN: Object to scope and form.

THE WITNESS: To the best of my recollection, if I have seen it, I don't remember it. This is very unfamiliar to me.

BY MR. SEGREST:

Q Okay. Let's flip over to page 388 out of 822. This is authored by the examiner. Do you see that item 6 there cites to the Bodor PCT application?

MR. McGUFFIN: Object to form; scope.

THE WITNESS: This is a page I have no idea where it comes from. You are -- and I don't know what it refers. This is a communication of Serono with the Patent Office? Or vice versa?

BY MR. SEGREST:

Q This is a communication -- this particular document is a communication from the Patent Office to Serono or to your legal representative that was handling this patent.

And my question is you see that on this page, right there, item 6, it cites to the Bodor

PCT application?

MR. McGUFFIN: Object to scope, form.

THE WITNESS: I can -- yeah, I can see reference to Bodor application in this paragraph starting number 6.

BY MR. SEGREST:

Q Okay. And on the next page, there's a sentence that starts "alternatively." No, sorry. The -- the third line, it says "in particular."

And it -- there's a sentence there after the words "in particular" that the examiner writes down something that he says "Bodor teaches." Right?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: I'm seeing on the screen a four-line sentence starting by in particular, Bodor teaches, et cetera, all the way to followed by 10 months of no treatment.

That's the sentence you want to refer to?

Q Uh-huh.

A So I can see it.
Q And then further down on that page --
A Sorry?
Q Further down on that page, the ninth line, you see cites to page 23, lines 7 through 24?
MR. McGUFFIN: Objection; scope.
THE WITNESS: You need to point me to where you're looking at. Because I'm lost.
Q Sure. Can you see the parentheses?
A And it's very small on my screen. Sorry.
Q Sorry. I'm trying to direct you to what I'm looking at.
Do you see the parentheses on -- I think it's the ninth line.
A Okay.
Q And --
A There's a parentheses saying "see page 23, lines 7 through 24."
Q Right.
A Okay.

Q So you see it's citing to the Bodor PCT application page 23, lines 7 through 24. Right?

MR. McGUFFIN: Objection; form, scope, foundation.

THE WITNESS: I see a whole sentence saying that, "Alternatively, the patient may be treated with 10 milligrams of cladribine in the dosage form once per day for a period of five to seven days per month for a total of six months, followed by eighteen months of no treatment, see page 23, lines 7 through 24."

BY MR. SEGREST:

Q And that citation, page 23, lines 7 through 24 of the Bodor PCT, includes the same passage that you quote from in paragraph 7 of your declaration. Right?

MR. McGUFFIN: Objection; form, scope.

THE WITNESS: This is referring to the -- to the '101 patent, so let me just check on page 23.

BY MR. SEGREST:

Q No, sir. The page 23, lines 7 through

24 is referring to the -- the Bodor PCT application, not the '947 patent. So I don't want you to be confused there. You're not going to find --

A Oh, the '101?

Q You're not going to find this in -- yes, the '101, which is, I think is Exhibit 1007.

But what I'm asking you really is this citation, page 23, lines 7 through 24. Doesn't that cover the same citation you have in paragraph 7 of your declaration for the language you quote from the Bodor PCT application?

MR. McGUFFIN: Object to form.

BY MR. SEGREST:

Q Which was page 23, lines 15 through 20?

MR. McGUFFIN: Object to form; scope.

THE WITNESS: I'm a bit lost with all this references. So.

BY MR. SEGREST:

Q Let me see if I can simplify it some. Have you got your declaration there?

A Yes.

Q The paper copy of it?
A Yes.
Q And if you can go to the sentence after paragraph 7, the one I pointed you to, the one that says "the Bodor PCT contains the same language"?
A On page 7, you said?
Q It's paragraph 7, it's on page 3.
A Ah, sorry. Sorry.
Bodor PCT contains the same language. Just before paragraph 8, right?
Q Right.
A Okay.
Q And you see it cites to page 23, lines 15 through 20?
A Yeah.
Q So that citation is included within this citation to page 23, lines 7 through 24 in Exhibit 1003 on page 389 of 822. Right?
MR. McGUFFIN: Object to form; scope.
THE WITNESS: So just to make sure, this reference on screen, page 23, lines 7 to 24, is

the -- the -- is the -- the Bodor PCT is the same as the Exhibit 1007 that we have in -- in my declaration?

BY MR. SEGREST:

Q Yes, and that's why I was asking you about the citations to -- do you want to go back to the previous page where it says WO 2004/087101?

A Okay. So you are asking whether the number 15 to 20 are included in the range 7 to 24?

Q Yes, sir.

A Arithmetically, yes.

MR. McGUFFIN: Object to scope.

BY MR. SEGREST:

Q Let's go to page 405 out of 822.

Doctor, have you seen examples of responses to office actions that gets filed in the U.S. Patent Office like this one?

MR. McGUFFIN: Objection to form, scope.

THE WITNESS: You speak -- you speak too fast and not directly --

BY MR. SEGREST:

Q I apologize.

Doctor, have you ever seen before examples of responses to office actions like this one that get filed in the U.S. Patent Office?

MR. McGUFFIN: Object to form; scope.

THE WITNESS: Again, this is one page, and I don't know if it is the first page or something else in this 822 pages. But I am not familiar with this kind of document.

BY MR. SEGREST:

Q Let's go to page 415 of 822.

And in the -- not the quote at the top of the page, but the paragraph that starts "with regard."

A What --

Q Last two lines of it.

A Yeah, I can see that paragraph, but I have no idea where we stand in context of this paragraph, so you need -- this is page 11 of a document that I -- I don't know what it is about.

Q Okay.

MR. McGUFFIN: And object to scope.

BY MR. SEGREST:

Q Okay. But you see that it says that:

"Bodor fails to teach a cladribine-free period of between 8 and 10 months followed by a, quote, maintenance period, close quote, during which a cladribine formulation is administered such that the total dose administered in the, quote, maintenance period, close quote, is lower than the total dose first administered to the patient which is then followed by another cladribine-free period."

Do you see that?

MR. McGUFFIN: Object to form; scope, foundation.

THE WITNESS: I -- I mean, I -- I can read what you just read.

BY MR. SEGREST:

Q Okay. As far as you know, during the prosecution that issued as the '947 patent, neither you nor any of the other applicants ever argued to the Patent Office that you were the source of this disclosure in Bodor. Right?

MR. McGUFFIN: Object to form; scope, foundation, relevance.

THE WITNESS: I -- sitting here today, I can only speak for myself, not for anyone else. And for my -- and myself, I have not been involved in any discussion, argumentation with -- with the Patent Office.

BY MR. SEGREST:

Q Okay.

We can close that and go back to document 2053, your declaration.

I'm looking at paragraph 3 on page 1. So, Doctor, are you being paid for your time on this case at a rate of 450 Swiss francs per hour?

A If your question is whether I'm compensated for the time in preparing this declaration and being here today at 450 Swiss francs per hour, my response is yes, this is correct.

Q And how much have you been paid in that compensation?

MR. McGUFFIN: Object to form.

THE WITNESS: As you asked the question earlier today, I have been deposing on several instances. And I have not kept records of the time spent on any of -- of this. And in particular, not on that one.

BY MR. SEGREST:

Q Do you know the total amount you've been paid?

A No --

MR. McGUFFIN: Object to form.

THE WITNESS: -- I have not -- I have not kept such records.

BY MR. SEGREST:

Q Were you being paid at the same rate on those other two proceedings as you are here? 450 Swiss francs per hour?

MR. McGUFFIN: Object to form.

THE WITNESS: Yes, I have.

BY MR. SEGREST:

Q How many hours did you spend preparing your declaration in this case?

MR. McGUFFIN: Object to form.

THE WITNESS: The process of writing this declaration spread over a certain duration, time duration. And I have not kept records on the specificities of neither the amount nor the time spent on this specific declaration.

BY MR. SEGREST:

Q Did you submit an invoice that indicated how many hours you had spent in preparing your declaration in order to be paid?

MR. McGUFFIN: Object to form.

THE WITNESS: I have submitted invoices, yes. But sitting here today, I am not able to describe on which topic I have invoiced in any detail.

BY MR. SEGREST:

Q Okay. But it would be true that you have made records of it, but you don't remember today what the amounts are. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: I made invoices stating the duration of my time spent on the case altogether, not necessarily separated by one IPR

or the other.

BY MR. SEGREST:

Q Look at paragraph 32 of your declaration.

And that first sentence, do you see the testimony that your team at Serono and the team at IVAX exchanged numerous emails and documents?

A I can read that the sentence says, "In addition to formal meetings of the Joint Development Committee, my team at Serono and the team at IVAX exchanged numerous emails and documents." Yes.

Q Have you retained copies of any of those emails and documents that were exchanged?

A No, I have not.

Q Okay. Other than Exhibits 2048, 49, and 50, did you look at any such emails and documents that were exchanged in the process of preparing your declaration?

MR. McGUFFIN: Object to privilege.

I'm going to instruct you not to discuss the contents of any communications with counsel.

To the extent you looked at any documents not with counsel, you can answer.

THE WITNESS: Can you then repeat your question?

BY MR. SEGREST:

Q Other than Exhibits 2048, 49, and 50, did you look at any such emails and documents that were exchanged in the process of preparing your declaration?

MR. McGUFFIN: Object; privileged.

I'm going to instruct you not to discuss the contents of any communications with counsel. To the extent you looked at any documents separately from counsel, you can answer.

THE WITNESS: I have not reviewed any document outside of discussion with my counsel -- with my counsels.

BY MR. SEGREST:

Q Let's look at paragraph 53.

Do you see it says that communications from your team at Serono included but were not limited to these two documented communications,

referring to Exhibit 2049 and 2050?

A I can read paragraph 53, yes.

Q Okay. Now, you haven't cited to or otherwise provided any copies of those other communications. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: I did not get the first word of your sentence. Excuse me.

BY MR. SEGREST:

Q Sorry.

You say these other communications are there, but you don't discuss those in your declaration, do you?

MR. McGUFFIN: Object to form.

THE WITNESS: I'm sorry. I must get tired. I'm going to have to request to repeat again your question. I'm sorry.

BY MR. SEGREST:

Q Sure.

This part of your testimony refers to other communications other than Exhibits 2049 and 2050, but you don't cite to those other

communications anywhere in your declaration, do you?

MR. McGUFFIN: Object to form.

THE WITNESS: The communication with -- within Serono and with IVAX was inquest to be open and free. This was -- we were instructed that this was a co-development between Serono and -- and IVAX. So the flow of information and -- that we exchanged with -- with -- with the other party was not restricted.

And sitting here today, I can't list all of them. What I remember is that we had free exchange and presented our design, for example, freely to -- to meetings where IVAX representatives were present either in person or remotely that we shared as you have seen in the -- we shared the briefing document with them. We had an open mindset in terms of collaboration and co-development.

But to be specific to your question, I cannot recall, sitting here today, of a specific slide deck or something like that. I can recall

me going, for example, to IVAX in January 2004 to discuss face-to-face on the same table with Dan Weiner there to review some -- some data.

I can recall also of some other meetings like we had in IVAX manufacturing. I think it was in Ireland. I can recall of various instances where we -- we shared information and opinions and ideas, but I don't have a track record of this.

BY MR. SEGREST:

Q And did you review any of those other communications from back then when you were preparing your declaration?

MR. McGUFFIN: Object to form.

THE WITNESS: Not other than what has been discussed with my counsel.

BY MR. SEGREST:

Q I'm not asking about what you discussed with your counsel. But did you review any of those other communications from back then when you were preparing your declaration?

MR. McGUFFIN: Object to form.

THE WITNESS: I -- sitting here today, I

don't -- I don't recall of having seen anything specific, and especially not outside of any discussion with my counsel.

BY MR. SEGREST:

Q [redacted]

MR. McGUFFIN: Object to form.

THE WITNESS: [redacted]

BY MR. SEGREST:

Q Okay.

MR. SEGREST: If we can take a -- really only a couple-minutes break. I want to look through my outline and see if I've missed anything.

MR. McGUFFIN: That's fine.

(Brief pause off the record.)

MR. SEGREST: I don't have any further questions subject to the dispute we've got about

some privilege instructions.

MR. McGUFFIN: Okay. Why don't we take another break just while I get my thoughts in order. I think we'll have a couple questions just to clarify the testimony.

(Whereupon, there was a recess in the proceedings.)

EXAMINATION BY COUNSEL FOR THE PATENT OWNER, MERCK SERONO SA

BY MR. McGUFFIN:

Q Dr. Munafo, I do want to ask a couple of questions to clarify some of your testimony.

And to start, can you please pull up Exhibit 2050? This is the August meeting minutes, Dr. Munafo. Can you go to page 4?

Right under the heading in the middle of the page, you were asked earlier by Counsel about the [redacted]

A [redacted]

[redacted]

Q [redacted]

[redacted]

A [redacted]

[redacted]

[redacted]

Q And then moving further down Exhibit 2050, in the section, Suggestions for Primary Phase III Study, Counsel asked you earlier about the third line which starts with "Arms." And specifically about the parentheses, .35 milligrams per kilogram times 5 days times 2 months and .35 milligrams per kilograms times 5 days times 6 months.

Do you see those?

A Yes, I do.

Q And you testified that there was a mistake in these parentheses. Do you remember that?

A When I read this again today, I realize that -- and, again, these are draft minutes. I'm not sure how it was in the final minutes.

But I realized that the mathematic that

the counsel was pointing to should have read differently in the sense that it should have been -- I think I would have to redo the mathematic. But .35 mgs per kilo over 5 days times 2 months rather than times 5 days times 2 months.

Q Thank you.

So you were asked some questions about an exhibit called 1008, which was a paper by Rice. Do you remember that?

A I see it on the screen right now for the record, yes.

Q So you were asked to compare a lot of numbers in this exhibit to numbers in regimens Serono had proposed. Do you remember that?

A Uh-huh. Yes. Sorry.

Q In your answers, you testified that they were numerically the same. What did you mean by "numerically the same"?

A I just see that 0.7 is 0.7 and 2.1 is 2.1. That's what I mean with "numerically."

Q And why is it important that they were

the same numerically as opposed to the same in any other way?

A Because a -- a dosing regimen includes many more elements than just the dose. It includes how often it is administered, to which frequency, to which interval. It includes also the fact that here it was parenteral formulation while our -- while we were looking at orally-administered drug.

And, again, a dosing regimen is much more than just comparing the total dose.

Q Is the regimen that Counsel read to you from Exhibit 1008 the same regimen you proposed to IVAX?

MR. SEGREST: Objection; leading.

THE WITNESS: No. Again, a regimen is -- is not just the dose. A regimen includes the whole set of -- of elements that come into it like -- like the -- not only the dose, but also the -- the frequency, the route of administration, the duration. Also, the fact that we have this unique retreatment on the second year.

And all of these aspects make it that the word "same," which is vague, does not really apply to -- to comparing to dosing regimen, no.

BY MR. McGUFFIN:

Q And was the regimen that Counsel read to you from Exhibit 1008 the same regimen claimed in the '947 and '903 patents?

MR. SEGREST: Objection; form, calls for expert opinion.

THE WITNESS: I -- when you say exhibit -- can you -- can you tell me what you mean with this exhibit, Counsel?

BY MR. McGUFFIN:

Q So I'm referring to Exhibit 1001 in each of the IPRs, which are the challenged patents, the '947 and '903 patents.

A So exhibit?

Q 1001.

A So this is the '947. Right?

Q Yes, this is the '947 patent.

A Okay. And your question is?

MR. McGUFFIN: Can we go to the claim at

the end? Which I think -- let's go to Claim 36, which I think is on the last page. It's on the second-to-last page. I forgot about the certificate.

So it's the bottom of Column 19.

Q So looking at the claim of this patent, is the regimen that Counsel read to you from Exhibit 1008 the same regimen claimed in the '947 patent?

A I am not a specialist of legal terms and the implication. The regimen that we have in the patent '947 is -- is elaborated for treating multiple sclerosis, which is already a difference with -- with respect to the other Rice paper.

And we have oral administration, which is not the case there. We have a clear description of an induction -- what was called at that time an induction period and a cladribine-free period. And then we have a maintenance or re-treatment period as we call it sometimes and then, again, a cladribine-free period.

So the articulation of the regimen is more specific and aimed at achieving the corridor of efficacy and safety in multiple -- in treating multiple sclerosis patient with -- with -- with cladribine being administered orally. All of this does not qualify to say that it is the same as -- as the one mentioned in -- in Rice or in former studies.

Q Thank you.

MR. McGUFFIN: We can take this exhibit down.

Q So Counsel also asked you questions about Exhibit 2049, which is the December briefing document. Do you remember Counsel asked you where on pages 47 to 51 it described two months of dosing for the low-dose arm followed by four months of placebo?

A Yes.

Q And in some of your answers, you said that in addition to your understanding of the document, this is what we had proposed and shared with -- within the company at meetings where IVAX

representatives were present.

So just to be clear, what are you saying that you proposed at meetings where representatives from IVAX were present?

MR. SEGREST: Objection; scope.

THE WITNESS: The collaboration of the dosing regimen is not only a complex process engaging many, many expertise, knowledge, and -- and internal know-how, but it is also lengthy and iterative. And that meeting internally and where we had IVAX representatives present, we shared freely the elaboration of our thoughts towards the dosing regimen and the design of the trial. And -- and for the dosing regimen, the fact of -- of dosing as described, in fact, in the briefing document that we -- we sent -- we prepared for sending to the health authority.

This elaborated -- this was an elaboration of thoughts and refinement of thoughts over several months. I'm not able, sitting here today, to say at what meeting we presented which level, but during the whole -- not the whole. But

at least the second half of the year 2003, this started to -- to concretize, to be more specific in terms of our proposal.

In particular, the dosing per kilo -- I should -- even when using strengths of 10-milligram, we wanted to still stay with the concept of dosing per kilo as well as introducing the -- the fact that we wanted to re-treat after -- in the second year.

BY MR. McGUFFIN:

Q And did communications at meetings where IVAX representatives were present include the proposal to treat the low-dose arm with two months of active treatment followed by four months of placebos?

A This is part of the concept that we elaborated from -- from early on. So yes, it was presented this way, that the low-dose would be two consecutive cycles. Then the high-dose would be six consecutive cycles. And in order to maintain blinding in the -- in the low-dose group, the next four cycles would be placebo so that the patient

nor the -- the treating physician would know in which group the patient was -- in which treatment group the patient was.

Q Now, you mentioned that -- excuse me. Let me clear my throat. Excuse me.

You mentioned that some of those meetings were in person. Were there any meetings by phone?

A Yes. There were. Sitting here today, I -- I am not able to remember all the meetings, the frequency, the number. But there were frequent -- this is a general term. There were meetings on -- on -- several meetings during the year, being either in person or in -- or remote by -- by phone.

And in addition, there was some email exchange, and there were, as -- as you said, I myself have been to -- to visit IVAX in the U.S. to discuss specifically the results.

And I speak only for me, but, again, the -- the organization was interested to have a total free flow of information, so this was both

frequent and intense.

Q Were there written records of every in-person meeting?

A Sitting here today, I'm not able to answer this question. There were some minutes for sure on -- of some meetings, but I am not sure that there were records of -- or minutes of every meeting.

Q And were there written records of every phone meeting?

A Sitting here today, I do not remember this. But I may not have the full picture here. I was not in -- in the group looking at project managements or the like.

Q Do you personally recall any meetings, either in-person or over the phone, with IVAX between August 2003 and the end of January 2004? And I don't -- I'm not asking if you recall the details of every meeting. I'm just asking if you recall some details of some meetings.

MR. SEGREST: Objection; form.

THE WITNESS: I recall, as I said, that

I went to Miami in January 2004. I -- I recall of a meeting, but I do not remember the date, where Serono team went to Ireland to visit IVAX facility. I am not 100 percent sure, but I think that we had another meeting in Miami, but this is really long ago, so I'm not confident in -- in saying that I recall all or any with respect to the exact dates beside what I just cited.

BY MR. McGUFFIN:

Q Yeah. Can you turn to Exhibit 2053, which is your declaration, and go to paragraph 47 on page 21? That's 22 of the PDF.

A I am on the -- yeah, I am there.

Q Do you see the second sentence starts, "The Serono inventors discussed, e.g. during joint meetings that IVAX attended"? Do you see that?

A Yeah. The sentence reads: "Serono inventors discussed, e.g. during joint meetings that IVAX attended, that certain parameters in the study protocol, such as the number of days of cladribine dosing each month, might need minor adjustment, e.g., to six or seven days per month."

Q Now, do you recall whether there were written records of the meetings you're referring to in this paragraph?

A I -- sitting here today, I cannot recall precisely at which meeting this was discussed and whether there are minutes or there were minutes of it. But this is a topic that has been discussed when I -- I was alluding to earlier to the iterative refinements of the dosing regimen in that -- in that time frame.

Q Just one moment.

MR. McGUFFIN: Yeah. I have no further questions, Dr. Munafo.

MR. SEGREST: Just a couple on recross.

FURTHER EXAMINATION BY COUNSEL FOR THE PETITIONER, TWI PHARMACEUTICALS, INC.

BY MR. SEGREST:

Q Have you still got Exhibit 2049 there?

A What is 2049?

Q 2049 is what you've referred to as the briefing document. Go to page 49 of 59.

I want to look at the study treatment.

So on redirect, Dr. Munafo, you were asked some questions about this regimen. Right?

A Sorry. I really need to ask you to speak louder.

Q Yes, sir.

A I apologize for this.

Q My apologies.

On redirect, you were asked some questions about the dose -- the treatment regimens in the study treatment. Right?

A The elaboration of the dosing regimen, which includes aspects like the dose, total dose, dose per day, frequency, duration, re-treatment, et cetera, has been a subject of discussion and adjustments over time. And this is what we presented in December 2003, given the dates.

I cannot comment, sitting here today, with certainty, whether we continued to discuss the duration after this briefing -- after this draft briefing document or not.

Q Okay. I want to ask you again about the strength 0, 3, and 10 milligrams. Do you see that

line?

A On the same -- are you on the same page 49 of the -- the briefing document?

Q Yes, sir. Page 49 of 59, "Study Treatment."

A Yes.

Q You've got formulation and you've got strength. Do you see strength 0, 3, and a 10-milligram?

A Yeah. There is not a second comma, but yes.

Q Oh, thank you.

And 10 milligrams, a 10-milligram tablet, for five consecutive days per cycle, per six cycles, is what would get you the high dosing arm in this study. Right?

MR. McGUFFIN: Object to form.

THE WITNESS: The dose was to be adjusted by kilo, and here you're talking about the strengths of 10-milligram, which is not the dose.

BY MR. SEGREST:

Q Would the high dosing arm require administration of the 10-milligram dosing strength for six cycles?

A The high dosing regimen was focusing on getting a total dose. And inasmuch as I recall sitting here today, at that time, we had not yet decided which strengths we would use to arrive to this dose.

Q Well, the high dosing regimen has the total dose of 2.1 milligrams per kilogram. Right?

A Total dose in the high -- high-dose treatment group was said to approximating cumulative dose of 2.1mgs per kilo.

Q Well, I thought you were saying that the high-dose was six cycles of 10 milligrams, and the low-dose was two cycles with the 10-milligram, filled out by a placebo. Was I wrong about that?

A I don't recall having said today that the strength at that time was fixed at 10-milligram, [redacted]

[redacted]

So the high-dose arm was designed to have or was -- was proposed to have, indeed, six cycle, the low-dose arm to have two cycle. And the target exposure that we wanted to have was defined, [redacted]

Q If you took six cycles of the 10-milligram dose to meet the total dose of the high dosing arm, then six cycles of the 3-milligram strength dose would not have been sufficient for the high dosing arm, would it?

A I did not --

MR. McGUFFIN: (Indiscernible.)

THE WITNESS: It would not have been what? Sorry.

BY MR. SEGREST:

Q It would not have been sufficient to reach the dose on the high dosing arm, would it?

MR. McGUFFIN: Can I ask you to pause before you answer, Dr. Munafo?

I object to form.

THE WITNESS: Yeah, I'm -- I don't understand the question, so can you perhaps rephrase it?

BY MR. SEGREST:

Q In your testimony, you've said that the target of 2.1 milligrams per kilogram would be six cycles of the 10-milligram dose strength, and that the target of .7 milligrams per kilogram would be two cycles of the 10-milligram dose strength.

Isn't that what you've said?

A I -- I --

MR. McGUFFIN: Object to form.

THE WITNESS: I don't recall having mentioned the strengths in that discussion, have I?

BY MR. SEGREST:

Q The total dose for administering 10 milligrams is going to be higher than the total dose for administering 3 milligrams on the same schedule, isn't it?

MR. McGUFFIN: Object to form.

THE WITNESS: I think you -- you made a hypothetical calculation using 10-milligram that I agreed on the arithmetic. But I don't think I have, and I would not have -- I should not have agreed on the strengths at this moment.

BY MR. SEGREST:

Q Well, you see for treatment regimen, this says five-day consecutive dosing within 28 cycles times six cycles per phase. Right?

A I'm getting tired. The -- the high dose --

Q No, it's the treatment regimen.

A Consisted.

Q You see it says five-day consecutive dosing within 28-day cycles times six cycles per phase?

A Which dosing regimen are you referring to here? The one in the briefing document, the cladribine one, the clarity one, the --

Q I'm referring to the page we're looking at, the briefing document, Exhibit 2049. The cell we're looking at on the study treatment --

A Okay.

Q -- and the underscore heading there, "treatment regimens."

A Yes.

Q Doesn't that say 5-day consecutive dosing within 28-day cycles times 6 cycles per phase?

A This is what it reads in this draft briefing document dated December 2003. But as I have already said, there have been discussions whether -- regarding the -- the number of consecutive days. And sitting here today, more than 20 years later, I cannot tell you whether this discussion of five, six, or seven had come to the conclusion this -- to conclusion, period.

This is a snapshot of what we had in December 2003 as a proposal to be submitted to the health authority in Sweden for their feedback.

Q So if you use the treating -- treatment regimen exactly as written here, 5-day consecutive dosing within a 28-day cycle times 6 cycles per phase, if you did that in one group with

10-milligram, following that same schedule with 3-milligram dosing strength, it's going to give you a much lower total dose, isn't it?

MR. McGUFFIN: Object to form. And also, this is well beyond the scope of the redirect examination.

You can answer --

MR. SEGREST: You can object to scope.

MR. McGUFFIN: -- Dr. Munafo. But --

MR. SEGREST: You can object to scope, but don't make a speaking objection on it.

THE WITNESS: I cannot object on the -- on the arithmetic of your calculation, but this was not what we had planned, what we had proposed, what we have discussed and shared with IVAX in -- or had shared in meeting where IVAX was present.

And the low-dose was -- was defined by two cycle, the high-dose by six cycle, and the strengths was not part of the discussion inasmuch as I remember sitting here today.

It was not part of the -- of the discussion or the argumentation with respect to

the low-dose or high-dose arm.

BY MR. SEGREST:

Q Five-day consecutive dosing within 28-day cycles for six cycles with a 3-milligram dosage strength oral formulation would only be about 30 percent of the total dose you would get with 5-day consecutive dosing within a 28-day cycle times 6 cycles per phase for a 10-milligram tablet. Right?

MR. McGUFFIN: Object to form; scope, asked and answered.

THE WITNESS: This is a hypothetical scenario that you present and was not part of our concept inasmuch as I remember sitting here today.

MR. SEGREST: Okay. That's all I've got.

MR. McGUFFIN: We have no further questions, Dr. Munafo. Thank you so much for your time today.

MR. SEGREST: Thank you, sir.

And as I said before, I think we've got an issue about privilege, but that's being

addressed separately. So that's all we've got for today.

MR. McGUFFIN: Yep.

MR. SEGREST: We can go off the record unless you've got something for the record.

MR. McGUFFIN: Before we go off the record, Merck designates the record protective order material under the Board's default protective order.

And I also just want to be -- make sure that the appearances at the start are correct, that I'm Asher S. McGuffin on behalf of both Dr. Munafo and Merck Group, the Patent Owner.

(Off the record at 6:29 p.m.)

CERTIFICATE OF SHORTHAND REPORTER - NOTARY PUBLIC

I, CASSIDY WESTERN, RPR, Certified Reporter and Notary Public within and for the Commonwealth of Pennsylvania, do hereby certify:

That ALAIN MUNAFO, Ph.D., the witness whose deposition is hereinbefore set forth was duly sworn by me before the commencement of such deposition and that such deposition was taken before me and is a true record of the testimony given by such witness.

I further certify that the adverse party, MERCK SERONO SA, was represented by counsel at the deposition.

I further certify that the deposition of ALAIN MUNAFO, Ph.D., occurred via videoconference on Friday, the 7th of June, 2024, commencing at 1:06 p.m. CEST to 6:29 p.m. CEST.

I further certify that I am not related to any of the parties to this action by blood or marriage, I am not employed by or an attorney to any of the parties to this action, and that I am in no way interested, financially or otherwise, in

the outcome of this matter.

IN WITNESS WHEREOF, I have hereunto set my hand this 10th day of June, 2024.

My commission expires August 4, 2025.

_____

Cassidy Western, RPR