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IN THE UNITED STATES DISTRICT COURT
IN AND FOR THE DISTRICT OF DELAWARE

- - -

VANDA PHARMACEUTICALS INC.,) Civil Action
)
Plaintiff,)
)
v.)
)
ROXANE LABORATORIES, INC.,)
)
Defendant.) No. 14-757-GMS

- - -

Wilmington, Delaware
Wednesday, March 2, 2016
9:00 a.m.
Trial Day 3

BEFORE: HONORABLE GREGORY M. SLEET, U.S.D.C.J.

APPEARANCES:

KAREN JACOBS, ESQ., and
ETHAN H. TOWNSEND, ESQ.
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-and-
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:16:36
:16:36

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:05:13

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Ratain - cross

:53:07 1 how iloperidone is metabolized. Correct?

:53:11 2 A. Can you point me to a specific page?

:53:14 3 Q. If we go to Page 6, for example -- I am sorry, Page

:53:21 4 13.

:53:24 5 Let's blow up Table 1 there, try and get that as

:53:28 6 large as we can, please, Mr. Lee.

:53:31 7 That is talking about the various enzymes that

:53:35 8 are involved in metabolizing iloperidone. Correct?

:53:39 9 A. That's correct.

:53:39 10 Q. And there are 11 of them?

:53:48 11 A. There are 11 P450 enzymes that have some level of

:53:56 12 activity on the metabolism of iloperidone.

:53:58 13 Q. CYP2D6 is one out of the 11. Correct?

:54:03 14 A. Yes. It's one out of the 11 and was the most

:54:07 15 efficient in the formation of metabolite P94, which is the

:54:11 16 precursor to P95.

:54:14 17 Q. While we are on that, the Percent of Total column,

:54:17 18 what does that mean?

:54:18 19 A. The percent of the total metabolites formed. This

:54:23 20 data comes from data that would have been submitted by the

:54:27 21 sponsor. I would have to, to really talk about this with

:54:32 22 any degree of certainty, I would really have to look at the

:54:35 23 submission data.

:54:35 24 Q. Fair enough. But this is telling us, at least in some

:54:38 25 fashion, the relative amounts of different metabolites.

:54:41 1 Correct?

:54:43 2 A. Yes. One would really have to see the submission data

:54:46 3 to really understand it. I think what one can primarily

:54:49 4 understand from this is that CYP2D6 was the most efficient.

:54:55 5 That is the conclusion of the FDA in regard to the data

:55:00 6 submitted by the sponsor.

:55:01 7 Q. Now, the list of items in the right-hand column, those

:55:05 8 are different metabolites. Correct?

:55:06 9 A. Yes.

:55:06 10 Q. And they are all prefixed with a P?

:55:10 11 A. That's correct.

:55:11 12 Q. So one of the ones that we see here is P88, for

:55:15 13 example. Am I right?

:55:16 14 A. Yes. I see that.

:55:17 15 Q. If we look down the table, CYP2D6 is shown as creating

:55:24 16 something called P94. Isn't that right?

:55:27 17 A. That's right.

:55:29 18 Q. It's known now that P94 is subsequently converted into

:55:34 19 P95. Correct?

:55:36 20 A. Yes.

:55:36 21 Q. But you are not suggesting that the knowledge was in

:55:39 22 the prior art, are you?

:55:40 23 A. I am suggesting that the prior art made it very clear

:55:43 24 that CYP2D6 was -- CYP2D6 activity was highly correlated

:55:50 25 with the metabolism of iloperidone from the Mutlib prior art

:55:54 1 **reference.**

:55:55 2 Q. I am going to come to Mutlib.

:55:56 3 To be clear, are you or are you not suggesting
:56:02 4 that in the prior art there was a teaching that metabolite
:56:06 5 P94 was converted by whatever process to metabolite P95?

:56:12 6 A. There is not anything in the prior art that refers to
:56:14 7 P94.

:56:15 8 Q. Now, just so we see here, there is also a reference to
:56:23 9 CYP3A4. Correct?

:56:26 10 A. Yes.

:56:26 11 Q. And that's another major metabolic pathway for the
:56:31 12 metabolism of iloperidone. Correct?

:56:34 13 A. That's a non-inheritable metabolic pathway. That is a
:56:39 14 very major important one, but for which no one has really
:56:44 15 found useful genetic predictors.

:56:46 16 Q. Let's tease that apart a little.

:56:49 17 First of all, we will agree that the CYP3A4 is a
:56:52 18 major metabolic pathway in the metabolism of iloperidone.
:56:56 19 Fair?

:56:57 20 A. Yes.

:56:57 21 Q. And you mentioned it being non-inheritable. What that
:57:00 22 means is I don't have variations in the part of my genetics
:57:05 23 that code for 3A4. Right?

:57:08 24 A. Not for 3A4. For 3A5, but not for 3A4.

:57:13 25 Q. Unlike 2D6, where, as we have heard quite a lot, I can

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