UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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TEVA PHARMACEUTICALS USA, INC., :
:
Petitioner, :
:
v. :
:
CORCEPT THERAPEUTICS, INC., :
:
Patent Owner. :
:
Case No. PCR2019-00048 :
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VIDEO DEPOSITION OF
Dr. David Greenblatt
February 14, 2020
Washington, D.C.
Lead: Eric Stops, Esquire
Firm: Quinn Emanuel Urquhart & Sullivan, LLP

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JANE ROSE REPORTING 1-800-825-3341

VIDEO DEPOSITION OF
DAVID J. GREENBLATT, M.D.

the witness, was called for examination by counsel for the Patent Owner, pursuant to notice, on Friday, February 14, 2020, commencing at 9:03 a.m., at the law offices of Sterne, Kessler, Goldstein & Fox, P.L.L.C., 1100 New York Avenue, NW, Suite 600, Washington, D.C., before Dawn A. Jaques, CSR, CLR, and Notary Public in and for the District of Columbia.

APPEARANCES:
On behalf of the Petitioner:
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I-N-D-E-X

P R O C E E D I N G S

THE VIDEOGRAPHER: We are now on the record. Here begins the video deposition of David J. Greenblatt, M.D., taken in the matter of Teva Pharmaceuticals USA, Inc., v. Corcept Therapeutics, Inc. Today's date is February 14, 2020. The time is 9:03.

This deposition is being held at 1100 New York Avenue, Northwest, in Washington, D.C. Our court reporter is Dawn Jaques. My name is Nat Pham, both on behalf of Jane Rose Reporting.

Will counsel please state your appearance for the record?

MR. STOPS: Eric Stops and Daniel Wiesner from Quinn Emanuel for Patent Owner, Corcept.

MS. STERLING: Deborah Sterling and Will Milliken from Sterne, Kessler, Goldstein & Fox for Teva Pharmaceuticals USA, Inc.

THE VIDEOGRAPHER: Will the court reporter please swear in the witness?

THE REPORTER: Raise your right hand, sir.

(The witness was administered the oath.)

Whereupon,

DAVID J. GREENBLATT, M.D.,

was called as a witness, after having been first duly sworn by the Notary Public, was examined and testified as follows:

EXAMINATION BY COUNSEL FOR THE PATENT OWNER

BY MR. STOPS:

Q Good morning, Dr. Greenblatt.

A Good morning.

Q Just a few instructions before we get into it. We need your answers orally because the court reporter cannot record nods of the head.

Do you understand?

A I do.

Q And if you don't answer a question, I need you to ask me for a clarification before you answer. If you do answer, that means you understood the question. Do you agree?

A Yes, I agree.

Q You've been deposed before, correct?

A Yes.

Q How many times?

A I don't have an exact number, but I estimate on average either a court or a deposition

appearance, on average, one to two times a year for the last 45 years.

Q Okay. And you've put in expert reports or expert declarations in the past, correct?

A Yes.

Q You submitted one declaration in this matter, correct?

A Correct.

Q Have you prepared any documents for this action beyond that declaration?

MS. STERLING: I'm going to object to the extent that that gets to privileged information.

You may answer yes or no, but not discuss any substance of any of the conversations you've had or any of the actions you've taken with your counsel.

THE WITNESS: No.

BY MR. STOPS:

Q Who retained you for this case?

A The Sterne Kessler firm.

Q Have you worked with Teva before?

A Yes.

Q How many times?

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A I don't have a number on it, but over the last decade, I served as a scientific consultant.
Q And have you worked with the Sterne Kessler law firm before?
A Yes.
Q How many times?
A That I don't know. I'd have to --
Q Okay.
A Without looking at the records, but sure, yeah.
Q What was the context? Was it a deposition like this?
A You know, apparently I can't trust my memory on that, so ...
Q Understood. Just so we keep the record clear, if I use the abbreviation PK for pharmacokinetics and PD for pharmacodynamics, you'll know what I mean, right?
A Yes.
Q And I've heard pharmacokinetics defined roughly as what a -- what your body does to a drug, and pharmacodynamics as what a drug does to your body.
Are those simplified definitions in

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accordance with your understanding?
A Those are simplified definitions. I would point to the declaration for more detailed discussion.
Q Okay. Enzymes in the cytochrome P4503A family are often referred to as just CYP3A, right?
A That is often the case, yes.
Q And if I call that CYP3A, you'll know what I mean, right?
A Yes, I will.
Q And a CYP3A is also written as P450-3A, correct?
A That's correct.
Q Okay. And there is a CYP3A enzyme in the intestines, correct?
A That is correct.
Q There's also a CYP3A enzyme in the liver, correct?
A Correct.
Q How would you define a CYP3A isoform?
MS. STERLING: Objection, form.
THE WITNESS: It is one of the specific proteins or enzymes in the cytochrome P4503A subfamily.
BY MR. STOPS:

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Q So a specific CYP3A subfamily member, such as CYP3A4, would be an isoform; is that right?
A Yes.
Q And the metabolism by the liver before a substrate reaches the rest of the body is referred to as first-pass metabolism, correct?
A That is one of the terms that's used. This -- and this refers to oral dosage.
Q Understood, because -- and it refers to oral dosage because IV dosing will bypass -- bypass first-pass metabolism, correct?
MS. STERLING: Objection, foundation.
THE WITNESS: The second statement is correct, yes.
BY MR. STOPS:
Q Oh, the second statement being IV dosing will bypass first-pass metabolism?
A Correct.
MS. STERLING: Same objection.
BY MR. STOPS:
Q Thank you. I'm sorry.
Is it -- is it proper to refer to the metabolism in the intestines and the first-pass liver metabolism collectively as presystemic

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metabolism?
MS. STERLING: Objection.
BY MR. STOPS:
Q Can I -- I'll rephrase that.
Is it proper to collectively refer to metabolism in the intestines and the first-pass liver metabolism as presystemic extraction?
A That -- that is partly -- partly correct.
Q Okay. What was incorrect?
A Well, the -- when a drug is given orally and incompletely reaches the systemic circulation, we collectively call that presystemic extraction or the first-pass effect. It can be due to metabolism, or there can be other things causing it.
Q Other things such as transporters?
A That's one of --
MS. STERLING: Objection, foundation.
THE WITNESS: Yes, that is one of the other things.
BY MR. STOPS:
Q Okay. And just so I'm clear on terminology, I had always thought first-pass metabolism referred to just the liver.

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Does first-pass metabolism also encompass the metabolism in the intestines?
A When it's used in that context, yes. It's a -- it's a combination of enteric and liver.
Q Would you agree that the most important mechanism of presystemic extraction is the first-pass hepatic metabolism?
MS. STERLING: Objection to form, scope.
THE WITNESS: No.
BY MR. STOPS:
Q Why do you disagree?
A It could be enteric metabolism, it could be hepatic metabolism, a combination of the two, or other factors preventing reaching of the systemic circulation.
Q So it depends on the context; is that correct?
MS. STERLING: Objection, form, scope.
THE WITNESS: Well, many factors determine the contributions or the determinants of first-pass metabolism or presystemic extraction.
BY MR. STOPS:
Q So sometimes the intestinal metabolism would be most important, sometimes the hepatic

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metabolism is the most important, sometimes it will be something else; is that right?
MS. STERLING: Objection, form.
THE WITNESS: Partially correct, but the point is that presystemic extraction or first-pass metabolism can be either hepatic or enteric biotransformation metabolism, it could be transport, and maybe other factors as well.
BY MR. STOPS:
Q Okay. And in all of the first-pass metabolism or the presystemic extraction, the common result is that some portion of the drug is biotransformed before reaching systemic circulation, correct?
MS. STERLING: Objection, foundation, form.
THE WITNESS: When there is first-pass metabolism or presystemic extraction, some fraction fails to reach the circulation after oral dosage.
BY MR. STOPS:
Q A POSA would have known prior to the critical date that for CYP3A substrates that ordinarily undergo high systemic -- sorry, high presystemic extraction after oral dosage, CYP3A

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inhibition may profoundly increase oral bioavailability through the impaired presystemic extraction, resulting in large substrate plasma concentrations, correct?
MS. STERLING: Objection, form, foundation.
THE WITNESS: A POSA would have known that after oral dosage of a CYP3A substrate, that inhibition of CYP3A could lead to increased systemic exposure in amounts ranging from small to very large.
BY MR. STOPS:
Q And a POSA would have known that such interactions may be clinically hazardous, correct?
MS. STERLING: Objection, form, foundation.
THE WITNESS: A POSA would have known that such interactions could be clinically beneficial, could be of no effect at all, or could be hazardous. All three are possible.
BY MR. STOPS:
Q In drug interactions, the drug causing the interaction can be referred to as the perpetrator, correct?
A It has been referred to as that, yes.

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Q And the drug being interacted with can be referred to as the victim or the substrate, correct?
A That is correct.
Q And the perpetrator can be, for example, an inhibitor of the victim's metabolism, correct?
A That is one possibility among many.
Q One of the references you refer to in your declaration is the -- is a 2006 draft FDA guidance, correct?
A I believe you're correct, that that's among the documents.
Q And it's your opinion that POSAs will follow FDA guidances, correct?
A My opinion is that a POSA could consider FDA guidance. Whether they follow it, I can't say.
Q Why can't you say?
A Because I don't know if they would follow it. Depends on what the objective is and what the clinical or scientific problem is.
Q In your opinions for this matter, is it your opinion that POSAs would follow the 2006 draft FDA guidance?

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MS. STERLING: Objection, form.
THE WITNESS: I think I just answered that.
BY MR. STOPS:
Q I was making sure you weren't answering the question in the abstract versus a different opinion for this case in particular.
A Okay. Well, my answer would then be the same. I think if -- if -- depending on the specific problem in question, they might consider the guidance; and whether they would follow it, I don't know.
Q You'd agree that the impact of a drug-drug interaction on the clearance of a victim drug is greatest when that drug is extensively metabolized and a single CYP isoform mediates clearance, correct?
MS. STERLING: Objection, form --
THE WITNESS: I can't --
MS. STERLING: -- foundation.
THE WITNESS: I'm sorry.
I can't agree with that. That's just not enough information.
MR. STOPS: Okay. So I'm going to continue the numbering from the last exhibit in

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the 2000 range that we put in. I think that's consistent with normal practice. So this is going to be --
MS. STERLING: It is.
MR. STOPS: Thank you. I think I'm going -- I'm going to mark this exhibit as 2049, please.
(Exhibit 2049 was marked for identification.)
BY MR. STOPS:
Q Doctor, I'm handing you an exhibit that is marked as 2049.
MS. STERLING: I'm going to object to the exhibit for authentication, scope, hearsay, relevance, and there may be others depending on where the questioning goes.
BY MR. STOPS:
Q Sure. Dr. Greenblatt, have you seen this Exhibit 2049 before?
A I have seen it, not in the context of the exhibit, but the internal part is a chapter written by me a number of years ago.
Q Sure. So after the first page, which is the cover of a -- cover of a book, the Chapter 24, which begins on page 625 of the

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exhibit, is a book chapter that you wrote, correct?
A That's correct. I see that.
Q Okay. And you recognize the book chapter?
A I do, yes.
Q And the book chapter is entitled "Clinical Studies of Drug-Drug Interactions: Design and Interpretation," correct?
A That is correct.
Q If you would turn to page 634 of Exhibit 2049, let me know when you're there, please.
A Yes, I see it. I'm there.
Q In the second full paragraph -- I'll direct you to the second full paragraph on the page. Do you see the first sentence, "The impact of a DDI on the clearance of a victim drug is greatest when that drug is extensively metabolized, and a single CYP isoform mediates clearance"?
A Yes, I see those words.
Q And you wrote those words, correct?
A That's correct. Also many other things in the -- in the chapter.

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Q In that same paragraph, the last sentence states, "Concern is augmented when the substrate victim has high clearance, and undergoes significant presystemic extraction after oral dosage." Do you see that?
A I see those words, yes.
Q And do you agree with those words?
A Well, I agree with the whole chapter, and I agree with the words in the context of the whole chapter, but not out of context. It's not relevant.
MS. STERLING: Excuse me. Sorry, Eric, I don't mean to interrupt your line. Our realtime has stopped.
MR. MILLIKEN: Mine stopped also.
THE VIDEOGRAPHER: Off the record, 9:23.
(Pause in the proceedings.)
THE VIDEOGRAPHER: Back on the record at 9:24.
BY MR. STOPS:
Q Mifepristone is metabolized entirely, or almost entirely, by CYP3A, correct?
MS. STERLING: Objection, foundation.
THE WITNESS: My understanding is that

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