1   UNITED STATES DISTRICT COURT
     FOR THE DISTRICT OF NEW JERSEY
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ASTRAZENECA PHARMACEUTICALS
4   LP, et al.,
                                          CIVIL ACTION NUMBERS:
5   Plaintiffs/Counterclaim-
     Defendants,
6
              -vs-   14-cv-03547-RMB-KMW
7
     SAGENT PHARMACEUTICALS, INC.,
8   Defendant/Counterclaim-Plaintiff.
     _____
9   ASTRAZENECA PHARMACEUTICALS
     LP, et al.,
10
     Plaintiffs/Counterclaim-
11   Defendants,

12   -vs-
                                          14-cv-05539-RMB-KMW
13   GLENMARK GENERICS, INC., USA,

14
     Defendant/Counterclaim-Plaintiff.
15

16

17

18   15-cv-00615-RMB-KMW
     _____
19   Mitchell H. Cohen United States Courthouse
         One John F. Gerry Plaza
20   Camden, New Jersey 08101
         July 14, 2016
21
     B E F O R E: THE HONORABLE RENÉE MARIE BUMB
22   UNITED STATES DISTRICT JUDGE
                                        AND A JURY
23

24

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                    United States District Court
                        Camden, New Jersey

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       Certified as true and correct as required by Title 28,
24     U.S.C., Section 753.

25                       /S/ Theodore M. Formaroli, CSR, CRR
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United States District Court
Camden, New Jersey

United States District Court
Camden, New Jersey

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3   DEFENDANT EXHIBITS DTX-545, 546 AND 548 WERE   912
     RECEIVED IN EVIDENCE
4   JOINT EXHIBITS JTX-6, JTX-7, AND JTX-8 WERE   949
     RECEIVED IN EVIDENCE
5   DEFENDANT EXHIBIT DTX-276 WAS RECEIVED IN   959
     EVIDENCE
6   DEFENDANT EXHIBITS' PTX-392, DTX-285, JTX-13,   1023
     DTX-39, DTX-48, JTX-16, DTX-49, JTX-17, JTX-15,
7   JTX-11, JTX-14, and JTX-10 WERE RECEIVED IN
     EVIDENCE
8   DEFENDANT EXHIBITS DTX-433, 881, 309, 320 AND 311   1039
     WERE RECEIVED IN EVIDENCE
9   DEFENDANT EXHIBITS DTX-317 AND DTX-318 WERE   1040
     RECEIVED IN EVIDENCE
10   DEFENDANT EXHIBITS JTX-1, JTX-3, JTX-4, PTX-432,   1047
     DTX-282, DTX-287, DTX-306 and DTX-307 WERE
11   RECEIVED IN EVIDENCE

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United States District Court
Camden, New Jersey

1   THE DEPUTY CLERK: All rise.

2   (OPEN COURT, July 14, 2016, 9:08 a.m.)

3   THE COURT: Good morning.

4   RESPONSE: Good morning, Your Honor.

09:08AM   5   THE COURT: Have a seat.

6   Okay. Are we ready to continue with the deposition

7   testimony?

8   MS. PIROZZOLO-MELLOWES: Yes, we are, Your Honor.

9   THE COURT: Ms. McCleskey, come forward.

09:09AM   10   MR. FREITAS: Yes, Your Honor.

11   (Laughter.)

12   THE COURT: Good morning.

13   MR. FREITAS: Good morning.

14   THE COURT: Okay. Whenever you're ready.

09:09AM   15   MS. PIROZZOLO-MELLOWES: We left off at Page 140 of

16 the transcript.

17   THE COURT: Yes, thank you.

18   MS. PIROZZOLO-MELLOWES: And Ms. Waldron continues

19 the questioning on behalf of defendants.

09:09AM   20 (Deposition read as follows:)

21 Q. Let's get back to the documents you kept when you were at

22 the Lombardi Cancer Center.

23   Did I understand you to say that you did keep

24 laboratory notebooks?

09:09AM   25 A. Yes.

1   Q.   Did you have any raw data of any kind?

2   A.   It was in the laboratory notebooks.

3   Q.   It would be pasted in the lab notebooks?

4   A.   Why do you think raw data would not be on the same piece

09:09AM   5   of paper as the lab notebook?

6   Q.   Actually, I don't know one way or the other. I want to

7   know what your particular procedure was.

8   A.   Well, most of the time, you're writing the laboratory

9   notebook. If you get, like, a printout or something, then you

09:09AM 10   would paste that in the laboratory notebook.

11   Q.   Got it. Did you keep anything on the computer?

12   A.   Yes.

13   Q.   What did you keep on the computer?

14   A.   Well, remembering that computers were not as good as they

09:10AM 15   are now, when I got data, I would have to enter it into the

16   computer, like, into a graphing program, for instance, and

17   then it would draw the graph and I would print the graph. But

18   the -- but the data in the computer was the same as in my --

19   hopefully, as in my lab notebook.

09:10AM 20   Q.   You didn't create, say, Word files and keep them on a

21   computer?

22   A.   Oh, yes, but that's not data.

23   Q.   Okay. I see. What type of information or documents, if

24   any, would you have saved on a computer?

09:10AM 25   A.   The drafts of the paper, the -- after I entered the data

1 to make a graph, that would be saved, of course, but it would

2 be the data from the lab notebook that I entered. So it's,

3 like, a copy and -- and also the graphics file, picture a

4 graph. I don't know how you would say that, but the graph

09:10AM   5 itself, I guess you would say, that was saved to the computer.

6 But I also, of course, printed it.

7 Q.   Do you have knowledge as to whether anyone in your group

8 had documents saved to a computer that had originated from

9 AstraZeneca?

09:11AM   10 A.   I don't have knowledge about anybody else in my group

11 except me.

12 Q.   Did you have any documents originating from AstraZeneca

13 that related to Ms. McCleskey 1998 saved to a computer?

14 A.   Are you speaking about data?

09:11AM   15 Q.   Anything. For example --

16 A.   Saved to a computer?

17 Q.   Yeah, like a statement of proposed investigation --

18 A.   Oh, no --

19 Q.   -- sample requests?

09:11AM   20 A.   -- no, no.

21 Q.   Did you have data that originated from AstraZeneca saved

22 to a computer?

23 A.   No.

24 Q.   Did you have any binders or personal notebooks separate

09:11AM   25 from your lab notebooks in which you kept information

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1 regarding McLeskey 1998?

2 A.   I had binders with the tumor data, the tumor measurements

3 in pictures of mice.

4 Q.   Any other places where you would have had information

09:11AM 5 related to McLeskey 1998, that we haven't talked about?

6 A.   No.

7 Q.   Now, you mentioned, if I understood you correctly, I

8 believe you testified that you destroyed your technical

9 documents related to McLeskey 1998 in the beginning of

09:12AM 10 June 2014; is that right?

11 A.   Correct.

12 Q.   What did you mean by "destroyed?" How did you destroy

13 them?

14 A.   I just threw them in the trash.

09:12AM 15 Q.   Just a regular trash bin?

16 A.   Yeah.

17 Q.   Where was this trash bin?

18 A.   At my school.

19 Q.   What school?

09:12AM 20 A.   The University of Maryland School of Nursing.

21 Q.   Do you know what happened to the documents after you

22 threw them in the trash bin?

23 A.   No.

24 Q.   When you left Lombardi Center and took your technical

09:12AM 25 documents with you, was it your understanding that that was

1   okay by the rules, by Lombardi's policies?

2   A.   I didn't have any understanding about that.

3   Q.   Did you know what document retention policies Lombardi

4   would have had in place at the time?

09:12AM   5   A.   No.

6   Q.   When you -- I'll just say "you" to start, and then we

7   will be talking about Lombardi Center. When you got a

8   document on a project, say, a certificate of service or MSDS

9   or something like that, what did you do with it? Where was

09:13AM   10   something like that kept?

11   A.   I don't know what a certificate of service is.

12   The -- we were required to keep MSDSs in the notebook

13   in the lab for all chemicals that we had in the lab, so that's

14   what we did.

09:13AM   15   So MSDSs would be kept in the laboratory notebooks,

16   correct?

17   (Reading stopped.)

18   MR. FREITAS: I apologize.

19   THE COURT: Ask it again.

09:13AM   20   MS. PIROZZOLO-MELLOWES: You have to read -- he

21   inadvertently reread the question.

22   THE COURT: Yes.

23   (Deposition read as follows:)

24   Q.   So MSDSs would be kept in the laboratory notebooks,

09:13AM   25   correct?

1 A. No, not in -- not where we had the data. We had separate

2 notebook for MSDSs.

3 Q. MSDSs had their own notebook?

4 A. That's correct.

09:13AM **5** Q. What about certificates of analysis?

6 A. Didn't usually keep those.

7 Q. They're -- why not?

8 A. Didn't feel that we needed them.

9 Q. Who retained custody of documents as they came in on the

09:14AM **10** McLeskey 1998 project?

11 A. I don't know what you're talking about, what documents.

12 Q. Do you recall how samples got shipped into the facility,

13 whether, say, they went to a mailroom or a specific sample

14 depository?

09:14AM **15** A. They went to the mailroom.

16 Q. And then that -- that would happen?

17 A. The mail people would bring them to us.

18 Q. Would you then keep the samples in your lab?

19 A. Yes.

09:14AM **20** Q. And did I understand you correctly that at the time you

21 were a postdoc in Dr. Kern's lab, you were not aware of the

22 policies and procedures that Lombardi Center had in place with

23 regard to retention of documents; is that right?

24 A. Not only was I not aware of anything they had in place, I

09:14AM **25** was not aware if -- whether they had anything in place.

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 1  Q.   If you received ancillary paperwork with samples, such as

 2  a certificate of analysis or something like that, what would

 3  you have recorded the receipt of that document --

 4  (Reading stopped.)

 5          THE COURT:  "Would you."

 6  (Deposition read as follows:)

 7  Q.   Would you have recorded the receipt of that document in

 8  your laboratory notebook?

 9  A.   No.

10  Q.   Did Lombardi require you to make copies of anything and

11  send them on to a document repository or anything like that?

12  A.   No.

13  Q.   To your knowledge, were the documents that you were

14  keeping in your lab the only copies?

15  A.   As far as I knew.

16  Q.   Are you aware of whether copies were ever made of your

17  laboratory notebooks?

18  A.   I think not.

19  Q.   Who had access to your laboratory notebooks besides you?

20  A.   Dr. Kern.

21  Q.   Anyone else?

22  A.   Well, the other people in the lab would have, had they

23  wanted it, but I don't know that they ever did --

24  (Reading stopped.)

25          THE COURT:  So could have.
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1   MR. FREITAS: Pardon me.

2   (Deposition read as follows:)

3   A. Well, the other people in the lab could have had they

4   wanted it, but I don't know what they ever did -- that they

09:15AM   5   ever did.

6   Q. In the conversation that you just referred to, when you

7   communicated with Mr. Trock, what did you discuss with

8   Mr. Trock?

9   A. He -- I think he, I don't remember a whole lot about the

09:16AM   10   conversation, but he said that he had been just about to

11   discard the data from -- from this paper when they called.

12   Q. When who called?

13   A. The -- the lawyers that were doing the Teva thing, Mary

14   Burke and company.

09:16AM   15   Q. I'm sorry. I believe you just said, "Mary Burke did not

16   ask me not to destroy documents."

17   A. She did not say, Don't destroy documents. When she said

18   that, I do not know.

19   Q. Mary Burke never told you to preserve your documents

09:16AM   20   related to McLeskey 1998?

21   A. Correct.

22   Q. Did anyone Mary Burke worked with ever tell you not to --

23   tell you that you must preserve your documents related to

24   McLeskey 1998?

09:16AM   25   A. No.

1 Q.   Now, I believe you said earlier that you recall speaking

2 with three people at AstraZeneca, Dr. Wakeling, Dr. Vose, and

3 a third person whose name you don't remember; is that correct?

4 A.   Correct.

09:16AM 5 Q.   Do you recall approximately how many times you spoke with

6 Dr. Wakeling?

7 A.   Twice.

8 Q.   Was this via telephone or by some other means of

9 communication?

09:17AM 10 A.   Telephone.

11 Q.   Who called who?

12 A.   I called him.

13 Q.   Both times?

14 A.   Yes.

09:17AM 15 Q.   Why did you call Dr. Wakeling?

16 A.   The first time I called to get him to send me the drug

17 and find out how to administer it to mice. The second time I

18 called to tell him we had used the drug he sent the first time

19 and that I needed more drug.

09:17AM 20 Q.   Did Dr. Wakeling require you to fill out any paperwork or

21 do anything in writing before you received samples of drugs?

22 A.   Not me.

23 Q.   Did he require that someone fill out some sort of

24 paperwork before samples would be shipped?

09:17AM 25 A.   I don't know.

1 Q.   What did Dr. Wakeling tell you in response to your

2 request that you wanted AstraZeneca to send you samples of

3 drugs?

4 A.   He told me that I should give it to the mice as it

09:17AM   5 outlined in this paper and that he would ship it.

6 Q.   Basically, an okay-I'll-take-care-of-it type thing?

7 A.   Um-hum.

8 Q.   How many times did you speak with Dr. Vose?

9 A.   Once -- that -- assume that he was not the second -- the

09:18AM 10 person I don't know who it is, but --

11 Q.   Right.

12 A.   -- I know I spoke with him once.

13 Q.   Did you ever communicate with Dr. Wakeling in writing

14 either by e-mail or letter?

09:18AM 15 A.   Not that I recall.

16 Q.   Okay. So you said you spoke with Dr. Vose once; is that

17 right?

18 A.   Um-hum.

19 Q.   Was this on the phone?

09:18AM 20 A.   Yes.

21 Q.   Did you ever have any written communications with him?

22 A.   Not to my -- not that I remember.

23 Q.   On the one incident -- one instance that you did speak

24 with Dr. Vose, who called who?

09:18AM 25 A.   I called him.

1 Q. Why did you call Dr. Vose?

2 A. Because Dr. Wakeling told me to call him to get

3 preformulated drug.

4 Q. Do I understand that you talked to Dr. Wakeling about

09:18AM 5 receiving powdered ICI 182,780 and Dr. Vose about obtaining

6 preformulated ICI 182,780?

7 A. At separate times.

8 Q. I'm just trying to understand. I think I understand the

9 -- that you talked to these guys about two different things.

09:19AM 10 Do I understand correctly that you talked to

11 Dr. Wakeling about receiving powdered ICI 182,780?

12 A. Correct.

13 Q. And then do I understand correctly that you talked to

14 Dr. Vose about receiving the preformulated ICI 182,780?

09:19AM 15 A. Much later.

16 Q. Much later? That's a good point.

17 Do you recall approximately when, or do you recall the

18 approximate dates on which you talked to Dr. Wakeling?

19 A. No.

09:19AM 20 Q. Year?

21 A. I don't know.

22 Q. But you know you talked to Dr. Vose much later. What do

23 you mean by "much later?"

24 A. When I talked to Dr. Wakeling initially, then he sent me

09:19AM 25 the drug, then we used the drug in mice and also in *in vitro*

1 studies and we used it all up. So I don't know how long that

2 took, but I would say a matter of months, anyway, maybe a

3 year. Then we needed more drug so I called Dr. Wakeling

4 again, that's when he told me to call Dr. Vose.

09:20AM 5 Q.   And the powdered ICI 182,780 would have been what you --

6 what was dissolved in ethanol and then spiked into the peanut

7 oil?

8 A.   Correct.

9 Q.   When you spoke to Dr. Vose, what did he tell you about

09:20AM 10 shipping you samples of preformulated 182,780?

11 A.   He said he would.

12 Q.   Did he say anything else?

13 A.   Not to my remembrance.

14 Q.   Did he require that you do anything before he sent the --

09:20AM 15 sent the files of preformulated ICI 182,780?

16 A.   No.

17 Q.   Do you know whether anyone in your lab had to complete

18 any type of paperwork before AstraZeneca would send the lab

19 preformulated 182,780?

09:20AM 20 A.   I do not know.

21 Q.   Who would know?

22 A.   Possibly Dr. Kern.

23 Q.   Okay. And now the third person that you spoke to, was

24 this before or after you talked to Dr. Vose?

09:21AM 25 A.   After.

1 Q. Who called who?

2 A. I called him.

3 Q. Did you have any communications in writing with this

4 third person?

09:21AM 5 A. No.

6 Q. And what was the purpose of calling this third person?

7 A. I wanted to find out what the -- what was in the drug

8 because I was getting ready to publish a paper. I was getting

9 ready to write the paper, actually.

09:21AM 10 Q. And what did he tell you?

11 A. He told me --

12 Q. Do you recall the words he used?

13 A. No.

14 Q. But he told you all of the excipients and their

09:21AM 15 percentages?

16 A. He told me what's in the paper: 10 percent ethanol,

17 10 percent benzyl benzoate and 10 percent benzyl alcohol

18 brought to volume with the castor oil.

19 (Reading stopped.)

09:21AM 20   MS. PIROZZOLO-MELLOWES: Your Honor, I think there

21 was a mistake in reading that.

22   THE COURT: It's -- no, the court reporter took it

23 down correctly, that's fine.

24 (Deposition read as follows:)

09:21AM 25 Q. You don't recall whether or not he specified the units of

1 measure?

2 A.   I do not recall.

3 Q.   How did you know to contact this third person?

4 A.   I called the number that was -- that I had been given for

09:22AM 5 Dr. Vose.

6 Q.   And somebody else answered?

7 A.   I don't know if it was somebody else or if it was

8 Dr. Vose.

9 Q.   So there -- you're saying -- if I'm understanding you

09:22AM 10 correctly, you believe it's possible that it was Dr. Vose that

11 told you the makeup of the formulation but you're not sure?

12 A.   Well, it was whoever answered the phone. That's all I

13 can say about it.

14 Q.   I see. But you called Dr. Vose's direct line?

09:22AM 15 A.   Yeah. I called the same number I had called previously

16 to speak with Dr. Vose.

17 Q.   Who gave you Dr. Vose's phone number?

18 A.   Dr. Wakeling.

19 Q.   Who gave you Dr. Wakeling's phone number?

09:22AM 20 A.   I don't remember.

21 Q.   Do you recall generally how you knew to call Dr. Wakeling

22 that he was the person to call?

23 A.   Either Dr. Lippman or Dr. Kern told me, but I don't know

24 who or when or anything.

09:23AM 25 Q.   But do I understand you correctly that you -- with regard

1   to this third person, that it was a man?

2   A.   Yes.

3   Q.   When you called Dr. Vose the first time, or when you

4   called Dr. Vose, how did you know it was him that answered the

09:23AM   5   phone?

6   A.   I don't remember.

7   Q.   But you feel confident that you were speaking to Dr. Vose

8   the first time?

9   A.   Well, I certainly believed that I was.

09:23AM   10   Q.   At the time, did you believe that the third person that

11   you were talking to was Dr. Vose?

12   A.   I don't recall what I believed.

13   Q.   What do you believe today?

14   A.   I don't believe.

09:23AM   15   Q.   You have no idea who you talked to?

16   A.   Right.

17   Q.   Did you send AstraZeneca drafts of the study protocol

18   that you were going to follow for the research described in

19   McLeskey 1998?

09:23AM   20   A.   No.

21   Q.   Did you ever provide your lab notebooks or raw data to

22   AstraZeneca?

23   A.   No.

24   Q.   Did you record when you received samples from AstraZeneca

09:23AM   25   in your laboratory notebooks?

1   A.   I don't recall.

2   Q.   What was your general practice with regard to recording

3   receipt of samples at the time you were postdoc in Dr. Kern's

4   lab?

09:24AM   5   A.   I would unpack them and if they needed refrigeration, I

6   would put them in the refrigerator or the freezer as

7   appropriate.

8   Q.   Did you have a separate practice as to what you would

9   record about the samples received?

09:24AM   10   A.   No.

11   Q.   Was it your understanding from the beginning of your

12   postdoc in Dr. Kern's lab that AstraZeneca was the source of

13   182,780 or was that something you learned later in time?

14   A.   At the beginning, I had no idea there was such a thing as

09:24AM   15   182,780.

16   Q.   How did you come to find out that? How did you come to

17   find out that AstraZeneca would supply 182,780 to the lab?

18   A.   I'm not sure.

19   Q.   What do you -- what is your best recollection?

09:24AM   20   A.   We had meetings of all the researchers, the breast cancer

21   researchers and it may have come up at that, one of those

22   meetings.

23   Q.   From the Lombardi side of things, not the AstraZeneca

24   side of things, but from the Lombardi side of things, was

09:25AM   25   procuring samples as simple as calling and asking for them, or

1   was there an internal protocol that had to be followed first?

2   A.   I was not aware of an internal protocol.

3   Q.   Do you know how long it took in between the time you

4   talked to Dr. Wakeling and the time that you received the

09:25AM   5   powdered ICI 182,780?

6   A.   I think it was a matter of weeks.

7   Q.   Do you recall how long it took from the time you talked

8   to Dr. Vose to then receive the preformulated ICI 182,780?

9   A.   Probably about the same.

09:25AM   10   Q.   And you personally do not recall filling out any forms or

11   signing anything in regard to samples, correct?

12   A.   Correct.

13   Q.   I want to make sure we're absolutely on the same page.

14   So before you started, at any time, did you send

09:25AM   15   AstraZeneca a statement of proposed investigation forms?

16   A.   No.

17   Q.   Do you know whether or not Dr. Kern had sent AstraZeneca

18   a statement of proposed investigation forms?

19   A.   No.

09:25AM   20   Q.   No, you do not know, or no, he did not?

21   A.   No, I don't know.

22   Q.   Did you fill out any other forms for AstraZeneca before

23   you started your work on McLeskey 1998?

24   A.   No.

09:26AM   25   Q.   Do you know whether anyone else in your group filled out

1 any other forms for AstraZeneca?

2 A.   I don't know.

3 Q.   Before starting the work on --

4 A.   I don't know. I know nothing.

09:26AM 5 Q.   Did you personally ever request any samples from

6 AstraZeneca in writing?

7 A.   No.

8 Q.   Okay. So you received powdered ICI 182,780 from Dr. Alan

9 Wakeling, correct?

09:26AM 10 A.   Correct.

11 Q.   Did Dr. Wakeling send the powdered samples directly to

12 you?

13 A.   I don't recall. I got them, but I don't remember who

14 they were addressed to.

09:26AM 15 Q.   You don't have a specific recollection of whether they

16 came directly to you or whether Dr. Kern gave them to you?

17 A.   I opened the package, or I got the package. I don't know

18 if I got the package from a mailman or from Dr. Kern. I don't

19 know.

09:27AM 20 Q.   Okay. But you opened the package?

21 A.   Yeah.

22 Q.   Do you recall approximately when that was when you opened

23 the package?

24 A.   No.

09:27AM 25 Q.   Was it in 1997?

1 A.   Oh, no. It was way before that.

2 Q.   Way before that? So 1996, 1995?

3 A.   It was before 1993.

4 Q.   Before 1993?

09:27AM 5 A.   Yes.

6 Q.   How was the powder sample packaged? Was it in a -- a

7 bottle or -- how did it arrive, do you recall?

8 A.   I think it was just in a little jar.

9 Q.   Would the receipt of that sample have been logged in the

09:27AM 10 lab?

11 A.   No.

12 Q.   Now, if I understand you correctly, Dr. Wakeling gave you

13 information on administration of the drug, correct?

14 A.   Correct.

09:27AM 15 Q.   Did Dr. Wakeling send you instructions on how to

16 formulate the 50-milligram per milliliter concentration of

17 ICI 182,780 and ethanol and peanut oil?

18 A.   He didn't send them to me, no.

19 Q.   Did he send you instructions regarding making the

09:28AM 20 formulation?

21 A.   No.

22 Q.   How did you know to do that?

23 A.   He told me over the phone.

24 Q.   Okay. So Dr. Wakeling told you how to administer it, and

09:28AM 25 he also told you how to make the formulation that's recorded

1 in McLeskey 1998 concerning ethanol and peanut oil?

2 A.   Exactly.

3 Q.   And you testified earlier, I think, that you were

4 actually the person that had actually dissolved the

09:28AM 5 ICI 182,780 in ethanol and then spiked it into the peanut oil?

6 A.   Correct.

7 Q.   Why did you use a concentration of 50-milligrams per

8 milliliter?

9 A.   Because that's what Dr. Wakeling said to do.

09:28AM 10 Q.   Dr. Wakeling did not discuss any sort of confidentiality

11 with you --

12 A.   No.

13 Q.   -- when -- when you spoke with him?

14 A.   No --

09:28AM 15 Q.   Sorry, it needs to be verbal.

16 A.   Sorry, no.

17 Q.   If you'll turn to Page 698 of Exhibit 5, do you see a

18 paragraph headed, the title Drugs, and then about seven lines

19 down, we see the lined sentence for the experiments depicted

09:29AM 20 in Figure 1, B and C, 50-milligram per milliliter

21 preformulated drug in a vehicle of 10 percent ethanol, 15

22 percent benzyl benzoate, 10 percent benzyl alcohol brought to

23 volume by castor oil was supplied by B.M. Vose, Zeneca

24 Pharmaceuticals.

09:29AM 25   Do you see that?

1 A. Yes.

2 Q. Is this the preformulated drug that we were just

3 discussing that you procured via telephone conference with

4 Dr. Vose?

09:29AM 5 A. Yes.

6 Q. Approximately when did you receive the preformulated

7 ICI 182,780 from Dr. Vose?

8 A. All I can tell you is it was before 1993.

9 Q. The preformed -- both -- you received both the powdered

09:29AM 10 ICI and the preformulated ICI before 1993. Is that what

11 you're saying?

12 A. Yes.

13 Q. How do you know that it was before 1993?

14 A. In 1993, I received a faculty appointment, and then I was

09:30AM 15 no longer a postdoc. And at that point, the animal

16 experiments were done.

17 Q. Were you the person that opened the package of the

18 preformulated ICI 182,780?

19 A. Yes.

09:30AM 20 Q. Do you recall how many preformulated samples were sent to

21 you?

22 A. No.

23 Q. Do you recall if those samples were in vials?

24 A. No.

09:30AM 25 Q. How were -- how were the preformulated samples packaged?

1 A. I don't recall.

2 Q. What documentation accompanied the preformulated

3 ICI 182,780?

4 A. I don't recall.

09:30AM 5 Q. Do you recall whether or not there was documentation

6 included with the preformulated ICI 182,780?

7 A. I don't recall.

8 Q. If you wanted to try to remember, who would you talk to?

9 A. Nobody. I mean, I -- there's nobody. I think it's lost

09:31AM 10 to posterity.

11 Q. So do I understand correctly that at the time you

12 received the preformulated ICI 182,780, you did not know what

13 excipients were present in the formulation -- in that

14 formulation?

09:31AM 15 A. Correct.

16 Q. Did you have an understanding that the preformulated

17 ICI 182,780 could not be used in humans?

18 A. Nothing we had in our lab could be used in humans.

19 Q. Were you given specific instructions from AstraZeneca

09:31AM 20 that it should not be used in humans?

21 A. I don't recall.

22 Q. Turning back to Page 698 in the drug section again, you

23 see the text that says, In a vehicle of 10 percent ethanol, 15

24 percent benzyl benzoate, 10 percent benzyl alcohol brought to

09:31AM 25 volume with castor oil.

1   Do you recall who actually wrote that text?

2   A.   I did.

3   Q.   Did you test or analyze the formulation in any way?

4   A.   No.

09:31AM   5   Q.   Were you told that the preformulated ICI 182,780 that you

6   received should not be administered intramuscularly?

7   A.   I was told to administer it subcutaneously to my --

8   Q.   When the person who answered Dr. Vose's phone gave you

9   the excipients present in the preformulated ICI 182,780, were

09:32AM   10   you sworn to secrecy?

11   A.   No.

12   Q.   Why did you want to include those details in McLeskey

13   1998?

14   A.   That's how I was instructed to write a paper when I was

09:32AM   15   in my predoctoral, was to include such things.

16   Q.   Have you searched your personal files for all documents

17   relating to either the powdered ICI 182,780 received or the

18   preformulated ICI 182,780 that you received?

19   A.   I don't have any personal files about this.

09:32AM   20   Q.   Did I understand you correctly that you do not recall

21   whether or not the person that answered Dr. Vose's phone told

22   you that the percentages were in weight to volume or

23   volume-to-volume?

24   A.   I do not recall.

09:33AM   25   Q.   Did you assume that the percentages were either in weight

1 to volume or volume-to-volume?

2 A.   I don't think I ever thought about it one way or the

3 other.

4 Q.   Have you thought about it since McLeskey 1998 was

09:33AM 5 published?

6 A.   Yes, but I have no basis for knowing which way it was.

7 Q.   So as you sit here today, you don't know whether or not

8 the percentages were in weight to volume or volume-to-volume?

9 A.   I do not know.

09:33AM 10 Q.   So what did you mean when you said "These studies

11 indicate that estrogen independence may be achieved"?

12 A.   I meant that in our engineered model, we achieved

13 estrogen-independent tumor growth in mice through engineering

14 the cell to express in FGF.

09:33AM 15 Q.   So in the context of your experiment, you wanted to use

16 the aromatase inhibitors and ICI 182,780 to shut down any

17 remaining estrogen that might have been present?

18 A.   Yes.

19 Q.   And you wanted to shut down any remaining estrogen so

09:34AM 20 that you could isolate or investigate the estrogen independent

21 cell growth; is that right?

22 A.   Well, we wanted to demonstrate that cells as -- when

23 injected into mice to form tumors, were not affected by -- by

24 different ways of shutting down the estrogen pathway.

09:34AM 25 Q.   So you used the aromatase inhibitors to shut down the

1 estrogen pathway so you could demonstrate that the hormonal

2 independent cancer cells were not affected and continued to

3 grow; is that right?

4 A.   Continued to make tumors --

09:34AM   5 Q.   Continued to make tumors.

6 A.   -- and grow as tumors.

7 Q.   And the same thing -- so you used the ICI 182,780 to act

8 as a pure antiestrogen, shut down any estrogen receptors so

9 that you could see if the estrogen-independent cells would

09:35AM   10 continue to grow?

11 A.   Correct. As tumors --

12 Q.   As tumors?

13 A.   -- in -- in mice.

14   The reason I keep saying that is, of course, we can

09:35AM   15 grow cells in tissue culture, but I wasn't talking about that.

16 I'm talking about mice.

17 Q.   Okay. So in order to study the hormonal-independent

18 cells, you wanted to deliberately target any remaining

19 estrogen production or any remaining estrogen receptors first;

09:35AM   20 is that right?

21 A.   Correct.

22 Q.   And the reason that you used the aromatase inhibitors in

23 the ICI 182,780 to shut down the remaining estrogen is because

24 they target the body's estrogen differently than tamoxifen

09:35AM   25 does; is that right?

1 A.   Correct.

2 Q.   Okay. At the time you were using the ICI 182,780,

3 because you understood that it would interrupt estrogen-based

4 pathways?

09:35AM   5 A.   It would inactivate the estrogen receptor.

6 Q.   Are you saying -- you keep directing me to the fact that

7 this was -- these experiments were done in mice.

8   Are you saying that this work has no applicability to

9 human subjects?

09:36AM   10 A.   I don't know of any applicability to humans.

11 Q.   The title says Cross-Resistant *in Vivo*.

12   What does "cross-resistant *in vivo*" mean?

13 A.   "Cross-resistant" means that the cells formed big tumors

14 even in the face of the ICI 182,780, or the aromatase

09:36AM   15 inhibitors. And "*in vivo*," refers to the fact that we used

16 mice or an animal to test it. *In vitro* would be, like, cell

17 culture.

18 Q.   So what does "cross-resistant" mean here? Resistance to

19 several different types of drugs?

09:36AM   20 A.   It means also resistant.

21 Q.   So it's basically saying resistant to several types of

22 drugs?

23 A.   Yes.

24 Q.   So this -- okay.

09:37AM   25   Now McLeskey 1998 was published in the Journal of

1 Clinical Cancer Research, correct?

2 A.   Correct.

3 Q.   And you were the person that determined whether or not

4 you wanted to cite references in McLeskey 1998?

09:37AM 5 A.   Me and Dr. Kern.

6 Q.   Did you keep laboratory notebooks from your lab when --

7 when you -- you were at Georgetown?

8 A.   Of course.

9 Q.   What happened to those lab notebooks?

09:37AM 10 A.   I brought them to Maryland with me and then when I was

11 getting ready to retire, I threw them away.

12 Q.   With the rest of the documents?

13 A.   Mm-hmm.

14 Q.   Going back to the preformulated samples that you received

09:37AM 15 from Dr. Vose, if I understand you -- understood you

16 correctly, you thought that you had received the samples

17 before 1993.

18 A.   Yes.

19 Q.   Is it possible that you received them in the first

09:37AM 20 quarter of 1993?

21 A.   I don't think so, but I don't know really.

22 Q.   You don't know for sure one way or the other?

23 A.   Well, we had finished the animal experiments by the time

24 I got my faculty appointment.

09:38AM 25 Q.   When exactly did you get your faculty appointment?

1 A.   I believe it was July 1st, 1993.

2 Q.   Okay. So you knew -- you think you received the samples

3 before July 1, 1993?

4 A.   Well, you know, the experiments with the tumors were

09:38AM 5 several months ago, several months long. So it had to have

6 been quite a bit before July.

7 Q.   Okay. So you do or do not think it's possible that you

8 received the samples in early 1993?

9 A.   I don't know.

09:38AM 10 Q.   Okay. When you were talking to the unnamed person that

11 answered Dr. Vose's phone, did you ask who you were talking

12 to?

13 A.   I don't recall.

14 Q.   But you do recall that you talked to Dr. Wakeling twice?

09:38AM 15 A.   Yes.

16 Q.   And you do recall that you were the one that called him

17 both times?

18 A.   Yes.

19 Q.   And you do recall that he gave you instructions on how to

09:38AM 20 make the peanut oil formulation?

21 A.   Yes.

22 Q.   And you do recall that he gave you instructions on

23 administration of the formulation?

24 A.   Correct.

09:39AM 25 Q.   And he's the person that told you to talk to Dr. Vose

1 about the preformulation -- preformulated ICI 182,780?

2 A.   Yes.

3 Q.   And you remember calling Dr. Vose regarding the

4 preformulated drug, correct?

09:39AM   5 A.   Yes.

6 Q.   Okay. But you don't remember whether there was a label

7 on the preformulated drug vials that you received, correct?

8 A.   I'm sure there was, but I don't remember one.

9 Q.   You don't recall whether there was any paperwork that you

09:39AM   10 received with the samples?

11 A.   I don't recall.

12 Q.   You can't remember the name of the person that told you

13 the identity of the formulation?

14 A.   No.

09:39AM   15 Q.   But do you remember that the person did not tell you to

16 keep the formulation secret, correct?

17 A.   Yes, I remember that.

18 Q.   You don't remember anything else in particular that he

19 said?

09:39AM   20 A.   No.

21 Q.   After you finished the experiments that are reflected in

22 McLeskey 1998, was there any preformulated drug left over?

23 A.   I don't remember.

24 Q.   If there had been drug left over, what would you have

09:40AM   25 done with it?

1 A.   Discard it.

2 Q.   How?

3 A.   Down the sink probably.

4 Q.   You don't recall any specific instructions from

09:40AM 5 AstraZeneca to return any unused material?

6 A.   No.

7 Q.   When you talked to Dr. Wakeling about the ethanol peanut

8 oil formulation, did he say anything other than tell you the

9 order of the steps?

09:40AM 10 A.   Not that I recall.

11 Q.   Did he tell you anything about the development of the

12 formulation within AstraZeneca?

13 A.   No.

14 Q.   I recall asking you about AstraZeneca, and I recall

09:40AM 15 asking you about O'Melveny & Myers. I just want to make sure

16 we're clear.

17   Did anyone at any time ever tell you to preserve your

18 documents that related to McLeskey 1998?

19 A.   No.

09:40AM 20 Q.   Did I understand you correctly that you were not privy to

21 any sort of confidentiality agreement between AstraZeneca at

22 Lombardi, correct?

23 A.   Correct.

24 Q.   Dr. Wakeling is the person that informed you of the

09:41AM 25 existence of the preformulated drug?

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 1  A.   Correct.

 2  Q.   Dr. McLeskey, may I direct your attention to Exhibit

 3  No. 9, that is the declaration of Sandra McLeskey, Ph.D.?

 4  A.   Yes.

 5  Q.   And feel free, of course, to review the declaration.

 6       My question is, is there anything sitting here today

 7  that you wish to change or correct in this declaration?

 8  A.   No.

 9  (Reading stopped.)

10       MS. PIROZZOLO-MELLOWES:  The questioning now

11  continues by Ms. Pensabene and I'll play the part of

12  Ms. Pensabene.

13       THE COURT:  Okay.  Well, as long as -- as long as the

14  record is clear who is doing the questioning.

15       So maybe Mr. Rizzi you should do it, so the court

16  reporter knows that when you're speaking, it's Ms. Pensabene.

17       MR. RIZZI:  Of course, Your Honor.

18       THE COURT:  Page 210.

19  (Deposition read as follows:)

20  Q.   Dr. McLeskey, at the time you were doing that research

21  that led to the paper of Exhibit 5, I think it is, was that

22  early in your career as a -- as a researcher?

23  A.   Yes.

24  Q.   Okay.  And at that time, were you experienced with

25  dealing with pharmaceutical companies?
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09:41AM 5
09:41AM 10
09:41AM 15
09:42AM 20
09:42AM 25

1   A.   No.

2   Q.   Was Dr. Kern the head of the lab you worked in at

3   Lombardi Cancer Center at Georgetown?

4   A.   Yes.

09:42AM   5   Q.   And was he your boss?

6   A.   Yes.

7   Q.   And what was Dr. -- and was Dr. Lippman the head of the

8   Cancer Center?

9   A.   Yes.

09:42AM   10   Q.   And was Dr. Lippman Dr. Kern's boss?

11   A.   Yes.

12   Q.   Back at the time that you were doing this research that

13   we've been talking about, were you familiar with the

14   statements of proposed investigations or forms or material

09:42AM   15   transfer agreements?

16   A.   No.

17   Q.   Okay. Who in the lab at that time would have signed a

18   statement of material -- of proposed investigation or a

19   material transfer agreement with regard to samples with

09:43AM   20   AstraZeneca?

21   A.   It would either have been Dr. Kern or Dr. Lippman.

22   Q.   Okay. You would not have done so?

23   A.   No.

24   Q.   Okay. And at the time, did you -- let me back up.

09:43AM   25   Did you have one way or another -- do you know one way

1 or another whether there was a statement of proposed

2 investigation or material transfer agreement with AstraZeneca?

3 A. I did not know.

4 Q. At the time, did you ever consider whether there was a --

09:43AM 5 some kind of an agreement or a statement of proposed

6 investigation or material transfer agreement with AstraZeneca

7 regarding samples?

8 A. I did not.

9 Q. Why not?

09:43AM 10 A. It just didn't occur to me.

11 Q. Okay. When you first called for samples, did you tell

12 Dr. Wakeling that you were calling from Dr. Lippman or

13 Dr. Kern's group?

14 A. I -- yes -- well, I don't know what I said, but I'm sure

09:44AM 15 I said something like that.

16 Q. When -- when you first called for samples, did you

17 understand whether Dr. Lippman or Dr. Kern had a preexisting

18 relationship with AstraZeneca?

19 A. I knew that Dr. Lippman knew.

09:44AM 20 Q. Now, once you got the preformulated ICI 182,780, was it

21 -- did you understand that its use was restricted to animals?

22 A. That's all I did was animals.

23 Q. Could you have used the preformulated ICI 182,780 in

24 people?

09:44AM 25 A. No.

1 Q. Could you have sent the preformulated ICI 182,780 to

2 anyone in the public to use?

3 A. No.

4 Q. Was it your understanding that the use of the

09:44AM 5 preformulated sample was restricted to use in the Georgetown

6 laboratory in animals?

7 A. I don't know how to answer that. That was -- that was

8 what I was going to use the drug for.

9 Q. Well, did you think that -- that you could give it to

09:44AM 10 anyone else to use in research in people?

11 A. No.

12 Q. Was the animal work in your laboratory publicly

13 available?

14 A. Not until it was published.

09:45AM 15 Q. Could members of the public have access to your

16 laboratory notebooks before they were -- before the paper was

17 published?

18 A. No.

19 Q. Did you send the manuscripts or the draft of Exhibit 5 to

09:45AM 20 AstraZeneca anyone at AstraZeneca to review?

21 A. No.

22 Q. Was sending the manuscript or draft of Exhibit 5 to

23 AstraZeneca to review have been your responsibility at the

24 time?

09:45AM 25 A. No.

1 Q.   Okay. When you called to ask for the formulation did you

2 tell anyone at AstraZeneca that you planned to publish the

3 formulation?

4 A.   I said I was preparing a manuscript.

09:45AM 5 Q.   Did you ask anyone at AstraZeneca permission to publish

6 the formulation?

7 A.   No.

8 Q.   Okay. I just want to ask a couple of questions about the

9 laboratory notebooks and materials that I know you said you

09:45AM 10 destroyed when you retired. Did AstraZeneca own those

11 laboratory notebooks that you described?

12 A.   No.

13 Q.   Did AstraZeneca have control over those laboratory

14 notebooks?

09:46AM 15 A.   No.

16 Q.   Could anyone at AstraZeneca have told you what to do with

17 your laboratory notebooks?

18 A.   No.

19 Q.   When you destroyed the -- threw away the laboratory

09:46AM 20 notebooks, were -- were you aware that the litigation with

21 Teva was over?

22 A.   Yes.

23 Q.   At the time you threw away the laboratory notebooks, did

24 you know about this litigation?

09:46AM 25 A.   No.

1   Q.   Did you learn about the litigation after you threw away

2   the notebooks?

3   A.   Yes.

4   Q.   Did you view -- with regard to the two different

09:46AM   5   formulations of ICI 182,780 in your paper, did you view the

6   ICI 182,780 in peanut oil and the preformulated ICI 182,780 as

7   interchangeable?

8   A.   Yes.

9   Q.   In your work did you do any pharmacokinetic analysis of

09:46AM   10   the drugs that you used in the paper at Exhibit 5?

11   A.   No.

12   Q.   Did you do any blood level analysis of the drugs you used

13   in the work that you did in the paper at Exhibit 5?

14   A.   No.

09:47AM   15   Q.   In your work at Exhibit 5 did the ICI 182,780 have any

16   effect on tumor growth or the metastasis of tumors?

17   A.   No.

18   MR. RIZZI: That's the end of Ms. Pensabene

19   questioning.

09:47AM   20   THE COURT: Thank you.

21   (The examination is continued by Ms. Waldron.)

22   Q.   But your testimony is that you believe that AstraZeneca

23   has paid you less than $10,000 to date; is that correct?

24   A.   Correct.

09:47AM   25   Q.   Yeah -- let's -- actually, that's a really good point.

1 Let me rephrase my question. Do you currently understand that

2 in the late nineties at the time you were doing your postdoc,

3 Dr. Ellis was doing clinical trials related to fulvestrant?

4 A.   I did.

09:47AM 5 Q.   When did Dr. Ellis come to Georgetown?

6 A.   I'm not sure, but it was in the late nineties I think.

7 Q.   Did the person who gave you the information about the

8 formulation understand that you were asking in connection with

9 publishing McLeskey 1998?

09:48AM 10 A.   I told him that I was preparing the manuscript.

11 Q.   I believe you testified earlier that you believed that

12 your current consultancy with O'Melveny & Myers began in June

13 of 2014; is that correct?

14 A.   Yes.

09:48AM 15 Q.   Do you know the date that you signed the agreement with

16 O'Melveny & Myers?

17 A.   No.

18 Q.   Do you know if it was late or early June?

19 A.   It was not early June.

09:48AM 20 Q.   Did the consultancy you had with regard to the Teva

21 litigation ever formally expire?

22 A.   I don't know.

23 Q.   Are you aware of being formally released from that

24 agreement?

09:48AM 25 A.   No.

        1   Q.   Do you have any reason to believe that it didn't

        2   continue -- continue on?

        3   A.   I'm under the impression that it did not continue.

        4   MS. PIROZZOLO-MELLOWES: That concludes the reading.

09:48AM 5   I'd like to offer into evidence the exhibits that

        6   were referenced --

        7   THE COURT: Yes.

        8   MS. PIROZZOLO-MELLOWES: -- in the transcript. They

        9   are DTX-545, DTX- 546, DTX-547, DTX- 548, DTX- 22, DTX- 552.

09:49AM 10   THE COURT: Mr. Prugo, any objections?

        11   MR. PRUGO: I'm not sure what all the exhibits are,

        12 your Honor, so.....

        13   THE COURT: They are in the binder. So two of them

        14 are the subpoenas, I don't know that they have any evidentiary

09:49AM 15 value.

        16   MR. PRUGO: No, I agree.

        17   THE COURT: The other are her declarations and

        18 responses.

        19   MR. PRUGO: No problem there, your Honor, that can go

09:49AM 20 into evidence. That's DTX-0552 to -- the McLeskey

        21 declaration, sure.

        22   THE COURT: What about DTX-547?

        23   MR. PRUGO: That seems to be another subpoena, your

        24 Honor. There is no evidentiary value of the subpoena.

09:50AM 25   THE COURT: Those are the responses and objections.

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09:50AM   1   MR. PRUGO: Well, if the subpoena doesn't go in -- I

2   guess we would maintain the objections. But, frankly, if we

3   haven't objected to the testimony, then I don't really see the

4   relevance of the objection to the subpoena.

09:50AM   5   THE COURT: DTX-547 is not a subpoena.

6   MR. PRUGO: My apologies, your Honor. No problem

7   with that exhibit.

8   THE COURT: Okay. So 547 and 552 are in evidence,

9   545, 546 are not in evidence.

09:50AM   10   And 22 is in, is it not?

11   MS. PIROZZOLO-MELLOWES: I believe it is.

12   THE COURT: DTX-22 is in, is it not?

13   MR. PRUGO: Yeah, that's already in, your Honor. I

14   believe that's already in.

09:50AM   15   MS. PIROZZOLO-MELLOWES: And DTX-548, additional

16   responses.

17   THE COURT: Yes. Any objection?

18   MR. PRUGO: Oh, of course not, no.

19   THE COURT: Okay in evidence.

09:51AM   20   (DEFENDANT EXHIBITS DTX-545, 546 AND 548 WERE RECEIVED IN

21   EVIDENCE)

22   MS. PIROZZOLO-MELLOWES: That conclude McLeskey.

23   We would like to read an additional transcript of Dr.

24   Francis Kern.

09:51AM   25   THE COURT: Okay. And are you playing the role Dr.

United States District Court
Camden, New Jersey

1 Kern?

2   THE COURT: Okay, when everybody is ready.

3 (THE DEPOSITION OF DR. FRANCIS G. KERN WAS READ BY MS.

4 PIROZZOLO-MELLOWES INTO THE RECORD)

09:52AM 5 MS. PIROZZOLO-MELLOWES:

6 Q.   Could you please state your full name for the record?

7 A.   Francis Gerard Kern.

8 Q.   Where do live?

9 A.   I live in Highland Park, New Jersey.

09:52AM 10 Q.   Do you understand that you are under oath today?

11 A.   Yes, I do.

12 Q.   Is there any reason that you cannot provide full and

13 honest testimony today?

14 A.   No, there is not.

09:52AM 15 Q.   Would it be okay with you if I call Exhibit 3 "McLeskey

16 1998?"

17 A.   Fine.

18 Q.   Did Dr. Gellert ask you anything about the samples that

19 your lab received from AstraZeneca?

09:53AM 20 A.   I don't know if it was Lisa or Dr. Gellert who answered

21 those -- asked those particular questions. I don't know the

22 direct question that -- that addressed what you have just

23 asked, but I think it became apparent that, yes, it was all

24 about us receiving some samples to accomplish this work.

09:53AM 25 Q.   What did you tell Dr. Gellert about your lab's receipt of

1 the samples from AstraZeneca?

2 A.   That it was 20 years ago, I didn't remember too much

3 about it.

4 Q.   Just to make sure I understand, did I understand you

09:53AM 5 correctly that you only talked to Dr. Gellert one time on the

6 phone?

7 A.   Correct.

8 Q.   Did you ever meet with Dr. Gellert in person?

9 A.   No.

09:53AM 10 Q.   Can you please tell me what your duties are, what's that

11 mean?

12 A.   I am the head of the oncology scouting. We do search and

13 evaluation of any licensing opportunities, partnering

14 opportunities, the academic medical centers to acquisitions of

09:54AM 15 company, biotech companies. So it spans that range, scouting

16 making recommendations as to who should be a partner or who

17 should be -- you know, who we should license from, who we

18 should acquire.

19 Q.   Going back now to Georgetown, approximately how long were

09:54AM 20 you at Georgetown?

21 A.   I left in '97.

22 Q.   Have you ever done any formulation work?

23 A.   Not personally, no.

24 Q.   Do you consider yourself a formulator?

09:54AM 25 A.   No.

1 Q. I assume this means you have not formulated any

2 parenteral drugs?

3 A. Personally myself? No.

4 Q. Did you have access to Dr. McLeskey's laboratory

09:54AM 5 notebooks and data?

6 A. Access? I guess I could ask to see them if I wanted to,

7 so in that sense I had access, yeah.

8 Q. Just to be clear, you never had copies of Dr. McLeskey's

9 notebooks or data underlying the McLeskey 1998?

09:55AM 10 A. No.

11 Q. When the lab received documentation, say with samples,

12 how would those documents have been kept in your lab?

13 A. You know, it's hard to say back in 1993, or -- I guess it

14 was just put in a file and put in a file cabinet.

09:55AM 15 Q. Do you have any specification recollection of your

16 procedures?

17 A. No.

18 Q. Who was in charge would you say, was in charge of the day

19 today activities concerning the research that led to McLeskey

09:55AM 20 1998?

21 A. I was.

22 Q. Would you say you directed the research?

23 A. Yes.

24 Q. What were your duties as they pertained to the research?

09:55AM 25 What does it mean to direct the research?

1 A.   You know, you'd meet maybe not daily but at least weekly

2 with Dr. McLeskey, go over the data that had been generated

3 the last week, make suggestions as to what new experiments

4 should be performed.

09:56AM 5 Q.   Who came up with the ideas for the research that led to

6 McLeskey 1998?

7 A.   Again, it's a long time ago, so generally I came up with

8 the ideas for the lab, for what was going on in that lab.

9 Q.   How did you decide what drugs you would study or what

09:56AM 10 drugs you would include in the research?

11 A.   Relating to this paper or --

12 Q.   Yeah. Let me take a step back.

13   How did you decide which drugs you would study in

14 relation to McLeskey 1998?

09:56AM 15 A.   We had earlier found that transfection of this particular

16 growth factor, okay, into these breast cancer cells that

17 originally required estrogen for their growth made them

18 resistant to a drug called tamoxifen. Tamoxifen also has what

19 are called estrogenic actions. Even though it functions

09:56AM 20 primarily as antiestrogen, it may -- it has some agnostic

21 effects to the estrogen receptors.

22   THE COURT: Agonistic.

23 A.   Agonistic effects to the estrogen receptors. Others had

24 shown that growth factors similarly could simulate the type of

09:57AM 25 agonistic effect on a estrogen receptor. We wanted to probe

1 into the question of whether the mechanism by which this

2 particular growth factor caused this resistance to this drug

3 tamoxifen was through this accentuating the agonistic effects

4 of tamoxifen. So we approached that question by using this

09:57AM 5 pure -- what's called pure antiestrogen, the ICI 182,780,

6 because that causes degradation of the estrogen receptor. So

7 if you could show that the cells could still grow in the

8 absence of estrogen when they had been treated with this drug,

9 that meant that the estrogen receptor was gone, okay, and

09:57AM 10 consequently they had bypassed the need for the estrogen

11 receptor signaling in this particular breast cancer cell.

12   Follow?

13 Q. Generally speaking, I think.

14 A. Okay.

09:58AM 15 Q. So, to hit the highlights, do I understand that you knew

16 that tamoxifen had partial agonist activity?

17 A. Right.

18 Q. But ICI 182,780 was a pure antiestrogen?

19 A. Right.

09:58AM 20 Q. And you new that ICI 182,780 would cause degradation of

21 the receptor?

22 A. Right.

23 Q. When did you learn about the resistance of ICI 182,780?

24 A. Hard to tell. You know, early nineties, probably.

09:58AM 25 Q. To the best of your recollection, how did you find out

1 about ICI 182,780?

2 A.   I, you know. I knew -- there were a lot of experiments

3 in the literature on precursor to this 162 something, 464,

4 perhaps. Was it 464?

09:58AM 5 Q.   That sound right. I'm not sure either.

6 A.   So, you know, there was a lot of publications on that. I

7 don't know how we became aware that that had been replaced,

8 you know, with 182,780. But when we started this work, we

9 wanted to get as close as we could to a drug that would

09:59AM 10 eventually make, or more likely to make its way to the clinic.

11 Q.   When did you start this work? When was the origin?

12 A.   You know, my guess it was probably in 1993. And we

13 published a paper in 1993 showing that tamoxifen resistance in

14 cancer research with FGF 4 transfected breast cancer cells, so

09:59AM 15 it was a continuation of that work. So my guess is 1993,

16 around there.

17 Q.   How did you first procure ICI 182,780 from AstraZeneca?

18 A.   Yeah. I'm not clear on that.

19 Q.   Was there already ICI 182,780 in the lab when you

09:59AM 20 started?

21 A.   I don't think so. You know, others at the Lombardi

22 Cancer Center may have been using it for other experiments. I

23 would assume, you know, that we would have had to request it,

24 the compound, for our particular experiments, you know. But

10:00AM 25 like I said, it was a long time ago. I noticed that Bob Dixon

1 is an author on this paper. You know, he had much better

2 relations with Alan Wakeling and with the two people who gave

3 us the aromatase inhibitors, you know. It could have been

4 either I requested it or he requested it, you know, but I'm

10:00AM 5 pretty sure that he had to have made that particular request

6 for these particular experiments.

7 When I moved to Southern Research I did make a

8 separate request to Zeneca, I believe, at the time, you know,

9 and I had to fill out their forms and describe the experiments

10:00AM 10 that I was going to perform at Southern Research. So that's

11 what's making me think we had to do something similar when we

12 were at the Lombardi Cancer Center.

13 Q.   During the telephone call in late August with Ms.

14 Pensabene, AstraZenica's representative, Arthur Mann and

10:01AM 15 yourself, were you asked about whether you had any documents

16 pertaining to McLeskey 1998?

17 A.   I believe so.

18 Q.   What did you say?

19 A.   I said I didn't think so.

10:01AM 20 Q.   Did you look for documents at that time?

21 A.   At that time?

22 Q.   Yes.

23 A.   No. I mean, I looked on a few thumb drives that I had

24 around from -- but they were actually from another -- another

10:01AM 25 job, you know. Nothing was on those.

1 Q.   Were you specifically asked to look for documents at that

2 teleconference?

3 A.   I don't recall.

4 Q.   Have you ever before read the subpoena that's marked as

10:01AM   5 Exhibit 2? Have you ever received a request from AstraZeneca

6 or any of AstraZenica's representatives requesting documents

7 related to McLeskey 1998?

8 A.   No.

9 Q.   Have you ever been told by AstraZeneca or any of its

10:02AM   10 representatives not to destroy any documents you had related

11 to McLeskey 1998?

12 A.   No not to destroy? I was never told that, no.

13 Q.   Okay. So you only talked to Dr. Gellert at one time?

14 A.   Right.

10:02AM   15 Q.   Dr. Gellert asked you about your recollection of

16 receiving samples from AstraZeneca?

17 A.   I don't know if it was Dr. Gellert or Lisa.

18 Q.   What did you say on this telephone conference regarding

19 your recollection about receiving samples from AstraZeneca?

10:02AM   20 A.   That we must have received them. I wasn't sure. I think

21 I said at the time I wasn't sure who was responsible at that

22 time.

23 Q.   Did you talk about whether or not you had a

24 confidentiality agreement with AstraZeneca?

10:02AM   25 A.   I believe we did.

1 Q. Did you have a confidentiality agreement with AstraZeneca

2 in the early nineties?

3 A. Well, confidentiality or material transfer?

4 Q. Well, let's start with confidentiality. Did you ever at

10:03AM 5 anytime enter into a confidentiality agreement with

6 AstraZeneca?

7 A. I don't recall. I don't know.

8 Q. Well --

9 A. Material transfer, or whatever, you know, they -- they

10:03AM 10 tend to call it. I don't know.

11 Q. Okay. Did you ever sign anything titled "confidentiality

12 agreement?"

13 A. I don't recall doing so.

14 Q. Do you have any reason to believe -- you have no reason

10:03AM 15 to believe that you did sign a document entitled

16 "confidentiality agreement?"

17 A. I have no reason to believe that I did not either. So,

18 yeah, I -- I just don't recall.

19 Q. You currently do not possess any copies of any

10:03AM 20 confidentiality agreements that you signed with AstraZeneca,

21 correct?

22 A. I do not.

23 Q. Do you have any documentation indicating that you signed

24 anything called a "confidentiality agreement" with

10:03AM 25 AstraZeneca?

1 A.   I do not.

2 Q.   Now, you've referred to a material transfer form. Did I

3 understand you correctly?

4 A.   Usually It's called a material transfer agreement, an

10:04AM 5 MTA.

6 Q.   Okay. In your words what is an MTA? What are you

7 referring to?

8 A.   You are asking a company for, you know, a portion of a

9 compound that is generally a proprietary compound not publicly

10:04AM 10 available, that you are asking them for a sample to allow you

11 to perform some laboratory experiments.

12 Q.   Can you say with certainty that you signed a material

13 transfer agreement with AstraZeneca in relation to McLeskey

14 1998?

10:04AM 15 A.   With certainty? No, I can't say with certainty.

16 Q.   You don't currently possess any copies of material

17 transfer agreements that you signed with AstraZeneca in

18 relation to McLeskey 1998, correct?

19 A.   I do not.

10:04AM 20 Q.   I will confess I barely remember where we just left off.

21 I believe you said that you did not have your own personal lab

22 notebooks or data relating to McLeskey 19918; is that right?

23 A.   Um-hum.

24 Q.   And did not copy for yourself Dr. McLeskey's laboratory

10:05AM 25 notebooks or data; is that correct?

1 A.   That's correct.

2 Q.   So, your edits and contributions continued after you left

3 Lombardi Center; is that correct?

4 A.   For this particular paper? Yes.

10:05AM 5 Q.   So, McLeskey 1998?

6 A.   Right.

7 Q.   Am I correct then that you would have had some sort of

8 documentation related to McLeskey 1998 with you at SM?

9 A.   It would have been at Southern Research.

10:05AM 10 Q.   At Southern Research with you?

11 A.   Maybe an electronic version of the file, yeah.

12 Q.   While you were at Lombardi Center did it have a

13 specification document retention policy?

14 A.   I don't know.

10:05AM 15 Q.   You were not made aware of a specific document retention

16 policy while you were at Lombardi?

17 A.   I don't recall whether I was or not.

18 Q.   As you sit here today, you don't recall a particular

19 document retention policy at Lombardi?

10:05AM 20 A.   I don't recall one, no.

21 Q.   Do you recall whether or not there were any rules or

22 restrictions on documents that you could take outside of

23 Lombardi, say to your new job?

24 A.   I don't recall there being any, no.

10:06AM 25 Q.   Did I understand you correctly that you directed the

1 research that led to McLeskey 1998, correct?

2 A.   Correct.

3 Q.   And I believe you said that you managed the day-to-day

4 activities; Is that right?

10:06AM 5 A.   To the extent possible, yeah, I guess, right.

6 Q.   Were you responsible for designing the studies described

7 in McLeskey 1998?

8 A.   Probably, yes.

9 Q.   Were you the primary individual responsible for actually

10:06AM 10 conducting the research described in McLeskey 1998?

11 A.   No.

12 Q.   Who was?

13 A.   McLeskey -- well, I mean the other authors had

14 contributions but the primary was McLeskey.

10:06AM 15 Q.   What was Dr. Sandra McLeskey's role in procuring samples

16 from AstraZeneca relating to McLeskey 19898?

17 A.   I'm not sure she had a role.

18 Q.   Do you have any personal knowledge as to if Dr. Sandra

19 McLeskey procured samples from AstraZeneca related to McLeskey

10:07AM 20 1998?

21 A.   Personal knowledge? I do not. I mean, you said that I

22 had told her -- or may have told her to go talk to Vose and, I

23 don't know, whoever, Vose and Wakeling, and it's possible that

24 I may have done that, right.

10:07AM 25 Q.   As you sit here today do you have a recollection of

1   instructing Dr. McLeskey to do that?

2   A.   I do not have a specific recollection, but it was

3   25 years ago.

4   Q.   Do you think it is possible that you told Dr. McLeskey to

10:07AM   5   call Drs. Wakeling and/or Vose?

6   A.   It's possible, yeah.

7   Q.   At the time that McLeskey 1998 was being researched and

8   drafted, could you describe the general process within your

9   group for submitting documents for publication to a journal?

10:07AM   10   A.   General process? It depends on who the first author was

11   and their capabilities with English. So Sandra was certainly

12   very capable with English, so she would have written the first

13   manuscript. She would have -- you know, the first draft. I

14   would have read the first draft and would have made editorial

10:08AM   15   changes, content changes, suggestions. Generally it was

16   between the two, first author and a senior author, that would

17   discuss this and then eventually would get to the rest the

18   authors.

19   Q.   In this case those two people would have been Dr.

10:08AM   20   McLeskey and yourself?

21   A.   Right. You know, it's also possible Dr. El-Ashry, who

22   has a very good command of English, would have written the

23   sections of the receptor binding assays.

24   Q.   Did you personally submit a draft of McLeskey 1998 to

10:08AM   25   AstraZeneca before it was publish?

1   A.   I don't have a recollection of doing so.

2   Q.   Do you believe at the time -- did you believe that you

3   needed to submit drafts of McLeskey 1998 to AstraZeneca before

4   it was published?

10:09AM   5   A.   Yeah.   Now that I think about it, it's usually -- it's

6   typically with MTA that they will want to see the data that's

7   been generated with the compound before publication, so -- but

8   it's quite possible, given the lapse of time that occurred

9   between the time of the manuscript, the material was acquired,

10:09AM   10   who was responsible for acquiring that material and the time

11   when the manuscript was submitted that it just slipped my mind

12   that that was an obligation.

13   Q.   So you have no recollection of telling Dr. McLeskey that

14   she should submit a draft to AstraZeneca; is that right?

10:09AM   15   A.   I have no recollection of doing so.

16   Q.   Did anyone from AstraZeneca ever contact you about

17   McLeskey 1998 after it was published?

18   A.   No.   Well, beyond the phone call.

19   Q.   In August of 2015?

10:09AM   20   A.   Right.

21   Q.   Has anyone from AstraZeneca ever told you that McLeskey

22   1998 violated any confidentiality provisions with AstraZeneca?

23   A.   No.

24   Q.   Were there ever any penalties or reprimands imposed upon

10:10AM   25   you by AstraZeneca for publishing McLeskey 1998?

1   A.   No.   For publishing?

2   Q.   For publishing McLeskey 1998?

3   A.   No.

4   Q.   To your knowledge were there ever any penalties or

10:10AM   5   reprimands imposed upon the Georgetown Lombardi Cancer Center

6   as a result of publishing McLeskey 1998?

7   A.   Not to my knowledge.

8   Q.   You said that you edited McLeskey 1998 before it was

9   published, correct?

10:10AM   10   A.   Right.

11   Q.   At that time did you have any qualms about publishing the

12   formulation data in McLeskey 1998?

13   A.   I did not.

14   Q.   Did anyone from AstraZeneca?

10:10AM   15   THE COURT: Mr. Rizzi?

16   MS. PENSABENE: I'm sorry.   I think you just

17   interrupted the witness.

18   MS. PIROZZOLO-MELLOWES: I'm sorry.

19   A.   Right.   I mean at the time I thought it was probably just

10:10AM   20   something that was a formulation for animal studies.

21   Q.   Did anyone from AstraZeneca ever specifically tell you to

22   keep the formulation secret?

23   A.   No.

24   Q.   Am I correct that you do not have any documentation

10:11AM   25   showing that you entered into a confidentiality agreement with

1 AstraZeneca?

2 A.   You are correct.

3 Q.   Am I correct that you do not have any documentation

4 showing that you signed a material transfer agreement for

10:11AM   5 AstraZeneca?

6 A.   You are correct.

7 Q.   Am I correct that you have no paperwork pertaining to the

8 samples you received from AstraZeneca; is that correct?

9 A.   You are correct.

10:11AM   10 Q.   But again, you are not the person that actually procured

11 of the samples that led to McLeskey 1998; is that correct

12 will?

13 A.   I don't know if I was or was not, right.

14 Q.   Do you have any reason to doubt that it was Dr. McLeskey

10:11AM   15 that procured the samples from AstraZeneca?

16 A.   I don't think she procured the samples, it was either

17 myself or Dr. Dixon, right.

18 Q.   So, at the time that the research leading to McLeskey

19 1998 was being done, you had no knowledge of Dr. McLeskey

10:12AM   20 calling Alan Wakeling; is that correct?

21 A.   I don't recall. You know, I would probably had -- had to

22 have been -- it would have either had to have been myself or

23 Dr. Dixon who signed the forms, right? It could have been we

24 told her, call up Dr. Wakeling and see, you know, if he'll

10:12AM   25 send this to us.

United States District Court
Camden, New Jersey

1 Q. So you are saying if there was a form signed it would not

2 have been Dr. McLeskey?

3 A. Right.

4 Q. But do you have any reason to doubt that Dr. McLeskey did

10:12AM 5 call Dr. Wakeling to procure samples of ICI 182,780?

6 A. I have no personal knowledge that she did, but she could

7 have, yes.

8 Q. Do you have any reason to doubt that Dr. McLeskey called

9 Dr. Vose for preformulated ICI 182,780?

10:12AM 10 A. Again, I have no personal knowledge that she did, but

11 it's quite possible that she did.

12 Q. Did you have any particular restrictions on Dr. McLeskey

13 as far as her communications with AstraZeneca?

14 A. No.

10:13AM 15 Q. Did you give Dr. McLeskey any specific instructions

16 regarding the confidentiality or secrecy of the samples

17 received from AstraZeneca?

18 A. Confidentiality? I'm not sure what you mean by that.

19 Samples aren't confidential.

10:13AM 20 Q. What do you mean?

21 A. Well, I mean information is confidential but samples

22 themselves, so I -- I don't quite understand your question.

23 Q. Did you ever give Dr. McLeskey any specific instructions

24 about keeping her work at Lombardi Center confidential?

10:13AM 25 A. I don't know if I gave her specific instructions, it's,

1 you know, sort of implied that you don't publicly announce

2 your work until it's published or ready for presentation.

3 Q.   Did Dr. McLeskey -- let me take a step back. At the time

4 you were doing the research leading to McLeskey 1998, did you

10:13AM 5 know the components of the preformulated ICI 182,780 received

6 from the lab, received from AstraZeneca?

7 A.   No, I don't think so. No. No reason for me to know.

8 Q.   Can you turn to Exhibit 3, which is a copy of McLeskey

9 1998.

10:14AM 10 A.   The paper?

11 Q.   Yeah. Okay. So in the journal page 698 --

12 A.   Right.

13 Q.   -- which is marked SAN.FUL 641, the second column there's

14 a paragraph headed "drugs."

10:14AM 15 A.   Right.

16 Q.   Do you see that?

17 A.   Yeah.

18 Q.   Seven lines down we see the sentence: For the

19 experiments depicted in Figure 1 B and C 50 mg per mL

10:14AM 20 preformulated drug in a vehicle of 10 percent ethanol,

21 15 percent benzyl benzoate, 10 percent benzyl alcohol brought

22 to volume with castor oil was supplied my B. M. Vose,

23 AstraZeneca Pharmaceuticals?

24 A.   Right.

10:14AM 25 Q.   Do you see that?

1 A.   Right.

2 Q.   Did I read that correctly?

3 A.   Yes, you did.

4 Q.   Do you know where the information that the preformulated

10:15AM 5 drug, 10 percent ethanol, 15 percent benzyl benzoate and

6 10 percent benzyl alcohol brought to volume with castor oil --

7 A.   I have no personal knowledge of where that information

8 came from.

9   You know, at the time I probably assumed it was

10:15AM 10 information that was provided when it was provided to us.

11 That would have been my logical assumption when reading this.

12 Q.   So, am I correct that you did not tell Dr. McLeskey not

13 to publish the details of the formulas, correct?

14 A.   Correct.

10:15AM 15 Q.   At some point we mention the phrase "the research

16 beginning." To the best of your recollection, when did you

17 begin the research that led to McLeskey 1998?

18 A.   Well, like I said, I assume it was following original

19 publications on this kind of -- line of work that appeared in

10:15AM 20 Cancer Research in 1993. So, around that time.

21 Q.   1993/1994?

22 A.   '92, '93, '94, in that range probably.

23 Q.   Do you think it's possible that your lab received the

24 samples that are discussed on page 698 of McLeskey 1998 in the

10:16AM 25 first quarter of 1993?

1 A. Do I think it's possible? Yeah, it's possible.

2 Q. Do you think it's possible that those samples were

3 received by your lab in the second quarter of 1993?

4 A. You know, I don't -- I don't know. I -- you know, I

10:16AM 5 can't tell if it's first quarter, second quarter. I can't

6 tell if we, you know, ran out of stuff or needed to get more,

7 you know, right.

8 Q. We've already discussed that on page 698 of McLeskey 1998

9 it states that preformulated drug in a vehicle of 10 percent

10:16AM 10 ethanol, 15 percent benzyl benzoate and 10 percent benzyl

11 alcohol brought to volume with castor oil was supplied by B.

12 M. Vose.

13 A. Right.

14 Q. Do you have any reason to doubt that those particular

10:17AM 15 samples were received by your lab in early 1993?

16 A. I have no reason to doubt that, no.

17 Q. Were you aware that it ws AstraZeneca or one of its

18 predecessors that was supplying ICI 182,780?

19 A. Yeah. One of its predecessors probably at the time.

10:17AM 20 Q. Do you believe that this research was important at that

21 time?

22 A. Yes.

23 Q. Why was it important?

24 A. You know, it showed that growth factors could get around

10:17AM 25 the need for estrogen receptors in a cell line that was

1 originally dependent on estrogen.

2 Q.   McLeskey 1998 was published in the Journal of Clinical

3 Cancer Research; is that right?

4 A.   Um-hum.

10:17AM 5 Q.   To your understanding, who are the people that read the

6 Journal of Clinical Cancer Research?

7 A.   In 1998? So, it's Volume 4, so it was a relatively new

8 journal. People engaged in what's called translational

9 research, I guess you would say.

10:18AM 10 Q.   Just so I understand, I guess, the structure with the

11 Lombardi Cancer Center, am I correct that Dr. McLeskey was a

12 postdoc, you were her supervisor and Dr. Lippman was your

13 supervisor in some way?

14 A.   Yeah, I guess you could put it that way.

10:18AM 15 Q.   To your knowledge after McLeskey 1998 was published did

16 AstraZeneca ever contact any of your coauthors regarding

17 McLeskey 19698?

18 A.   Not to my knowledge.

19 Q.   Do you have a specific recollection of filling out any

10:18AM 20 particular forms for AstraZeneca before you started your work

21 on McLeskey 1998?

22 A.   No specific recollection.

23 Q.   Dr. Kern, I know we have been talking about samples a lot

24 today, but I know I didn't actually ask you about the receipt

10:18AM 25 of the samples themselves. Were you actually the person that

1 received the physical samples from AstraZeneca relating to

2 McLeskey 1998?

3 A.   I don't know for certain but it's quite possible I was.

4 Q.   Do you have any recollection of what the packaging looked

10:19AM 5 like for the preformulated ICI 182,780 that was received?

6 A.   No.

7 Q.   Do you recall if there was any documentation that

8 accompanied the samples of the preformulated ICI 182,780?

9 A.   There usually is but, you know, a packing slip at least.

10:19AM 10 Right?

11 Q.   Do you have any specific recollection of what was

12 included with the samples?

13 A.   No.

14 Q.   What is your best recollection of the documentation that

10:19AM 15 was accompanying the preformulated ICI 182,780 samples?

16 A.   My best recollection is no recollection at this point.

17 Q.   So am I correct that you don't know if the Lombardi

18 Center received a certificate of analysis with the

19 preformulated drug samples?

10:19AM 20 A.   Yeah, I don't know. I do not know if they did or not.

21 Q.   Am I correct that you do not know if the Lombardi Center

22 would have received MSDS sheets with the preformulated drug

23 samples?

24 A.   Usually that comes with it, yeah, an MSDS sheet.

10:20AM 25 Q.   An MSDS sheet for each excipient?

1 A.   I don't know. I don't -- I don't know what's on the MSD

2 sheet, yeah.

3 Q.   At the time McLeskey 1998 was published, did you have an

4 understanding of whether those percentages were in

10:20AM 5 weight/volume or volume to volume?

6 A.   Weight/volume or volume to volume, I think they're all

7 liquids, so probably would have been volume to volume.

8 Q.   Do you know one way or the other?

9 A.   I mean, looking at it, I would say they're liquids, so

10:20AM 10 it's volume to volume. I'm not sure about benzyl benzoate,

11 whether that's a liquid or --

12 Q.   Did you test the samples yourself?

13 A.   No.

14 Q.   And as I understand you earlier, that you do not consider

10:21AM 15 yourself a formulator; is that correct?

16 A.   That's correct, right.

17 Q.   Have you had any formulation classes?

18 A.   No.

19 Q.   When vials containing preformulated ICI 182,780 were

10:21AM 20 received at Lombardi Cancer Center, would they have been

21 logged or recorded in some way?

22 A.   I -- I don't know.

23 Q.   And did I understand you correctly earlier that you never

24 talked to anybody at AstraZeneca regarding the components of

10:21AM 25 the preformulated ICI 182,780 received by Lombardi Cancer

1 Center?

2 A. That's correct.

3 Q. And you're not paying for any of the lawyers that are

4 here representing you, right?

10:21AM 5 A. No.

6 Q. And neither is Daiichi?

7 A. Not that I know of.

8 Q. You had referenced earlier, I think, something called an

9 MTA.

10:21AM 10 A. MTA, material transfer agreement.

11 Q. And I think you referenced one specifically in connection

12 with some work you did at Southern Research -- at SRI,

13 Southern Research Institute?

14 A. Right, yes.

10:22AM 15 Q. Now, were you referring to a specific MTA that you

16 recall?

17 A. Yes.

18 Q. Was that with AstraZeneca?

19 A. That was. Well, I don't know if it's Zeneca.

10:22AM 20 Q. When I say AstraZeneca, I mean any predecessor.

21 A. Right.

22 Q. Have you seen that particular MTA recently?

23 A. No.

24 Q. You haven't seen it?

10:22AM 25 A. No.

1 Q. What made you recall that?

2 A. Just when the issue came up, I remembered that I did

3 contact Vose in order to get more compound because I needed it

4 to continue the work, once I moved institutions.

10:22AM 5 Q. This was after you had moved to SRI?

6 A. Right.

7 Q. So you recalled specifically making a request to

8 Dr. Vose?

9 A. Right.

10:22AM 10 Q. Has anyone shown you actual -- you an actual material

11 transfer agreement that you entered into with --

12 A. No.

13 Q. -- AstraZeneca?

14 A. No.

10:23AM 15 Q. In that laboratory at that time, in let's just say '93 to

16 '98 time frame, approximately how many other research projects

17 were going on at that time?

18 A. In?

19 Q. In your laboratory.

10:23AM 20 A. In my laboratory, four or five, in that range, something

21 like that.

22 Q. And these were all projects that you were responsible

23 for?

24 A. Yeah. You know, each postdoc kind of had a project, so

10:23AM 25 yeah.

1 Q.   You may have answered this before, but there was no --

2 for people who worked in the Cancer Center or in your lab,

3 there was no confidentiality, general confidentiality

4 agreement they had to sign in order to do work in the lab?

10:23AM 5 A.   I don't recall, no.

6 Q.   Would you say it was sort of a collaborative environment

7 at the time in terms of sharing --

8 A.   Yes.

9 Q.   -- information with colleagues?

10:24AM 10 A.   Yes.

11 Q.   So you would discuss with colleagues projects you were

12 working on, you would share what you were working on?

13 A.   Yeah.

14 Q.   Prior to the research -- sorry, let me back up.

10:24AM 15   Throughout the course of your career, just roughly, on

16 how many occasions do you recall, in connection with research

17 you were doing, making a request for a drug, whether from

18 AstraZeneca or anybody, in order to conduct research?

19 A.   Not too often. A lot of -- I mean, a lot of times,

10:24AM 20 things were commercially available, and that's sort of the

21 first preference, so you don't have to go through that type of

22 paperwork. So, you know, I've had people approach me for cell

23 lines, where we would have to send them Georgetown's MTA.

24 Q.   Okay. Going in the other direction?

10:24AM 25 A.   Going in, mostly going in the other direction, yeah.

1 Q.   Okay. Well, so you're saying it wasn't a regular

2 occurrence that you would enter into an MTA in order to obtain

3 a drug for you to conduct research?

4 A.   No, I don't think so, no.

10:25AM 5   You know, we would ask for plasmids. Again, we would

6 have to ask for an MTA for those from other academic

7 laboratories.

8 Q.   Specifically, with regard to McLeskey 1998, I'm not sure

9 the record was clear. Maybe you weren't asked.

10:25AM 10   Approximately for how many years did the research go

11 on?

12 A.   For this particular paper?

13 Q.   Yes.

14 A.   Hard to estimate, but, you know, my guess is it started

10:25AM 15 around '93, '94, in that range, and went to the time that it

16 was finally accepted, which was November, '97, I think.

17 Q.   So you believe that for that entire time, there was

18 research going on towards this?

19 A.   Related to this paper, yeah.

10:26AM 20 Q.   And during that time, is it fair to say that you would

21 discuss with colleagues the nature of that research?

22 A.   Yeah, it would be fair to say that.

23 Q.   And you didn't understand that there was any prohibition

24 or restriction on you doing that, did you?

10:26AM 25 A.   Not within the Lombardi Cancer Center, certainly, there

1 was no -- no restriction.

2 Q.   Before the paper was published, in that time frame that

3 the research was going on, did you give any talks or report

4 progress to anyone?

10:26AM 5 A.   You know, it's possible some of this work may have been

6 presented at the annual meeting of the AACR as a poster or

7 possibly as a talk. I just don't recall.

8 Q.   Okay.

9 A.   There would be records of abstracts with those people.

10:26AM 10 Q.   Approximately what time frame are you talking about?

11 A.   Same time frame. Well, it would be before it was

12 published, yeah.

13 Q.   What is the AACR?

14 A.   American Association of Cancer Research. That's most

10:27AM 15 likely where it would have been presented, if it was.

16 Q.   And is it fair to say that when you undertook to begin a

17 research project at Lombardi, you would do so with the hope

18 and expectation that the work results in a publication?

19 A.   Yes.

10:27AM 20 Q.   And that's true with McLeskey 1998?

21 A.   Yes.

22 Q.   Sorry, just going back to relationship with Ms. Pensabene

23 and her first, which is O'Melveny and Meyer, for the record.

24 Is there an actual engagement agreement in place between you

10:27AM 25 and O'Melveny?

1   A.   No.

2   Q.   When did O'Melveny actually start representing you in

3   connection with this case?

4   A.   I think after Arthur -- after the subpoena was delivered,

10:27AM 5   Arthur sent me an e-mail saying that Lisa had offered to

6   represent me, and I think that -- the day after I received the

7   e-mail, the day I received -- I forget which document here --

8   the request for documents subpoena.

9   Q.   Before that, did you have any reason to believe that you

10:28AM 10   needed counsel in connection with the subpoena?

11   A.   No, I guess not.

12   Q.   Did Mr. Mann explain to you or provide you any

13   information as to why O'Melveny was offering to represent you

14   in this case?

10:28AM 15   A.   No.

16   Q.   Going back to the Lombardi Center when you were there.

17   Was there any control on access to the actual facility

18   starting in 1993?

19   A.   Control on access to?

10:28AM 20   Q.   To the building.

21   A.   To the building? The doors were locked, yeah.

22   Q.   Well, was --

23   A.   Certainly, the animal facilities were locked up.

24   Q.   Where the animals were?

10:28AM 25   A.   Yeah.

1   Q.   So the animals couldn't get out?

2   A.   Well, so other people couldn't get in.

3   Q.   No animals, human or otherwise, okay.

4   Who actually had access to the lab itself? Did you

10:29AM 5   have to be a employee or somebody working for the Cancer

6   Center to be able to get into the building?

7   A.   Yes. I mean, you know, students could be -- come down

8   because there was -- the faculty at their offices in the

9   proximity of the laboratories.

10:29AM 10   Q.   So if you were a student of undergrad or the medical

11   school --

12   A.   We had some undergraduates who were working in the

13   laboratories, right.

14   Q.   Was there some sort of special ID issued to those

10:29AM 15   students so they could get access to the laboratory?

16   A.   I don't think so, but I don't recall.

17   Q.   Beyond student ID, was there any other ID that had to be

18   shown to get access to the lab?

19   A.   Yeah, I just don't recall. I'm fairly certain that there

10:29AM 20   were guards there, right. You know, so anybody just coming on

21   and off the street would have difficulty going down into the

22   laboratories.

23   Q.   There was no ID issued by the Cancer Center itself that

24   you needed to get into the Cancer Center lab?

10:30AM 25   A.   I don't recall there being so.

1 Q.   Before making the request to AstraZeneca for the samples

2 that were used in McLeskey 1998, did you have any prior

3 dealings with AstraZeneca in terms of requesting samples for a

4 research project?

10:30AM 5 A.   No.

6 Q.   And since that time, you referenced the occasion at SRI?

7 A.   Right.

8 Q.   Any others besides that?

9 A.   I don't think so, no.

10:30AM 10 Q.   At any time when you working on the project, McLeskey

11 1998, did you have any understanding that you would not be

12 able to publish the results of the work?

13 A.   No. I mean, I thought I had freedom to publish the work.

14 Q.   During the time you were working on this project, which

10:30AM 15 is described in McLeskey, 1998, did you have any understanding

16 that there was any restriction on publishing the formulation

17 of ICI 182,780 in any publication resulting from the work?

18 A.   Okay. Yeah, I would say if I were -- if I was the one

19 that signed the MTA, I probably would have understood that

10:31AM 20 they wanted to see the paper, the manuscript, before it was

21 submitted, right. That would have been the only limitation

22 that I would have been aware of, right. And I think in there,

23 they usually would have said they're not going to block

24 publication, the publication itself, right, yeah.

10:31AM 25 Q.   Okay. So the only -- and, again, you have no

1   recollection of actually signing anything in connection with

2   this particular project, do you?

3   A.   No.

4   Q.   You're saying hypothetically, if you had, the only

10:31AM 5   restriction you were aware of --

6   A.   I think what I said was it was probably either me or

7   Dickson, we signed that form. If it was Dickson, I might not

8   have been aware of limitation. If it was me, I would have

9   read those terms and, you know, would have been aware of that

10:32AM 10   limitation.

11   Q.   And what terms specifically?

12   A.   You know, usually, there's -- when a company gives you

13   something that's not publicly available yet, they'll ask to

14   see the manuscript before you submit.

10:32AM 15   Q.   And that was the only restriction you might have been

16   aware of?

17   A.   Correct.

18   Q.   Okay. And, again, you have no knowledge that the

19   manuscript or any version of the manuscript was sent to

10:32AM 20   AstraZeneca?

21   A.   I have no knowledge that it was.

22   Q.   Let me ask you this. So, I know you looked at this

23   before and you saw that it was submitted originally --

24   A.   July 3rd.

10:32AM 25   Q.   '97.

1   A.   Yeah.

2   Q.   What's your best understanding as to when a first draft

3   would have been prepared, I believe you said probably by

4   Dr. McLeskey?

10:32AM   5   A.   Two to three months previous, probably. That would be my

6   estimate. Could have been earlier, little earlier, in that

7   range.

8   Q.   So, for the work at SRI, you said you do recall there was

9   an MTA.

10:33AM   10   A.   Yeah.

11   Q.   And you do recall that the MTA obligated you to provide a

12   manuscript to AstraZeneca.

13   A.   I don't recall that.

14   Q.   You don't recall that?

10:33AM   15   A.   No.

16   Q.   So you're not sure if there was an obligation?

17   A.   Not at that time.

18   Q.   But if there was, it didn't happen?

19   A.   Yeah. Somebody screwed up.

10:33AM   20   Q.   Was there any other occasion, besides the two we have

21   talked about at Georgetown and SRI, where you received

22   material potentially under an MTA from AstraZeneca?

23   A.   No, I don't think so.

24   Q.   Well, throughout the course of your career, do you have a

10:33AM   25   recollection of any occasion where you sent a draft manuscript

1 to a drug supplier?

2 A.   Throughout my career? No, I guess not.

3 Q.   Well, wasn't your objective to clearly convey to the

4 research community the work you did; is that fair? That was

10:34AM 5 part of the purpose of the paper, no?

6 A.   That's correct, right.

7 Q.   And the formulation is there, right? So the formulation

8 is there for what it's worth?

9 A.   The formulation is there, right. Somehow or other, we

10:34AM 10 got that information.

11 Q.   And isn't it fair to say that if any of the authors

12 thought that it was important to be more explicit in

13 describing the formulation for purposes of conveying that

14 research, then that would have been done in the paper?

10:34AM 15 A.   I -- I'm, you know, fairly certain that we felt we met

16 our obligation for materials and methods section.

17 Q.   And that you had clearly conveyed to the research

18 community what the formulation was?

19 A.   That we had clearly relayed to the research community

10:34AM 20 what the formulation was?

21 Q.   Yes.

22 A.   You know, like I said previously, at the time I didn't

23 really know what a formulation was, to tell you the truth.

24 Okay? So it's -- this is information that was conveyed to us

10:35AM 25 and, you know, that's what we put into the paper.

1 Q.   And you were the one who was ultimately responsible for

2 signing off on the final version of the paper, right?

3 A.   Yeah.

4 Q.   You didn't have any reason to believe when you read it

10:35AM 5 and signed off on the final version -- you read it carefully,

6 didn't you?

7 A.   Yeah.

8 Q.   And you didn't have any reason to believe that there was

9 anything unclear or incomplete about the description of the

10:35AM 10 formulation?

11 A.   I had no reason to believe that.

12 Q.   Sorry. You didn't have any reason to believe that the

13 description of the formulation would in any way prevent

14 researchers in the field from making full use of the results

10:35AM 15 that were -- that you were publishing?

16 A.   No, I didn't have any reason to believe that.

17

18   MS. PIROZZOLO-MELLOWES: That concludes Dr. Kern's

19 testimony.

10:35AM 20   THE COURT: Okay.

21   (The read in concluded.)

22   MR. RIZZI: Your Honor, the next witness is a live

23 witness.

24   THE COURT: Okay.

10:36AM 25   MS. PETERSON: Dr. Mehta.

1   THE COURT: Thank you. You may step down.

2   MR. RIZZI: Can we take a short break?

3   THE COURT: Yes, why don't we take a five-minute

4   break. Okay?

10:36AM 5   THE DEPUTY CLERK: All rise.

6   (A recess was taken at 10:36 a.m.)

7   THE DEPUTY CLERK: All rise.

8   THE COURT: Okay. Be seated.

9   MS. PENSABENE: Your Honor, I understand that there

10:53AM 10   was a question about PTX-6, 7 and 8. They are the prosecution

11   histories.

12   THE COURT: Are they in evidence?

13   MS. PENSABENE: The parties have agreed that they

14   should be in evidence. Happily, I can say the parties have

10:54AM 15   agreed.

16   THE COURT: That's nice to hear.

17   So what are the document numbers? 6, 7, and 8?

18   MS. PENSABENE: PTX-6, 7, and 8.

19   THE COURT: Okay.

10:54AM 20   MS. PETERSON: And I think there is a corresponding

21   set of exhibits on JTX-6, 7, and 8 as well. They were

22   produced -- one set was produced by the plaintiff and one set

23   was produced by the defendants.

24   THE COURT: Yes. So which are the exhibits coming

10:54AM 25   in?

United States District Court
Camden, New Jersey

1   MS. PETERSON: I think we should agree's it's the JTX

2   numbers since that's the joint list.

3   MS. PENSABENE: That's absolutely fine, Your Honor.

4   They are the certified file histories that come from the

10:54AM 5   Patent Office.

6   THE COURT: Okay. So JTX-6, 7, and 8 are in

7   evidence.

8   MS. PENSABENE: Yes. Thank you, your Honor.

9   THE COURT: Okay.

10:54AM 10   (JOINT EXHIBITS JTX-6, JTX-7, AND JTX-8 WERE RECEIVED IN

11   EVIDENCE.)

12   THE COURT: Okay.

13   MS. PETERSON: The defendants call Dr. Mehta to the

14   stand.

10:54AM 15   THE COURT: Okay. Come forward.

16   THE DEPUTY CLERK: Good morning.

17   THE WITNESS: Good morning.

18   THE DEPUTY CLERK: If you could please take a step in

19   the witness stand, place your left hand on the Bible and raise

10:55AM 20   your right hand.

21   (DIVYESH MEHTA, HAVING BEEN DULY SWORN/AFFIRMED, TESTIFIED AS

22   FOLLOWS:)

23   THE WITNESS: I do.

24   THE DEPUTY CLERK: Can you please state and spell

10:55AM 25   your full name for the record.

1   THE WITNESS: Divyesh Mehta.

2   THE DEPUTY CLERK: Will you please spell it.

3   THE WITNESS: Divyesh, D-I-V-Y-E-S-H, Mehta,

4 M-E-H-T-A.

10:55AM 5   THE DEPUTY CLERK: Thank you.

6   THE COURT: Okay. Doctor, have a seat, make yourself

7 comfortable.

8   THE WITNESS: Thank you.

9   THE COURT: Please speak loudly into the microphone,

10:55AM 10 please. Okay.

11   MS. PETERSON: May I proceed?

12   THE COURT: You may.

13 (DIRECT EXAMINATION OF DIVYESH MEHTA BY MS. PETERSON:)

14 Q.   Good morning.

10:56AM 15 A.   Good morning.

16 Q.   Can you please start by introducing yourself to the

17 Court.

18 A.   My name is Dr. Divyesh Mehta. I am a medical oncologist

19 and licensed to practice medicine in the State of Arizona.

10:56AM 20 Q.   And do you hold any other titles?

21 A.   I am the chief of oncology services at the Maricopa

22 Integrated Health Services, which is the County Hospital for

23 Phoenix, Arizona.

24 Q.   Anything else?

10:56AM 25 A.   I'm also professor of medicine at the University of

1 Arizona, College of Medicine in Phoenix.

2 Q.   And can you tell us a little bit about your educational

3 background?

4 A.   So I graduated in 1971 from Baroda, India.

10:56AM 5   I came to the United States in 1972. Before that, I

6 had done a year of internship in India and another internship

7 in Chicago, a residency in internal medicine, and then a

8 fellowship at the University of Illinois in Chicago, in

9 hematology and oncology.

10:57AM 10 Q.   And are you currently a practicing physician?

11 A.   Yes, I am.

12 Q.   In what areas do you practice?

13 A.   I practice in hematology and oncology, specializing in

14 breast medicine.

10:57AM 15 Q.   And you mentioned hematology. What is that?

16 A.   Hematology is diagnosis and treatment of blood diseases,

17 including blood cancer.

18 Q.   And what portion of your clinical practice is devoted to

19 oncology and, in particular, the treatment of breast cancer?

10:57AM 20 A.   It has varied over the last 15 years.

21   While I was in Chicago, from 2003, most all of my

22 clinical practice was breast cancer.

23   When since coming to Phoenix, Arizona in 2011, 60

24 percent of what I see are breast cancer; the rest is assorted

10:57AM 25 tumors and some blood conditions which I also see.

1   Q.   And how many breast cancer patients have you treated over

2   the course of your career as a clinician?

3   A.   The number must be in thousands.

4   Q.   And how many patients do you see a month?

10:58AM   5   A.   At the moment I see about ten new breast cancer patients

6   a month, and maybe 30 to 50 patients in follow-up or in

7   hormonal or chemotherapy.

8   Q.   And what other prior academic positions have you held?

9   A.   So, I was assistant professor of medicine in -- from late

10:58AM   10   '70s to 1985.

11   I was associate professor of medicine in Chicago from

12   2003 to 2011. And during that time, I was also the chair for

13   the Division of Hematology and Oncology at the University of

14   Illinois, and I was also the director of clinical oncology

10:59AM   15   services, which means I ran the chemotherapy services for the

16   University Hospital for the entire program.

17   Q.   And what did you do during the time period from 1985 to

18   2003?

19   A.   So I returned to India to my hometown, where I graduated

10:59AM   20   from and where I grew up.

21   I set up a practice as well as I set up three tertiary

22   care hospitals which would provide cancer care. I set up a

23   breast clinic, and I also set up a mammography unit for -- one

24   of the first in Western India.

10:59AM   25   One of the problems we found when we did that was that

1   most breast cancers came late in India because there were no

2   mammographies, and women would come with a lump that had

3   spread. And so we tried to introduce mammography, and we

4   learned that women were somewhat shy and not really trusting

10:59AM   5   that this would not be photographed or something, and they

6   were worried that there would be man technicians, so we began

7   an education program of why it was important, how it was done.

8   And by that time, we started to educate people to get that

9   done. So that was in the initial part of my return to India.

11:00AM   10   Besides starting a hormonal and chemotherapy treatment

11   program for breast cancer patients, I was involved in getting

12   diagnostic setups going.

13   And then I set up ICON.

14   Q.   And what is ICON?

11:00AM   15   A.   So ICON, I-C-O-N, stands for Indian Cooperative Oncology

16   Network. This is a cooperative group, a mentoring group, we

17   set up in Mumbai, and the whole idea was this: There were

18   lots of patients who could benefit from new drugs, but they

19   had no funds to access them.

11:00AM   20   There were a hundred plus physicians in India treating

21   all kinds of cancer, including breast cancer. They did not

22   know how to put these patients on trials.

23   And there were drug companies and universities across

24   the world who wanted large number of patients for their

11:01AM   25   trials.

1   So we became the fulcrum that brought the pharma and

2 the universities to the physicians and the patients.

3   We also then had to set up education programs, so we

4 set up programs for doctors to be able to do good clinical

11:01AM 5 research, human rights and research, consenting. We focalized

6 what was there, being floated between the drug companies and

7 the doctors, and we monitored it was ethically and

8 transparently carried out.

9   So this was basically a process that started in mid

11:01AM 10 '90s and now it's in full force. It's become a force that has

11 linked up 300 different institutions in India and covers a

12 population of about 750 million people. So now they have

13 access to modern drugs, and the doctors have access to modern

14 methods of research.

11:01AM 15 Q.   And over the course of your career, have you engaged in

16 any clinical research activities associated with the treatment

17 of cancer?

18 A.   So, we just finished a study on impact of HPV in triple

19 negative breast cancer.

11:02AM 20   THE COURT: In what?

21   THE WITNESS: HPV is an infection that is present on

22 female cervix, and it seems to be responsible for cancer of

23 cervix, certain genital cancers, lung cancer, and ENT cancers,

24 and we had a feeling that it may be linked to the last kind of

11:02AM 25 breast cancer, which is triple negative cancer, the ER

1 negative, the PR negative, the HER2 negative, the most

2 difficult to treat breast cancer.

3   And we wondered, there was some evidence in the

4 literature that suggested that it may be related to HPV

11:02AM 5 infection, so we basically studied the last 15 years of our

6 data. The data are basically being presented next month at an

7 oncology meeting.

8   We also studied --

9   THE COURT: Doctor, can you slow down just a little?

11:02AM 10   THE WITNESS: Sure.

11   THE COURT: Thank you.

12   THE WITNESS: We also studied breast cancer in

13 Hispanic women and presented two abstracts last year at the

14 San Antonio Breast Cancer Conference which kind of looked at

11:03AM 15 impact of access, impact of insurance, and outcomes. And,

16 obviously, that was of major interest because at County

17 Hospital, we have maybe 30 to 40 percent of women who have no

18 insurance, and we try to give them modern treatment while

19 keeping their financial needs in our sight.

11:03AM 20   And, of course, I was the part of the team that brought

21 a new molecule called p28. It's a molecule licensed by

22 University of Illinois, and one of the researchers who was

23 working with us. It's a molecule that's a novel molecule,

24 underwent Phase 1 trial, which means we did safety and

11:03AM 25 toxicity and dosing setup trials. The data was presented at

1   the American Society of Clinical Oncology meeting in Chicago

2   in 2011. And that molecule is now into its Phase II trials.

3   Q.   Thank you.

4   And have you been involved in any clinical trials

11:04AM   5   for the -- involving endocrine therapy for treatment of breast

6   cancer?

7   A.   So the major one was ATAC trial which compared

8   anastrozole to tamoxifen. And the trial was a national trial,

9   and I enrolled patients on it, and I was the principal

11:04AM   10   investigator for the site of University of Illinois in

11   Chicago. The trial looked at anastrozole versus tamoxifen

12   versus combination.

13   I also was the principal investigator for Chicago site

14   for a Tailor Rx trial, which basically asked the question if a

11:04AM   15   woman has a early ER cause to breast cancer, do all of them

16   require chemotherapy? And if all of them don't require

17   chemotherapy, some can be simply cured by surgery followed by

18   hormonal treatment alone, how would we detect that these are

19   the patients who can be spared chemotherapy?

11:05AM   20   And so the trial looked at the genomic makeup of the

21   tumor cell and distinguished who had a high lethal score and

22   would benefit from chemo, and who were slow-growing tumors

23   like turtles that were going to keep going for years and the

24   chemo would really not have any impact on it? So those trial

11:05AM   25   results are just coming out.

11:05AM

11:06AM

11:06AM

11:06AM

11:07AM

1   And then participated in a Phase III trial looking at

2   avastin versus chemotherapy, a Phase II trial of a new

3   molecule called Epithalone B. It was a negative trial, didn't

4   work in breast cancer.

5   And, of course, as I mentioned, the Phase I for p28.

6   Q. Have you been involved in any animal research studies

7   over the course of your career?

8   A. So, during my fellowship at UIC, my boss used to have a

9   lab where we worked. This was a lab that basically worked on

10 mice. And the idea was to look at impact of removing kidneys

11 and how they affected the blood of the -- the animal.

12 And subsequently during that time of my fellowship, I,

13 along with other trainees, would also look after the dogs who

14 were going through experimental bone-marrow transplants, and

15 we would come in over the weekend and week and basically

16 manage the dogs.

17 Over the time I was the chair for the oncology program

18 at the University of Illinois, Chicago, I was instrumental in

19 directing the Ph.D.s which were under my division. I would

20 approve their funding. I would approve -- look at the

21 research that is basically going up for further funding. I

22 would look at and mentor them about the animal research that

23 was going on to be published. And my team acted as a liaison

24 between the lab research and what the clinicians wanted the

25 question to be answered in the lab. This was during the

1 period I was in Chicago.

2 Q. And over the course of your career, have you presented or

3 published on topics of treatment of breast cancer?

4 A. Yes. So I have been a speaker all my life and a teacher

11:07AM 5 all my life, the last 15 years, I have addressed physician

6 audiences which sometimes included nurses and pharmacists on

7 breast cancer across United States and abroad, approximately

8 150 docs on treatment of breast cancer, management of breast

9 cancer, ER positive breast cancer as well as chemotherapy of

11:07AM 10 breast cancer.

11 Q. And Dr. Mehta, can you please take your binder that's

12 sitting in front of you and turn to the tab that's marked

13 DTX-276. It should be your first binder.

14 A. Absolutely.

11:07AM 15   MS. PENSABENE: Counsel, do you have a copy for us?

16   THE WITNESS: 276? Got it. 276?

17   THE COURT: It's about the fifth one, tab in.

18   MS. PETERSON: Is it not in your binder?

19   THE COURT: It's about the fifth tab in.

11:08AM 20   THE WITNESS: 276, right? Yeah. Got it.

21 BY MS. PETERSON:

22 Q. Sorry for that, Dr. Mehta. Can you identify DTX-276?

23 A. Yes.

24 Q. And what is this?

11:08AM 25 A. It's my copy of my CV.

1   MS. PETERSON: Your Honor, defendants move to enter

2   DTX-276 into evidence.

3   THE COURT: Any objection?

4   MS. PENSABENE: No objection.

11:09AM 5   THE COURT: In evidence.

6   (DEFENDANT EXHIBIT DTX-276 WAS RECEIVED IN EVIDENCE)

7   MS. PETERSON: At this point, defendants proffer

8   Dr. Mehta as an expert on the clinical treatment and research

9   of breast cancer.

11:09AM 10   THE COURT: Any objection, any voir dire?

11   MS. PENSABENE: No, Your Honor.

12   THE COURT: Okay. Subject to Rule 702, Dr. Mehta

13   will be permitted to testify in the areas identified by

14   counsel as an expert.

11:09AM 15   BY MS. PETERSON:

16   Q.   Now, Dr. Mehta, are you here to testify today about the

17   opinions you have offered concerning invalidity of the patents

18   in suit?

19   A.   Yes.

11:09AM 20   Q.   And were all of the facts and data that you considered in

21   forming your opinions in this case disclosed in your expert

22   reports?

23   A.   Yes.

24   Q.   Dr. Mehta, can you just briefly explain for the Court

11:09AM 25   what the primary options are for treating hormonal-dependent

1 breast cancer?

2 A.   So this is a tumor that is fed and nourished by

3 estrogens, and one of the main strategy was to withdraw

4 estrogen either surgically by removing ovaries or chemically

11:10AM 5 producing menopause. Then the same concept progressed to have

6 agents which would be blocking the estrogen receptors which

7 are like switches on the cells, turning the cells on and

8 egging the cell on for division and -- and of course, all

9 strategy that would reduce circulating estrogen around the

11:10AM 10 cancer cell.

11 Q.   And what types of drugs would fall into the antiestrogen

12 category that you described?

13 A.   So principally, there were three categories. First were

14 the drugs that were selected to be modified, the estrogen

11:10AM 15 receptors were concerned, tamoxifen being the principle

16 example. Other categories were aromatase inhibitors which

17 block the enzyme aromatase and made estrogen non-available to

18 the cell. And the third category where your antiestrogen or

19 estrogen down regulators, ERDs, and the example being

11:11AM 20 Faslodex.

21 Q.   And as of the 1990s, how did clinicians determine what

22 treatment option to use for a patient?

23 A.   Since most of the tumors, since most of the tumors were

24 estrogen receptor positive, the strategy largely had to decide

11:11AM 25 if the estrogen was -- the manipulation was the first

1   treatment to go to, and if not, if you actually wanted

2   chemotherapy, why.

3   So as the algorithm on these slides suggest, if you had

4   a life-threatening disease or the patient was extremely

11:12AM   5   symptomatic involving some important vital organ then

6   chemotherapy was fast, it would control the tumor and one

7   would go that route. But otherwise, almost everybody would

8   proceed to options that were listed on the left side of the

9   column where you begin your first line hormonal therapy.

11:12AM   10   Q.   Dr. Mehta, were there different options for endocrine

11   therapy available in the 1990s?

12   A.   So if you look at the slide again, talking about the

13   premenopausal versus postmenopausal. In the postmenopausal,

14   tamoxifen was still a major drug which was for the entire

11:12AM   15   decade, sort of dominated the breast cancer therapy. The

16   aromatase inhibitors that arrived and Anastrazole as an

17   example. Megestrol which used the mechanism to block the

18   progesterone receptor was a standard of care if there was

19   tamoxifen failure, and this was an old drug and sort of left

11:13AM   20   over from earlier part of the decade.

21   And there was also knowledge that if you could block

22   the androgens by just like hetero tested, breast cancer

23   sometimes responded and hetero testing was androgen blocking

24   was an option.

11:13AM   25   On the other end, in the premenopausal, bulk of the

1 strategies were around tamoxifen or making a woman menopausal.

2 To do -- to put a woman in menopause, the options included a

3 drug that would interrupt the pathway between pituitary and

4 ovary or actually physically taking the ovaries out, so called

11:13AM 5 oophorectomy.

6 And of course, down the line, the products that were

7 coming were looking at the fact that the post -- the

8 premenopausal woman couldn't be given the aromatase inhibitor

9 if she was made to resemble a postmenopausal woman by using

11:14AM 10 Anastrozole.

11 Megestrol and androgen, as I had mentioned in the

12 postmenopausal, they were leftovers from earlier part of the

13 decade were still options being used but less and less so.

14 Q.   And just to be clear, looking at your demonstrative up on

11:14AM 15 the screen, DTX-1006, I think you were referring to the

16 treatments for postmenopausal which are on the left side --

17 A.   Right.

18 Q.   -- is that right?

19 A.   Yes.

11:14AM 20 Q.   And then the right-hand side of the screen?

21 A.   Is the premenopausal.

22 Q.   Were other candidate drugs and developments under

23 consideration at that time as well in the late 1990s?

24 A.   So, on one hand, the aromatase inhibitors were already on

11:14AM 25 their way and they were successfully headed for clinical use,

1   and on the other hand, there were a very powerful group of

2   drugs known as antiestrogens.

3   Q.   Other than the aromatase inhibitors and the pure

4   antiestrogen, were there any other categories of drugs that

11:15AM 5   were under development for hormone-dependent breast cancer?

6   A.   There was more an attempt to also create better

7   tamoxifens. As tamoxifen was a drug that had basically

8   dominated breast cancer care, the question was, could you

9   create a better tamoxifen, higher efficacy or lower side

11:15AM 10   effects, and those were some of the products also being tried.

11   Q.   So out of those three categories of drug candidates, did

12   any of the candidates within those categories appear to be

13   promising as a potential new therapy for hormone-dependent

14   breast cancer at the time?

11:15AM 15   A.   So the prior art during that time identified fulvestrant

16   as a very promising candidate.

17   Q.   Why do you say that?

18   A.   Because there was strong preclinical data suggesting that

19   it was efficacious, it was a novel product, in terms of a new

11:16AM 20   mechanism of action, so it was likely to work when other drugs

21   had failed. The preclinical and clinical data was showing

22   that it did work when tamoxifen had failed. The data also

23   suggested that it being pure antiestrogen had no side effects

24   that would come if we were using tamoxifen, such as

11:16AM 25   endometrial and other changes.

1   So it had promise in terms of being novel, new

2 mechanism of action, efficacy and safety, and also the prior

3 art was suggesting that this was going to be delivered by a

4 mechanism or a method which would make sure that the patient

11:16AM 5 is compliant and the drug is in, based on the injections.

6 Q.   Now, you mentioned one of the properties of fulvestrant

7 that it had been shown to work when tamoxifen had failed.

8 What's the significance of that?

9 A.   So one of the important lessons of hormonal treatment has

11:17AM 10 been that if you go from one successful treatment to the

11 other, if the next one is effective and not basically negated

12 by prior treatment, you added life and survival to the

13 patient. So as you -- even though one drug fails, you go to

14 the next paradigm and next paradigm and next paradigm.

11:17AM 15   That's how -- I have had patients who have survived

16 five, ten, 15 years with Stage 4 disease and are doing well

17 because something works and then the cells start to become

18 resistant, something else works. That's what cross-resistant,

19 non-cross-resistant. So not being cross-resistant to

11:17AM 20 tamoxifen was a major attribute here.

21 Q.   And I think you mentioned that fulvestrant was -- or the

22 category that fulvestrant belongs to, the pure antiestrogens,

23 there were no approved drugs within that category, is that

24 right?

11:17AM 25 A.   That is correct.

1 Q. And what about the other two categories, were there

2 already approved drugs within those two categories?

3 A. So, the premenopausal group of course had tamoxifen and

4 all of the options of depriving ovarian outputs, such it LHRH

11:18AM 5 antagonists or removal --

6 THE COURT: Or what? Wait, slow down.

7 THE WITNESS: LHRH antagonist, the interpreter -- the

8 interrupter of pituitary to ovary access. On the other end,

9 in the postmenopausal group, there were -- one agent was

11:18AM 10 already there, which was a group in Europe and two more were

11 on their way, which was very, very promising.

12 Q. Now, within the category of the pure antiestrogens, was

13 there any one candidate or -- within that group, that

14 demonstrated more promise than the others?

11:18AM 15 A. I would say that would be fulvestrant.

16 Q. And why do you say that?

17 A. The prior art of fulvestrant and the excitement about

18 this being a new novel molecule can be illustrated by this

19 particular slide.

11:19AM 20 Your Honor, the San Antonio Breast Conference is a big

21 pow-wow of breast cancer focused physicians, researchers, even

22 patient care groups arrive and everybody has a way of

23 interacting and learning what's coming new.

24 So 1999, there were 440 studies presented of all kinds

11:19AM 25 of research on breast cancer of which the most prominent, most

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1 promising 40 abstracts were chosen for a general session,

2 which meant that everybody who came to San Antonio would be

3 likely to attend the general sessions before the sessions

4 break out in smaller rooms. And of those, eight focused on

11:20AM 5 hormonal therapies -- studies. So there were a few of these

6 studies as abstracts presented to this general audience that

7 came from all over the world, including from United States,

8 and of all those studies presented, there was only one new

9 novel product at that time introduced and that was Faslodex.

11:20AM 10 Q.   The other seven hormonal therapy studies that were

11 presented at that general session, did those not involve new

12 or novel products?

13 A.   So some of them are comparing tamoxifen to some other

14 methods. Some of them had also talking about aromatase

11:20AM 15 inhibitors. Some had -- but none of them had any product that

16 was not yet in the approval process, and there was excitement

17 about it.

18   In fact, Dr. Robertson in his presentation on this

19 product was from Dr. Robertson, and he categorized the product

11:21AM 20 as the most advanced pure antiestrogen available in the

21 research community at that time.

22 Q.   If I could actually ask you to turn to the tab marked

23 JTX-13 in your binder. I believe it should be towards the

24 end.

11:21AM 25   Can you identify JTX-13 for the record?

1 A.   Yeah. It covers the abstracts from the general sessions,

2 Page 31.

3 Q.   This is the Robertson abstract that you just referenced

4 in your prior demonstrative?

11:21AM 5 A.   Yes.

6 Q.   Marked DDX-10-07?

7 A.   Yes.

8 Q.   And how did Dr. Robertson describe Faslodex in his

9 abstract?

11:22AM 10 A.   Simply the first line, he says that Faslodex is the most

11 advanced, of a new class of drugs, a non-agonist, which means

12 a pure steroidal antiestrogen currently in clinical trials in

13 postmenopausal women in the United States, I guess.

14   MS. PETERSON: Can you go back to JTX-13 first. I

11:22AM 15 think it was asking for the first few sentences.

16   THE WITNESS: Correct.

17   MS. PETERSON: Keep going. Yep. Blow that up.

18 Right where it starts, Faslodex.

19   THE WITNESS: It says, I was seeing the most advanced

11:22AM 20 of the new class of drugs, the non-agonist pure steroidal

21 antiestrogen currently in clinical trials in postmenopausal

22 women with advanced breast cancer.

23   He was reporting on a randomized, partially blind trial

24 of this particular product in three different dose categories,

11:23AM 25 50 milligrams, 125 and 250 milligrams in association with

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1 tamoxifen or tamoxifen placebo to see if this drug added any

2 value to tamoxifen and several therapeutic efficacy biomarkers

3 were also measured in that trial.

4 BY MS. PETERSON:

11:23AM 5 Q.   Now, Dr. Mehta, are you familiar with the term a person

6 of ordinary skill in the art?

7 A.   Yes, I am.

8 Q.   And have you provided an opinion as to the

9 characteristics of that -- of that person?

11:23AM 10 A.   Yes, I have.

11 Q.   Is it referenced here up on your demonstrative,

12 DDX-10-08? Can you explain?

13 A.   So this person is a hypothetical person but highly

14 educated, having, for example, a Ph.D. or an MB, many years of

11:24AM 15 training and experience in the field of treating

16 hormone-dependent diseases of the breast. This is a person

17 who would understand that the drug development process is a

18 teamwork that requires input from various individuals with

19 various background. For example, a person of ordinary skill

11:24AM 20 in the art would have familiarity with the pharmaceutical

21 formulations or would call on a colleague or a team member for

22 such expertise to collaborate.

23 Q.   And Dr. Mehta, would you consider yourself to have been a

24 person of ordinary skill in the art as of 2000?

11:24AM 25 A.   Yes.

1 Q.   Now, prior to 2000, would a person of ordinary skill in

2 the art have been interested in developing a new treatment

3 method with fulvestrant for treating hormone-dependent breast

4 cancer?

11:25AM 5 A.   Yes.

6 Q.   And I see you've prepared a demonstrative timeline here,

7 DDX-10-09.

8   Can you explain?

9 A.   So this looks at a stage of -- stages of drug development

11:25AM 10 for fulvestrant, in terms of preclinical, clinical and some

11 corroborative evidence that came subsequently. For

12 preclinical, 2002, the evidence that then begins to look at

13 actual patient drugs.

14 Q.   And when you said some corroborative evidence that came

11:25AM 15 subsequently, what was the date of those publications?

16 A.   '97, '98, '99.

17 Q.   So they followed the preclinical and clinical studies

18 that you referenced?

19 A.   Yes.

11:25AM 20 Q.   But they occurred before 2000, is that right?

21 A.   They did.

22 Q.   Now, who was authoring this literature in the 1990s?

23 A.   So there was a group of physicians and researchers who

24 were very focused on estrogen receptor positive breast cancer.

11:26AM 25 Some of these people were originally being part of the team

1   that developed tamoxifen, and now we're on to a new product.

2   This is the team -- lot of -- each of these initial studies,

3   the preclinical and clinical had input or team members from

4   the Imperial Chemical Industry, ICI, the team members

11:26AM   5   subsequently Zeneca, AstraZeneca. It was a group that was

6   mentoring and testing a novel compound with a new mechanism of

7   action.

8   Q.   And why is that significant, who these authors were?

9   A.   It sort of -- if you, if you like that work and if these

11:26AM   10   are the people you follow, there is a linear progression of

11   research from their preclinical work which is handed on to

12   clinical work and the same group is now in the corroborative

13   phase talking about the same product.

14   Q.   And where were these results being published?

11:27AM   15   A.   In various, very prestigious journals.

16   Q.   And what was the typical audience for these journals?

17   A.   These were breast cancer clinicians, breast cancer

18   academicians, breast cancer experts, surgeons, pathologists,

19   entire group of doctors who would be interested in treatment

11:27AM   20   of breast cancer.

21   Q.   And let's move on to your next demonstrative, DDX-10-10.

22   Can you -- can you describe this for us?

23   A.   So in a broad overview, we see paper from Wakeling and

24   that basically looked at rational for this product of a pure

11:28AM   25   antiestrogen. The testing was in mice and this was a single

1 dose given every four weeks.

2   Moving on to Wakeling further, it was again looking at

3 rational testing in mice and the dose every four weeks. Dukes

4 data was in monkeys, long-acting castor oil formulation. IM

11:28AM 5 injections, 4 milligrams per kilogram every four weeks and

6 then Wakeling and Duke again revisiting the dose and frequency

7 of these treatments in hormone-dependent breast cancer, and

8 again, Dukes '93 going on with further research in the same

9 area.

11:28AM 10 Q. So does this demonstrative, DDX-10-10, does this describe

11 what you were referring to as the preclinical phase?

12 A. That is correct.

13 Q. Okay. Well, let's take a look at the first reference on

14 your list. This is Wakeling 1991.

11:28AM 15   Can you tell us actually a little bit about the

16 Wakeling study from 1991?

17 A. So this study basically looks at fulvestrant and

18 describes it as being a potent and specific inhibitor of

19 estrogen action, and it states that it demonstrated excellent

11:29AM 20 growth suppressive effects in both cells and animals in breast

21 cancer.

22 Q. And what journal was Wakeling 1991 published in?

23 A. This was published in Cancer Research.

24 Q. And who were the authors?

11:29AM 25 A. Dr. Wakeling, Dr. Dukes and Jean Bowler.

1	Q. And does the article indicate where they worked?
2	A. They were all part of ICI Pharmaceuticals.
3	Q. And what results does Wakeling 1991 report?
4	A. The most relevant part of the study was that this, in a
5	cell line, it compared the new product, fulvestrant, to
6	tamoxifen and on breast cancer cell lines, and it also tried
7	to see one of the criticisms of tamoxifen was that it was
8	stimulating the uterine lining and led to problems,
9	subsequently even endometrial cancer. So it was basically
10	showing an anti-uterotrophic action. So anti means against,
11	utero means uterus, trophic means stimulation of uterine
12	lining. It showed excellent anti-uterotrophic action, and
13	this was achieved without having other side effects of
14	tamoxifen; namely, body weight and impact on gonadotrophic
15	secretion. It was not really working in any other fashion
16	except as a pure antiestrogen.
17	Q. And these results that you were just referring to,
18	they're described on your demonstrative, DDX-10-12?
19	A. Yes.
20	Q. And why were these findings important?
21	A. This established the fact that you have a potent new
22	mechanism of action with a product that can -- in comparison
23	with tamoxifen, have an improved efficacy and without the
24	uncomfortable side effects that you worried about. So you saw
25	improved the efficacy, reduced toxicity. The therapy index

Timestamps: 11:29AM (line 5), 11:30AM (line 10), 11:30AM (line 15), 11:30AM (line 20), 11:31AM (line 25)

1 sort of goes up and so it points towards the possibility that

2 this product would have that kind of improved treatment

3 ability.

4 Q.   And what animals were studied in Wakeling 1991?

11:31AM 5 A.   So he used MCF-7 cell lines, these are the famous human

6 cell lines that have been nurtured, and are responsible for so

7 many advances in hormone treatment of breast cancer and these

8 were these cell lines on which he tested the first hypothesis,

9 which was the efficacy. He also used rats, and giving this

11:31AM 10 particular product, he also showed that the vaginal

11 cornification, which was one of the changes they described to

12 suggest that there was an estrogenic stimulation of uterus was

13 absent and he also showed in nude mice where he took these --

14 these MCF-7 cell lines, created a xenograft on the animal and

11:32AM 15 then see -- saw how the fulvestrant acted to see the efficacy.

16   So I think the -- all three models that he describes, I

17 believe he also worked on monkeys. So the Macaca monkeys,

18 they were basically looking at the same action. He basically

19 demonstrated that if you use fulvestrant, the weight increase

11:32AM 20 of the uterus did not happen, which means the uterus was

21 protected from the uterotrophic action.

22   THE COURT: Can you just spell what type of monkey

23 you said.

24   THE WITNESS: Macaca, M-A-C-A-C-A. It's a species

11:33AM 25 they used.

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1   THE COURT: How do you spell it?

2   THE WITNESS: M-A-C-A-C-A.

3 BY MS. PETERSON:

4 Q.   Were the animals that Dr. Wakeling studied -- were the

11:33AM 5 animals that were studied in Wakeling 1991, were they

6 ovariectomized?

7 A.   Yes.

8 Q.   What does that mean?

9 A.   It basically means you created a physiological condition,

11:33AM 10 that is, simulating postmenopausal women.

11   THE COURT: What was the word you said?

12   MS. PETERSON: Ovariectomized.

13   THE COURT: Thank you.

14 BY MS. PETERSON

11:33AM 15 Q.   Dr. Mehta, did Wakeling 1991 teach any information about

16 the preferred method of administration of fulvestrant?

17 A.   So it looked at bioavailability of the drug in all the

18 works in its injectable form, and found this drug to have a

19 very poor bioavailability, and this study also then

11:34AM 20 demonstrated, had a potential efficacy of a depot oil

21 preparation in the nude mouse that were implanted with the

22 xenografts.

23 Q.   And what is a depot formulation?

24 A.   So it's usually a drug given as a -- it's part of an oil

11:34AM 25 depot and depot meaning it sort of stores the drug, releases

1 it slowly so you have blood levels in a sustained long-term

2 fashion, rather than immediately rising and dissipating

3 themselves.

4 Q.   And why would a depot formulation be desirable?

11:34AM 5 A.   In the typical route, it would reduce the frequency of

6 injection, it would also give a very sustained dependable

7 control of tumor. In real-life setting for patients, that

8 basically means that patient would have come less frequently,

9 be monitored with much more efficacy and the problems of

11:35AM 10 compliance that we see with pills would not exist, because we

11 would know the injection is given and it's in there. So if

12 it's working, it's working.

13 Q.   And does Wakeling 1991 demonstrate the frequency of the

14 treatment with the oil depot formulation?

11:35AM 15 A.   It was given once every four weeks.

16 Q.   And what does Wakeling 1991 tell a person of skill in the

17 art about using fulvestrant to treat hormone-positive breast

18 cancer?

19 A.   So if you look at the last line of what is put up there,

11:35AM 20 it says that data available for fulvestrant indicate that pure

21 antiestrogens may find a valuable place in treatment of breast

22 cancer. This product will be used to test this proposition.

23 So it kind of carries it forward and offers it for further

24 research to the colleagues as well as their own lab.

11:35AM 25 Q.   And you're referring to DDX-10-14?

1 A.   Yes, I am.

2 Q.   Did Wakeling 1991 indicate whether further study with

3 fulvestrant would continue?

4 A.   Yes, it did. The last line again states that this would

11:36AM 5 be used to test this proposition, which means further studies

6 would continue.

7 Q.   Thank you. Let's move on to Wakeling's next publication

8 in 1992. And can you explain what was disclosed in Wakeling

9 1992?

11:36AM 10 A.   Wakeling 1992 was a summary of what his findings were

11 from Wakeling 1991, being presented in sort of a review

12 fashion so that it was a -- his attempt to capsulize what they

13 found, his attempt to also disseminate information so other

14 researchers in the field would also move on with their

11:36AM 15 research with this product, and sort of set the standard of

16 care for what was available, known about this product at that

17 time.

18 Q.   Okay. Let's go on to the next piece of literature, then,

19 Dukes 1992. And in what journal was Dukes 1992 published?

11:37AM 20 A.   It was published in the Journal of Endocrinology.

21 Q.   And who were the authors?

22 A.   Authors again were Dr. Dukes, Dr. Miller, Dr. Wakeling

23 again and Waterton.

24 Q.   And would the Journal of Endocrinology be reviewed by

11:37AM 25 breast cancer researchers?

1 A.   Yes, it was a major journal to look at because bulk of

2 breast cancers were endocrine positive, ER positive and lot of

3 endocrine related research was appearing in the journals that

4 were dealing with endocrinology. So it was a major area where

11:37AM 5 these teams were being laid out.

6 Q.   And what does Dukes 1992 indicate to a person of skill in

7 the art who would be interested in developing a treatment for

8 hormone-positive breast cancer?

9 A.   So this study further explored the -- for potency and

11:38AM 10 efficacy of fulvestrant by studying the ovariectomized monkeys

11 and, in fact, on the uterus of these monkeys. They basically

12 used a novel technique which was an MRI scan. So they didn't

13 actually have to weigh the uterus, they would simply estimate

14 the growth of the lining of the uterus by doing sequential

11:38AM 15 MRIs, and this was important study in its own way because it

16 attained sustained blockade effect of estrogen on monkey

17 uterus in a dose-dependent manner for three to six weeks.

18   He also demonstrated that repeated injections of

19 4 milligrams per kilogram at four weekly intervals provided an

11:39AM 20 effective blockade for uterine proliferation.

21   This was an extension of what Dr. Wakeling had

22 suggested, but in a slightly more sophisticated technology.

23 This was confirming what had been seen earlier.

24 Q.   And Dr. Mehta, just for the aid of the court reporters

11:39AM 25 here, if they have a question, if you can just --

1 A. Absolutely, I'm answering, I'm looking at them, I'm

2 answering. I speed up sometimes and I will slow down and

3 utter each word, no problem.

4   THE COURT: Was the objective of the Dukes 1992, was

11:39AM 5 it to study the uterine issue?

6   THE WITNESS: So it basically, yeah, it wanted to

7 study the uterine issue but it also wanted to study the

8 administration, the dose, the injectability. So it wasn't --

9 Macaca monkey is a larger animal and easier to study than

11:40AM 10 practices for mice, and I think the two things we established

11 here, one was that, yes, he proved again that the uterine

12 simulation was no longer happening with, because of this

13 product, and he showed that this was the way it could happen.

14   THE COURT: So it seems that it wasn't really related

11:40AM 15 to the treatment of breast cancer, but more so towards --

16   THE WITNESS: If the treatment was efficacious

17 towards the side effect, right.

18   THE COURT: Yes.

19 BY MS. PETERSON:

11:40AM 20 Q. And what was the significance of the monkeys in the study

21 having been treated with estrogen?

22 A. And so they were ovariectomized, which means there's a

23 physiological model resembling a postmenopausal woman, and

24 then being given estrogen means that they were challenged with

11:40AM 25 estrogen, but these powerful antiestrogen could block that and

1 not let the estrogens create increase in the size of the

2 lining of uterus. It would basically prove the hypothesis

3 that this was a product that protected the uterus.

4 Q.   And was your testimony just now, that was a -- just for

11:41AM 5 the record, that was in relation to DDX-10-016?

6 A.   Yes.

7 Q.   And what other results did Dukes 1992 report?

8 A.   So basically, the Dukes, again, from my vantage point,

9 brought the dose of 4 milligrams per kilogram and also showed

11:41AM 10 that there could be a sustained blockade for one month with

11 this dose, and this dosing interval is likely to be clinically

12 relevant in therapeutic studies of breast cancer. This is

13 from the abstract itself, largely because this would translate

14 into monthly visits and monthly injections.

11:41AM 15 Q.   And you're referring to the language on DDX-10-17?

16 A.   Yes, I am.

17 Q.   Can you determine how the 4-milligram per kilogram

18 formulation tested in Dukes 1992 would compare to a dose for

19 breast cancer patients?

11:42AM 20 A.   So, in '90s, when we calculated dose or ordered drugs,

21 the ruling paradigm was, we would say for a 60 to 70 kilogram

22 woman. And if you say 70 kilo, then you're coming to

23 280 milligrams of dose. If you do 60, then it's slightly less

24 than 250. So it sort of approximates the dose that was to

11:42AM 25 come in future.

1   Q.   And does Dukes 1992 report on the duration of action of

2   fulvestrant?

3   A.   Yes, it does, it says that the blockade continued for

4   four weeks.

11:43AM   5   Q.   And how would that four week time period inform a person

6   of skill in the art about the use of fulvestrant for treating

7   breast cancer?

8   A.   It would translate into a depot injection once every

9   month.

11:43AM   10   Q.   Let's move on to the next preclinical study from your

11   overview, Wakeling 1993.

12   Did Wakeling 1993 report on another animal study?

13   A.   He summarized the available state of art at San Antonio

14   Symposium of this new pure antiestrogen that got eventually

11:44AM   15   published in Breast Cancer Research and Treatment.

16   Q.   And what does Wakeling 1993 report?

17   A.   It again goes over these studies we have covered, it

18   looks at the -- can I have the available piece? Okay.

19   So Wakeling goes on to say that the oil base

11:44AM   20   formulation of fulvestrant in experimental studies in rats

21   showed that the antiestrogen activity could be sustained for

22   long periods with single injection.

23   Q.   And what does Wakeling mention is described about the

24   administration of fulvestrant?

11:44AM   25   A.   So it's basically describing an oil depot injection, a

1 single injection intramuscularly -- single injection at four

2 weekly intervals giving an effective blockade of the same

3 duration, four weeks.

4 Q. And does Wakeling 1993 provide any information to a

11:45AM 5 person of skill in the art as to what the dose and frequency

6 of administration should be for fulvestrant?

7 A. So again, as I indicated earlier, a 65, 60, 70 kilo

8 woman, the dose starts to approximate 250 milligrams, it's

9 given in a once a month oil depot injection and it allows you

11:45AM 10 to have a sustained blockade for about a month. So those are

11 the things that are starting to become somewhat clear in the

12 preclinical science.

13 Q. And this is in reference to your demonstrative DDX-10-19?

14 A. That is correct.

11:45AM 15 Q. What does Wakeling 1993 tell the person of skill in the

16 art about the mechanism of action of the fulvestrant?

17 A. Basically it talks about very powerful antiestrogen

18 reaction of this particular product, which can probably

19 sustain 100 percent blockade of the estrogen receptor. And

11:46AM 20 finally concludes by saying that there is a powerful rationale

21 which argues for the superiority of this particular

22 antiestrogen over other treatments.

23   THE COURT: Antagonist.

24   THE WITNESS: Antagonist.

11:46AM 25 BY MS. PETERSON:

United States District Court
Camden, New Jersey

1 Q. Did Wakeling 1993 provided any teaching as to the

2 sequence in which fulvestrant could be used as a potential

3 endocrine agent for the treatment of hormonal dependent breast

4 cancer?

11:46AM 5 A. It does, because these were oophorectomized patients and

6 the treatment of choice for patients who had relapsed after

7 tamoxifen was becoming an increasingly important subject. So

8 what Wakeling in his particular article surmises is that

9 there's a sound rationale for treating patients who have

11:47AM 10 relapsed on adjuvant tamoxifen therapy with the pure

11 antiestrogens.

12 Q. And you're referring to DDX-10-21 in connection with your

13 testimony here?

14 A. Yes, I am.

11:47AM 15 Q. What other conclusions did Wakeling 1993 provide?

16 A. So summarizing the fact that this was the results that he

17 found impressive for potentially this group of patients, he

18 goes on to say that an initial therapeutic trial has started

19 in patients with advance breast cancer who have failed on

11:47AM 20 tamoxifen.

21 Q. Let's go to the last of the preclinical publications from

22 your overview. Can you tell me what generally is reported in

23 Dukes 1993?

24 A. So again, looks at an antiuterotrophic effect of pure

11:48AM 25 antiestrogens on female monkeys with sequential MRI's.

1 Q.   What would a person interested in developing a treatment

2 for hormonal dependent breast cancer take away from this

3 article?

4 A.   So basically it's again validation of the earlier idea

11:48AM 5 that this was an important new mechanism of action. I think

6 the only difference about this particular group was that these

7 were not oophorectomize animals.

8 Q.   And what does that mean?

9 A.   That basically means that this particular physiological

11:49AM 10 system tried to resemble a premenopausal woman.

11 Q.   And what were the results?

12 A.   The results were described as being unpredictable and

13 variable, which means that they did not produce the kind of

14 results one saw in a postmenopausal mortal, these results were

11:49AM 15 not very, very predictable and reliable.

16 Q.   Now, overall looking at all of these preclinical studies,

17 what do they tell a person of ordinary skill in the art

18 looking for new treatments for hormone positive breast cancer?

19 A.   That there was a new agent, that it had a new mechanism

11:49AM 20 of action. That it did not have cross-resistance with the

21 drug in question, tamoxifen. That it was working very well in

22 postmenopausal women. That there was a way of administering

23 it at 4 milligrams per kilogram dose and in an oil based depot

24 injection that could be given for sustained blockade for four

11:50AM 25 weeks.

United States District Court
Camden, New Jersey

1   Q.   So let's talk now about your clinical study slides.

2   What is depicted in this slide as it relates to the

3   clinical studies?

4   A.   So DeFriend basically looked at tolerance,

11:50AM   5   pharmacokinetics, and short term biological effects in women

6   with primary breast cancer. This was a short-acting

7   formulation. They were able to reach plasma levels of 27

8   nanogram per mL. And was very well tolerated.

9   Howell, going on from there, established safety in

11:50AM   10   dosing in some owes. Howell went on to look at this in actual

11   patients who had relapsed on tamoxifen. So he looked at

12   pharmacokinetic, as well as therapeutic effects in advance

13   breast cancer. Again, having used a caster oil base injection

14   long-acting. Use 250 milligrams per month. And 13 out of 19

11:51AM   15   patients responded.

16   Q.   Let's take a closer look at DeFriend 1994.

17   Can you identify who the authors were of DeFriend 1994?

18   A.   We can see familiar names. Beside that of Dr. DeFriend,

19   we have Anthony Howell, we have Nicholson, we have Mitch

11:51AM   20   Dowsett, we have Dr. Robertson, we have Alan Wakeling, several

21   of the researchers from that time in the UK and several of the

22   team from AstraZeneca.

23   Q.   And what does the fact that these authors were studying

24   fulvestrant, what does that mean to you?

11:52AM   25   A.   These were all very leading authors in their field with

good track records, so they were focused on this product in

terms of bringing it to further in its research, the product

definitely meriting attention.

Q.   Now, how many patients were included in the DeFriend

study?

A.   So he had a control group of 19 patients and a treatment

group of 37 patients, they received daily intramuscular

injections of fulvestrant in two dose settings, 6 milligrams

and 18 milligrams for seven days and then they were taken for

surgery.

Q.   And did the study include postmenopausal or premenopausal

women?

A.   They were only considered for the study if the women were

postmenopausal.

Q.   And what does DeFriend tell us about how the product was

administered?

A.   He gave as an intramuscular injection in the buttocks of

a short-acting formulation.

Q.   And what else does DeFriend tell us about the

short-acting formulation?

A.   So he gave it for seven days and he used it in two doses,

so 6 milligrams versus 18 milligrams, and he was able to

measure impact in terms of estrogen receptors, clinical

biochemistries, and serum levels of certain hormones.

Q.   And what was the dose that was administered?

er

1 A.   Two kinds of dose, 6 and 18.

2 Q.   I meant the concentration.

3 A.   20 milligrams per mL.

4 Q.   And what were the results of this trial reported in

11:54AM 5 DeFriend 1994?

6 A.   So one of the things reported were the blood levels he

7 got with the lower dose and the higher dose. And, as you can

8 see in the demonstrative, the higher dose, those levels go all

9 the way up to 25. So when we have 18 milligrams for seven

11:54AM 10 days, the end point seems to be ending at 25 and when we have

11 6 milligrams for seven days, the end point seems to be under

12 10.

13 Q.   And is the DeFriend reference you're referring to

14 DDX-10-27?

11:54AM 15 A.   I am.

16 Q.   And does DeFriend report any information concerning the

17 biological activity of the drug?

18 A.   He does. He found --

19 Q.   Go ahead.

11:54AM 20 A.   He found significant reductions in the estrogen receptor

21 levels in estrogen positive tumors in the group both at the 6

22 milligram level and 18 milligram level but very profound

23 reduction at the 18 milligram level. And the 18 milligram

24 level was statistically very significant, 0.01, and it brought

11:55AM 25 the level down from .73 to .01, which is an extremely low

1 estrogen level and impressive.

2   THE COURT: What dose levels, the 6 milligram and --

3   THE WITNESS: 18.

4   THE COURT: 18.

11:55AM 5   THE WITNESS: Only those levels, so we have the

6 lowest and highest possibly is there.

7 BY MS. PETERSON:

8 Q.   Is reduction of receptor expression a measure of

9 efficacy?

11:55AM 10 A.   It would translate into efficacy because if you have less

11 receptors, there's less switches to turn on this cancer and

12 its activity.

13   THE COURT: Can you explain that, please?

14   THE WITNESS: If you have less receptors -- each

11:56AM 15 receptor is like a switch on a tumor cell and it turns on the

16 electrical, the chemical messages start to go to the cell to

17 divide, multiple, spread, and having less number of estrogen

18 receptors would basically mean that it would be that much less

19 chance for the tumor to progress and grow.

11:56AM 20 BY MS. PETERSON:

21 Q.   Did DeFriend report any information about side effects in

22 the patients?

23 A.   Well, it was a seven day study and they saw no adverse

24 side effects, no patients were withdrawn from the study

11:56AM 25 because of drug toxicity.

1 Q.   What does DeFriend 1994 teach a person of skill in the

2 art who would be interested in developing a treatment for

3 hormone positive breast cancer?

4 A.   So this was a Phase II -- Phase I study in my mind, it

11:56AM 5 looked at the doses, it looked at safety, and it established

6 safety and established some guidelines for doses, and went on

7 to say that this was a new generation of potent pure

8 antiestrogens and is the first therapeutic agent to be

9 investigated in clinical trials with a potential so completely

11:57AM 10 to deprive breast cancer tumors of estrogenic stimulation.

11 And he goes on to say that Phase II trials with a long-acting

12 formulation of this agent are now in progress.

13 Q.   Now, DeFriend 1994 used a short-acting formulation that

14 was administered once a day. Would that be feasible for

11:57AM 15 further clinical studies in humans?

16 A.   In actual patient care that would be absolutely difficult

17 to administer because you cannot expect for months for a woman

18 to have daily injections, so this was impractical. For a

19 presurgical seven day trial it was okay.

11:58AM 20 Q.   Okay. Let's move on to the next piece of literature from

21 your clinical study section.

22   This is the Howell 1996 article?

23 A.   Yes.

24 Q.   And what type of study was conducted in Howell 1996?

11:58AM 25 A.   It was a pharmacokinetic, pharmacological in studying

1 antitumor effects of fulvestrant in women with advanced breast

2 cancer.

3 Q.   And do you recognize the authors of Howell 1996?

4 A.   They're all very well known. Dr. Howell, Dr. DeFriend,

11:58AM 5 Dr. Robertson, Sutcliffe, Walton, several from the labs of

6 Zeneca Pharmaceuticals.

7 Q.   Would you refer to this as a Phase II clinical trial?

8 A.   It was.

9 Q.   And what journal is Howell 1996 published in?

11:59AM 10 A.   It was published in the prestigious British Journal of

11 Cancer.

12 Q.   Is that a journal read by breast cancer researchers?

13 A.   Absolutely.

14 Q.   What was the purpose of the study in 1996.

11:59AM 15 A.   So this was the first investigation of an antiestrogen

16 fulvestrant in patients with breast cancer, and the

17 demonstrative that predicted levels of the drug from animal

18 experiments can be achieved and maintained for one month.

19   THE COURT: Are you saying predicted?

11:59AM 20   THE WITNESS: Predicted. Right.

21   Following intramuscular injections of the long-acting

22 formulation.

23   Can I have the next?

24 BY MS. PETERSON:

11:59AM 25 Q.   Okay. How was the study designed?

1   MS. PETERSON: Next slide.

2   THE WITNESS: So these were again postmenopausal

3   women who had either become refractory to tamoxifen after

4   being given tamoxifen in an adjuvant setting or had disease

12:00PM   5   stabilization and then subsequently progressed and so now they

6   were not responding to tamoxifen.

7   THE COURT: Schooch the microphone away just a little

8   bit.

9   THE WITNESS: Yeah.

12:00PM   10 BY MS. PETERSON:

11 Q.   How many patients were in the study?

12 A.   The study, I believe, had -- I'm having a block for a

13 second.

14   19 patients.

12:00PM   15 Q.   And what does Howell say about the dosage that was

16 administered?

17 A.   So they gave a 5 mL depot intramuscular injection, which

18 was a castor oil base vehicle, and he started first five

19 patients at 100 milligrams to make sure there was no new

12:01PM   20 toxicity. And at the end of the month when they did not see

21 that, they upgraded all those patients to the 250 milligram

22 dose and started the new group of patients on 250 milligram

23 dose.

24 Q.   And you're referring to DDX-10-32?

12:01PM   25 A.   Yes, I am.

1 Q. What were the results reported in Howell 1996?

2 A. So all 19 patients were evaluated, six were unresponsive

3 and 13, 69 percent, responded. And they had a median

4 durational response of 25 months, which was pretty impressive

12:01PM 5 for a Phase II.

6 Q. Were some of the 13 patients that were designated as

7 responders, did they all show progression or did they all show

8 a partial response to the drug?

9 A. So I think six of them had stable disease and the rest

12:02PM 10 showed actual shrinkage of tumor.

11 Q. And would it be typical to categorize results, a new

12 change being an actual response to the drug?

13 A. So, number one, the group that published this, and we

14 even now basically consider no news is good news, there's no

12:02PM 15 progression in the disease, that means the patient is

16 responding. Because if the patient is not responding, there

17 would be progression and there would be proof of that, so

18 stable disease at this moment is considered a very effective

19 indicator of efficacy. One would obviously hope for shrinkage

12:03PM 20 of tumor evidence. Patients who actually responded were in

21 one category but people who were stable were sort of lumped

22 with people who responded.

23 Q. So I understand, you're saying the authors categorized

24 the patients who were stable or no change as also being

12:03PM 25 responders to the drug?

1 A.   That is correct.

2 Q.   The reference you're referring to is DDX-10-33, is that

3 right?

4 A.   Yes.

12:03PM 5 Q.   What does Howell say about the side effects of the dose

6 that was administered to the patients?

7 A.   No side effects, serious side effects were seen in the 19

8 patients.

9 Q.   And you are referring to DTX-10-34?

12:03PM 10 A.   Yes, I am.

11 Q.   Does Howell make any conclusions with respect to the

12 volume of the drug that was administered?

13 A.   They were all either mLs in the buttock. And again,

14 talking about the side effects there were no local side

12:03PM 15 effects, no pain, no sciatica, no abscesses, things that we

16 worry about with large injections in that site.

17 Q.   What do the authors ultimately conclude about the

18 clinical trial results reported in Howell?

19 A.   So, this is a pure antiestrogen in long term treatment.

12:04PM 20 It seems to be active as an antitumor agent in patients with

21 advanced breast cancer who have relapsed previously on

22 tamoxifen.

23 Q.   And for reference you are referring to DTX-10-35?

24 A.   I am.

12:04PM 25 Q.   Now, what is the significance of Howell 1996's conclusion

1 that fulvestrant is active as an antitumor agent in patients

2 who had previously relapsed on tamoxifen?

3 A.   It tells you that there is no cross-resistance with

4 tamoxifen. People who failed tamoxifen will still respond to

12:05PM 5 this drug. That basically mean it's active in that particular

6 group and something worth exploring.

7 Q.   Let's take a look now, shift to what you had referred to

8 earlier as the corroborative studies, I believe. Turning to

9 the first one in the group, Robinson 1997. What is that?

12:05PM 10 A.   So, Robinson 1997 was a study where he took the data from

11 Howell, the patients -- 19 patients and he took his patients,

12 who were on metrozole acetate.

13   Let me digress and give a little idea of metrozole

14 acetate. So until that point before these other drugs were to

12:05PM 15 arrive on the horizon when people failed on tamoxifen,

16 megestrol acetate was considered to be standard of care second

17 line drug. And so we said okay, if this is the standard

18 second line drug, let's compared it to this new product, is it

19 the same or better or what. But this was not the same trial,

12:06PM 20 these people were not in the same trial, he took Howell's

21 trial, which he was part of, and he took another trial where

22 his be patients failed on megestrol and he compared efficacy.

23   And he came up with the findings that in case of

24 those who were treating with fulvestrant, the duration of

12:06PM 25 remission, whether they have partial remission or stable

1 disease, was 26 months. And if you went to the standard of

2 care at that time for failure, which was megestrol, it was

3 14 months. So it was an almost doubling of the duration. And

4 this -- basically they concluded, this particular study in the

12:06PM 5 paper by saying that these finding support further clinical

6 comparisons between established estrogen therapies and

7 fulvestrant.

8 Q.   What journal was Robinson 1997 published in?

9 A.   The Breast.

12:07PM 10 Q.   And would breast cancer researches in the nineteen

11 nineties have been following that journal?

12 A.   Absolutely.

13 Q.   For reference, you've been referring to DTX-10-37 as part

14 of your testimony just now?

12:07PM 15 A.   Yes, I am.

16 Q.   Now, did Robinson 1997 describe the Howell 1996 in any

17 other way?

18 A.   He goes on to say that a -- number one, he calls it Phase

19 II study, so he's basically looking at efficacy. And he goes

12:07PM 20 onto say rather surprisingly for a second antiestrogen not

21 only did most patients respond, but the median duration was

22 longer than suspected. So they were basically taken by

23 surprise that this drug suddenly was far better than what they

24 were using in clinical practice to treat women who had failed

12:08PM 25 on tamoxifen. Rather surprisingly, it's just their major

1 comment.

2 Q.   And you are referring to your demonstrative DDX- 10-3?

3 A.   Yes, I am.

4 Q.   In what your opinion, what does Robinson 1997 teach the

12:08PM 5 person of ordinary skill in the art about the use of

6 fulvestrant to treat hormone positive breast cancer?

7 A.   It basically again confirms that there is an antitumor

8 efficacy. It confirms that there is -- there are no signs of

9 agonist activity that one sees with tamoxifen. It sort of

12:08PM 10 sets up the stage for him being able to say that this was a

11 exciting new product and seems to be working in patients who

12 have progressed on tamoxifen.

13 Q.   And I think you had explained earlier that this wasn't

14 actually a real study between two -- between the two drugs,

12:09PM 15 right?

16 A.   So, the classic Phase III study would be randomized where

17 half would be on one and half would be on the other. The one

18 would be the standard of care and the other arm would be the

19 new drug. And then this would then be tested to see if one

12:09PM 20 was better than the other.

21   He did do a comparison to standard of care, but not

22 within the umbrella of single trial. He used Howell's

23 patients and looked at their response and then looked at other

24 patients that were in his trial on megestrol and compared it.

12:09PM 25 That's called cross-trial comparison and it's used basically

1 to see if the hypothesis seems to be working.

2 Q. Now, earlier this week Dr. Robinson testified that there

3 were several questions remaining about the use of fulvestrant

4 to treat hormone positive breast cancer after the results of

12:10PM 5 Howell 1996 were reported. Do you recall his testimony?

6 A. Yes, I do.

7 Q. Chris, could you bring up slide number 45 from Dr.

8 Robinson's direct testimony?

9 THE COURT: Were you here when he testified?

12:10PM 10 THE WITNESS: Yes.

11 MS. PENSABENE: I'm going to object to this as not

12 having any notice from the defendants that they were going to

13 use this slide with this witness.

14 MS. PETERSON: Well, it's not one of our

12:10PM 15 demonstratives, it's one your demonstratives.

16 MS. PENSABENE: Your Honor, the pretrial order is

17 really clear, the demonstratives that are going to be used on

18 direct examination have to be identified prior to the witness.

19 This is a demonstrative, it's being used on direct examination

12:10PM 20 with their witness.

21 MS. PETERSON: We can do the examination without the

22 demonstrative.

23 THE COURT: Okay.

24 BY MS. PETERSON:

12:10PM 25 Q. So, Dr. Mehta, you were here when Dr. Robinson testified

	1 on Monday, right?
	2 A. Yes, I was.
	3 Q. Do you recall Dr. Robinson testifying that there were
	4 several questions remaining about the use of fulvestrant to
12:11PM	5 treat a hormone-positive breast cancer, right?
	6 A. Yes.
	7 Q. Did Dr. Robinson reference Howell 1996 containing a group
	8 of favorably selected patients? Do you recall that?
	9 A. Yes, he did.
12:11PM	10 Q. Do you agree with Dr. Robinson that that was a concern
	11 with the Howell results?
	12 A. I don't.
	13 THE COURT: Was it the patients the 19, were favored?
	14 THE WITNESS: Highly selected group. Highly, that's
12:11PM	15 what he said.
	16 THE COURT: What was the word he used, biased or --
	17 THE WITNESS: Highly selected or, you know, the ones
	18 they were probably likely to respond and so subsequently they
	19 felt that maybe in a more generic group the similarly
12:11PM	20 responses might not have come. So his words were "highly
	21 selected group."
	22 THE COURT: Yes. Do you disagree with him?
	23 THE WITNESS: I do.
	24 THE COURT: Why?
12:11PM	25 THE WITNESS: So, the drug paradigm we were looking

1 for in this time frame would be postmenopause women that had

2 taken tamoxifen, and that's all these women were. They were

3 highly selected in a way, but yes, they were not triple

4 negative. They are highly selected in the way --

12:12PM 5   THE COURT: They were not what?

6   THE WITNESS: Triple negative. They were also not

7 ones that had failed other compounds. Like, if this was a

8 second line trial of this drug, it is likely to be quite

9 successful, but not third for people who had not yet been

12:12PM 10 exposed to aromatase inhibitors which were in trial. So,

11 subsequently criticism was that, okay, this is a selected

12 group because you pick patients who had just failed tamoxifen

13 and they were not down the line in terms of lines of therapy.

14 That's what I understand. Nobody has actually in the

12:12PM 15 literature explained what they meant by highly selected.

16   But the group was basically, by Howell's own

17 admission, postmenopausal women who had progressed on

18 tamoxifen. And these were women who were -- either failed on

19 tamoxifen and progressed or they stopped tamoxifen and then

12:12PM 20 the disease had come back and now they had progressed. So,

21 it's sort of the classic patient where such a drug would be

22 looked for but certainly not a patient who has been failing

23 several lines of treatment where this drug would have been

24 introduced. That's what I think he meant and I think I don't

12:13PM 25 agree.

1 BY MS. PETERSON:

2 Q.   And do you also recall Dr. Robinson's testimony about

3 Howell 1996's categorization of patients with no change as

4 responders?

12:13PM 5 A.   Yes, I do.

6 Q.   Would you have found that to be a clinically relevant

7 finding?

8 A.   I think no change is response. Because in oncology in

9 stage four disease no news is good news. So if a patient does

12:13PM 10 not show progressive tumor and the tumor is stable, achieving

11 stability means you are controlling the growth. So

12 controlling growth is what we are trying to do. And stable

13 patients without symptoms and without anything is good news.

14 Q.   What about tamoxifen withdrawal? What does that refer

12:14PM 15 to?

16   THE COURT: Can we put up that chart?

17   MS. PETERSON: Sure.

18   THE COURT: From Howell?

19   MS. PETERSON: Oh.

12:14PM 20   THE COURT: Isn't that the chart he's referring to?

21 The responders?

22   MS. PETERSON: Yeah, sure. That would --

23   MR. PRUGO: You are referring to Table 2?

24   THE COURT: Yes. Could I just see it?

12:14PM 25   So, you disagree with how Dr. Robinson broke down the

1 A.   So, patients who are failing on tamoxifen, there is one

2 small group that is -- actually, tamoxifen is fueling the

3 growth of the tumor because it also has the estrogen

4 stimulating faculties. And it does that. And in that case,

12:16PM 5 if you withdraw tamoxifen, that small group, you will see a

6 short response as the stimulators disappear and then the tumor

7 would start to grow again.

8 Q.   Now, do you agree with Dr. Robinson's conclusions about

9 Howell 1996 and the effect of tamoxifen withdrawal?

12:16PM 10 A.   So, I don't think one can quantify it because, again,

11 when you have tamoxifen withdrawal, this is a short-lived

12 phenomenon, can't really use it for therapeutic action. I

13 mean, yes, you can stop tamoxifen, there may be some time

14 during which the tumor may stop progressing, but soon tumor

12:17PM 15 will start to grow again. So I'm not exactly sure how it

16 impacted the numbers. The overall numbers are small, so,

17 again, I'm not sure how much impact it would have had. It's

18 sort of conceptual.

19 Q.   And are you familiar with the term "estrogen

12:17PM 20 sensitivity?"

21 A.   Yes, I am.

22 Q.   Can you explain that?

23 A.   So, to prolong life a woman in stage four breast cancer,

24 as you proceed down the treatment line, first line, second

12:17PM 25 line, third line, it's important that the tumor cells retain

1 endocrine sensitivity. If the endocrine sensitivity goes way,

2 then the tumor becomes unresponsive.

3 Q. And do you recall what Dr. Robinson's testimony was

4 regarding the endocrine sensitivity that was reported?

12:17PM 5 A. He was worried that in 10 patients, patients stopped

6 responding to megestrol after the antiestrogen fulvestrant was

7 used and he wondered at that time that -- whether that would

8 mean that if you used fulvestrant would the woman be deprived

9 of any further treatment options.

12:18PM 10 Q. So, was Dr. Robinson -- is the suggestion -- strike that.

11 Is the suggestion that if you take someone off of

12 fulvestrant that they would become sensitive to all other

13 endocrine therapies?

14 A. No. The suggestion was that would fulvestrant cause a

12:18PM 15 situation where subsequent treatments would fail. That was

16 his main concern that he voiced.

17 Q. And the subsequent treatment at issue in Robinson 1997,

18 what drug was that?

19 A. That was megestrol.

12:18PM 20 Q. And so do you agree necessarily with the hypothesis that

21 the patients who later became insensitive to the megestrol

22 acetate, that would mean that they have demonstrated an

23 endocrine sensitivity profile overall?

24 A. Again, I don't agree.

12:19PM 25 Q. Why not?

1   A.   So, you already have proven by also prior art that the

2   fulvestrant is a far more powerful agent. And what we are

3   finding on quality is if you use a powerful targeting agent to

4   block a target such as an endocrine receptor, the agents which

12:19PM 5   were of an earlier era, which were much weaker, would now not

6   work. You could only use the most powerful weapon. And if

7   the disease progresses, you cannot go back to drugs which were

8   inferior to that.

9   THE COURT: Hold on a second.

12:19PM 10   MS. PENSABENE: Your Honor, we've been really patient

11   with this outside the scope, but this is way outside of the

12   scope of the expert reports here.

13   MS. PETERSON: I think I'm almost done with this. We

14   can move on.

12:19PM 15   MS. PENSABENE: I move to have this testimony

16   stricken, your Honor.

17   THE COURT: I don't know what's outside the scope.

18   The last answer?

19   MS. PENSABENE: His whole last answer, this last two

12:19PM 20   answers.

21   MS. PETERSON: The ones on the endocrine

22   insensitivity.

23   MS. PENSABENE: This witness never testify about

24   that, never expressed such an opinion in his expert reports.

12:20PM 25   THE COURT: Okay.

1   Do you agree with that? I mean, unless there is an

2 objection I'm assuming that it's all relevant and within the

3 scope of the expert report. It's much harder for the court to

4 go back and strike testimony because much of it becomes

5 intertwined. So, do you agree that his opinions relating

6 to -- I guess it's the endocrine sensitivity issue, those are

7 all outside the scope?

8   MS. PETERSON: Well, Dr. Mehta did include the

9 Robinson and discussed the Robinson '97 publication in his

10 expert reports, and in particular the subsequent treatments

11 with megestrol acetate. I don't know if he specifically

12 mentioned the words "endocrine sensitivity" in his report, but

13 he certainly did discuss the Robinson 1997 article and the

14 impact of it.

15   THE COURT: So, the objection goes to the

16 insensitivity to the megestrol acetate? Is that the issue?

17   MS. PENSABENE: That is correct, your Honor, that was

18 never discussed in --

19   THE COURT: Okay.

20   MS. PENSABENE: -- Dr. Mehta's report.

21   THE COURT: So that testimony will not be considered.

22   MS. PETERSON: And just to confirm, you are talking

23 about the endocrine sensitivity testimony?

24   THE COURT: Apparently, yes.

25 BY MS. PETERSON:

1 Q.   Okay. Moving on. Are you familiar with the term of an

2 off target effect?

3 A.   Yes, I am.

4 Q.   And do you recall criticism by Dr. Robinson about

12:21PM 5 fulvestrant relative to impacts on other off target tissues?

6 A.   Yes.

7 Q.   What does that mean, this off target effect?

8 A.   If the target is the estrogen receptor positive breast

9 cancer, then all other organs outside that domain would be off

12:22PM 10 target. And what he was referring to was the effect of this

11 particular agent on other organ systems, bones, heart,

12 etcetera.

13 Q.   And had that already been reported in the prior art?

14 A.   There is reference in the prior art where there is a

12:22PM 15 suggestion that there is no impact on bone health.

16   THE COURT: On what?

17   THE WITNESS: On bone health.

18 Q.   And when you have potential downsides like that, how does

19 a clinician weigh those in view of the other benefits of the

12:22PM 20 drug?

21 A.   So, all new therapies have obviously some drawbacks. One

22 has to see what you are trying to achieve. If you are trying

23 to achieve efficacy for long life and provide one more mode of

24 bringing the disease in control, and if there were some side

12:23PM 25 effects that did not seem to be as important as controlling

1 the disease, that would be a tradeoff that one would be able

2 to accept as the therapy index. You have this much of

3 efficacy and you accept this much of toxicity.

4 Q. In your opinion, would the fact that fulvestrant had been

12:23PM 5 administered as an intramuscular injection in the Howell

6 study, would that have dissuaded a person of skill in the art

7 from continuing work with fulvestrant?

8 A. No.

9 Q. Why not?

12:23PM 10 A. Because I think intramuscular is the route that ensures

11 compliance, close physician visits and takes away the chance

12 of patients missing their oral pills. So it's actually a very

13 good way of dealing with a very difficult stage of disease.

14 Q. And another aspect of Howell was the five mL injections

12:24PM 15 volume. Do you recall that?

16 A. Yes.

17 Q. In your opinion, would a 5 mL injection volume, would

18 that have been too large to have been considered as a possible

19 route of administration?

12:24PM 20 A. No. And there were no side effects reported of that.

21 Q. Are you familiar with the concept of maximum tolerated

22 dose?

23 A. Yes, I am.

24 Q. Can you describe what that is?

12:24PM 25 A. So, when you are doing Phase I studies, one of the

1 objectives is to say what's the maximum tolerated dose, and

2 what kind of toxicities it will produce. And based on the

3 toxicities, a dose is set which is then moved on to Phase II

4 trials to see efficacy. In oncology, sometimes maximum

12:25PM 5 tolerated doses is what you want to use because underdosing

6 can lead to tumor resistance and progression. Underdosing can

7 lead to a tumor line to evolve and get out of control, and

8 then subsequently not respond to even higher doses. So

9 maximum tolerated dose basically insures that you have

12:25PM 10 no emergence of resistance or late emergence of resistance and

11 that's what you want to administer to get maximum benefit for

12 what you are doing.

13 Q. Is that concept applicable to treatments for breast

14 cancer?

12:25PM 15 A. Yes, it is.

16 Q. And is it also applicable to treatments -- hormonal

17 therapy treatments?

18 A. Yes, it is.

19 Q. Why is that?

12:25PM 20 A. Because for every drug there is a optimum dose. And when

21 you are trying to set a dose, if the evidence suggests, like

22 in Howell it was 250 mg and it was tolerated without major

23 side effects and showed efficacy, I would stay with that dose

24 because in subsequent studies I would not like to tinker with

12:26PM 25 the possibility that the efficacy would drop.

1   THE COURT: But do you agree that he taught a lower

2 dose?

3   THE WITNESS: The Howell does say that one should try

4 lower doses, yes.

12:26PM 5 BY MS. PETERSON:

6 Q.   But despite that, did researches, including Howell and

7 Dr. Robinson, continue testing the 250 mg dose?

8 A.   They did. And that went into the Phase III trials.

9 Q.   And the suggestion in Howell that you should be lower

12:26PM 10 than 250 mg, would that have motivated researches to not even

11 look at the 250 mg dose anymore?

12 A.   The most impressive prior art was Howell's one study at

13 125 and 250, and so why would anybody try to change that?

14 Because you would base your further clinical studies on most

12:27PM 15 effective dose at a Phase II trial.

16 Q.   Does it negate the results that were reported in Howell

17 with that 250 does?

18 A.   It doesn't negate the results.

19 Q.   Was the 250 mg dose in Howell 1996 the maximum tolerated

12:27PM 20 dose for fulvestrant?

21   MS. PENSABENE: Objection. That's outside the scope

22 of this witness' expert reports.

23   MS. PETERSON: We disagree. This opinion was

24 disclosed in his reply report.

12:27PM 25   THE COURT: Do I have it?

1   MS. PETERSON: Paragraph 16.

2   THE COURT: Do you recall rendering that opinion?

3   THE WITNESS: Yes, I do.

4   MS. PETERSON: Would you like a copy?

12:28PM 5   THE COURT: Yes. I don't think I have it up here.

6 Is it in his binder?

7   MS. PETERSON: It's not in his binder, your Honor.

8   THE COURT: Okay, thank you.

9   What was the question that was asked? Was the 250 mg

12:28PM 10 dose in Howell the most tolerated dose for fulvestrant? Is

11 that the question?

12   MS. MORAN: Maximum tolerated dose.

13   THE COURT: Excuse me, maximum.

14   MS. PETERSON: Yes, that was the question.

12:29PM 15   Okay. I'm sorry, your Honor, actually it's paragraph

16 17 of his report. Would you like a copy? May I approach?

17   THE COURT: Yes, please.

18   MS. PENSABENE: Now that counsel submits that, your

19 Honor, I'll withdraw the objection.

12:29PM 20   THE COURT: It seems it was. I'll keep it up here if

21 there is another objection. Thank you.

22   I think we're going to break it there. Why don't you

23 answer the question and we'll break for lunch.

24   THE WITNESS: I'm sorry?

12:29PM 25   THE COURT: Continue to answer the question.

1   THE WITNESS: If I remember the question correctly,

2   was that the maximum tolerated dose or not?

3   THE COURT: Was the dose that is disclosed in Howell,

4   which what was the 250 mg, was that the maximum tolerated dose

12:29PM   5   of fulvestrant?

6   THE WITNESS: No. I believe if you consider the

7   DeFriend trials, they had gone with 6 mg versus 18 mg dose.

8   That was given once a day for 7 days. If that was given once

9   a day for 7 days and if you take a 4-week interval where it

12:30PM 10   could be repeated and extrapolate to a 28-day cycle and

11   multiplication of 28 by 18 leads to a dose that is closer to

12   500 mg. So the dose disclosed in the Phase I trial seems to

13   have no side effects in that particular trial of DeFriend.

14   So, the dose disclosed seems to be around 500 milligrams of

12:30PM 15   fulvestrant.

16   THE COURT: Okay. We'll leave it at that.

17   We'll break for lunch. And if counsel many recall, I

18   will see you back at 2 o'clock. Okay? Thank you.

19   THE DEPUTY CLERK: All rise.

12:30PM 20   (Luncheon Recess 12:30 p.m.)

21   THE DEPUTY CLERK: All rise.

22   THE COURT: Okay. Great. Thank you. You may be

23   seated.

24   So, my criminal matter has been adjourned, and I

01:52PM 25   thought we would make use of the time. So we'll go about an

1   hour-ish or so, and then we will take our afternoon break.

2   Okay? So we can continue on.

3   MS. PETERSON: Actually, your Honor, before we

4   continue, upon further review, we did go back and look at

01:52PM   5   Dr. Mehta's expert reports with respect to the objection about

6   whether he had disclosed testimony concerning the endocrine

7   resistance, and we do think that it was properly disclosed in

8   his reply report, which you do have a copy of in front of you,

9   at Paragraph 15.

01:52PM   10   THE COURT: Did you share it with Ms. Pensabene?

11   MS. PETERSON: We have not yet.

12   THE COURT: You didn't talk to her about this?

13   MS. PETERSON: No.

14   But in Paragraph 15, he does -- Dr. Mehta does refer

01:52PM   15   to this portion of Robertson 1997 and the possibility of

16   fulvestrant resistance precluding further endocrine treatments

17   as a cause for concern. And then throughout the paragraph, he

18   discusses the benefits and down sides in the analysis that

19   would apply there. So we would ask for a reconsideration of

01:53PM   20   your ruling.

21   MS. PENSABENE: Your Honor, that is not about this

22   further endocrine insensitivity that's discussed in Robertson

23   1997. Robertson 1997 is not cited here; nor are the opinions

24   that were provided by Dr. Mehta on further endocrine

01:53PM   25   insensitivity. So I would stand by my objection that this is

            1   not disclosed in his expert report.

            2   THE COURT: So it doesn't seem to be within the scope

            3   of what he was testifying to, but I would prefer to have the

            4   benefit of the transcript. So were you through with the

01:53PM   5   questioning?

            6   MS. PETERSON: I was through with the questioning,

            7   and the witness was through with his answer, as well.

            8   THE COURT: Okay. So there is a motion to

            9   reconsider, and I'll reserve.

01:53PM   10   MS. PETERSON: Okay. Thank you, Your Honor.

           11   Defendants will recall and resume the testimony of

           12   Dr. Mehta.

           13   BY MS. PETERSON:

           14   Q.   Dr. Mehta, if we could move on to the next publication

01:54PM   15   discussed in your overview timeline. This would be McLeskey

           16   1998. Can you tell us what journal McLeskey 1998 was

           17   published in?

           18   A.   *Clinical Cancer Research*.

           19   Q.   And tell me about the *Clinical Cancer Research* journal.

01:54PM   20   Is that something that breast cancer researchers would be

           21   interested in?

           22   A.   Yes. It is the official journal of the American

           23   Association of Cancer Research, and something that sort of is

           24   offered just to clinicians, researchers, and people who are

01:54PM   25   doing bench and animal research. So it's kind of a place

1   where all research streams come together.

2   Q.   And what was -- and, for the record, Dr. Mehta's

3   testimony here, he is referring to DDX-10-040.

4   Dr. Mehta, what was the purpose of McLeskey 1998?

01:55PM 5   A.   So, McLeskey had a very unique idea. She basically was

6   looking at the MCF-7 cell line, which was until then the most

7   estrogen-sensitive cell LINE for experimentation. She changed

8   it in an -- she changed it in her laboratory, in her lab, and

9   created a cell line.

01:55PM 10   THE COURT: In her laboratory.

11   THE WITNESS: In her laboratory, and went on to

12   create a cell line that was totally independent, she thought,

13   of endocrine manipulation.

14   Now, to test her hypothesis, what she needed to do

01:55PM 15   was to try and bring two to three most powerful antiestrogenic

16   agents of that time, and what she chose were three agents that

17   she would test on the cell line and see if it retains its

18   independence, because her further research depended on showing

19   it, because this cell line was not manipulatable by changing

01:56PM 20   anything about the estrogen receptivity.

21   Q.   So, if I could just make sure that we all understand,

22   Dr. McLeskey had taken a -- a cell line that was typically

23   hormone --

24   A.   Sensitive.

01:56PM 25   Q.   -- sensitive, and what did she do to it?

1   A.   She changed it in her lab to make it a hormone

2   independent cell line. It's called transfection. And it was

3   basically a application of a growth factor, which then created

4   a cell line that would not respond to hormonal manipulation.

01:56PM   5   Q.   And then what was the purpose for which she used the

6   fulvestrant on that cell line?

7   A.   To prove that -- her hypothesis that this was not a

8   hormone manipulative cell line.

9   Q.   And what other compounds did Dr. McLeskey use?

01:56PM 10   A.   So she used a -- two aromatase inhibitor and one pure

11   antiestrogen. So she used letrozole, which was then

12   considered to be one of the powerful aromatase inhibitors; she

13   used formestane which, until mid-90s, was proved in Europe and

14   a major aromatase inhibitor; and for the antiestrogen, she

01:57PM 15   chose Faslodex® which was, in her mind, a very powerful new

16   antiestrogen agent.

17   Q.   And, for the record, in your testimony, were you

18   referring to DDX-10-41 and -42?

19   A.   Yes.

01:57PM 20   Q.   Does Dr. -- or does McLeskey 1998 describe the

21   formulations of the fulvestrant that were used in this study?

22   A.   She does. She uses two kinds of formulation. One is

23   a -- is a injectable in warm peanut oil, and she uses a second

24   formulation which is a injectable in castor oil. And these

01:58PM 25   are the two things that she basically is using as a source

1 material for fulvestrant.

2 Q.   And does McLeskey 1998 provide any further description of

3 the composition of the castor oil formulation?

4 A.   Yes, it does. It basically says it was a 50 milligram

01:58PM 5 per mL preformulated drug, in a vehicle of 10 percent ethanol,

6 15 percent benzyl benzoate, 10 percent benzyl alcohol, and

7 brought to volume with castor oil.

8 Q.   And who supplied the formulation, the castor oil

9 formulation, to Dr. McLeskey?

01:58PM 10 A.   This was supplied by Mr. B.M. Vose of AstraZeneca.

11 Q.   And, for the record, Dr. Mehta's testimony -- was your

12 testimony related to DDX-10-043?

13 A.   Yes.

14 Q.   Now, why would McLeskey 1998 be relevant, in your

01:59PM 15 opinion, to a person of skill in the art who would be

16 interested in treating hormone-positive breast cancer?

17 A.   So if you are looking for options in women who had

18 basically progressed on tamoxifen, and the prior art has

19 suggested that there was a powerful new antiestrogen, and you

01:59PM 20 were looking for validation that that was considered to be a

21 new agent with fairly reproducible efficacy, this particular

22 this particular article in this particular experiment goes on

23 to prove that Dr. McLeskey and her group also considered among

24 the three major agents to use to try and prove a hypothesis

01:59PM 25 that they had cell line that were resistant to hormone

1 manipulation. So, of the three agents she chose, she chose

2 fulvestrant, and this kind of, for me, would, again, reinforce

3 my interest in this product as being something I would be

4 interested in treating ER-positive breast cancer.

02:00PM 5   THE COURT: Could you try that again?

6   THE WITNESS: So, I think this particular piece of

7 art identifies and sort of says, okay, if you were to choose

8 the most interesting and powerful agents of that time to test

9 the hypothesis that we have a cell line that if we try to

02:00PM 10 manipulate with a hormonal treatment, it will still remain

11 independent, because there is a theory that you must

12 eventually develop a cell line that is completely hormone

13 independent. Eventually ER-positive cancer requires

14 chemotherapy because the hormonal manipulations eventually

02:00PM 15 fail to do anything. And even then, they are basically moving

16 on to chemo when tamoxifen and subsequent drugs fail. So

17 this -- basically, she -- her hypothesis was that these cells

18 are independent because there is another pathway in progress.

19   And so, if the estrogen manipulation blocks one

02:01PM 20 pathway, the cancer cells find a way and keep growing because

21 they are being driven by a different pathway. So when they

22 start to grow, the tumor grows, and now, manipulating estrogen

23 receptor by any kind of pharmacological agent would not lead

24 to any kind of efficacy.

02:01PM 25   And, to prove that point, she selected three major

1 agents of that time. One was letrozole, which was a very

2 powerful aromatase inhibitor. Another was formestane. And

3 what antiestrogen did she choose? Fulvestrant. And all three

4 failed to affect her independent cell line, proving her point

02:01PM 5 that she had an independent cell line. But point for me of

6 interest is that she picked fulvestrant as one of the three.

7 　　　　MS. PETERSON: Maybe I could ask a few follow-up

8 questions to maybe clarify.

9 　　　　THE COURT: Okay.

02:01PM 10 BY MS. PETERSON:

11 Q. So would you expect an antiestrogen like fulvestrant to

12 block the tumor activity in an estrogen-dependent cell line?

13 A. Yes.

14 Q. Now, would you expect an antiestrogen like fulvestrant to

02:02PM 15 block the tumor activity in an estrogen-independent cell line?

16 A. No.

17 Q. Now, had Dr. McLeskey created an estrogen-independent

18 cell line?

19 A. That is correct.

02:02PM 20 Q. What was she trying to prove?

21 A. That it was estrogen independent.

22 Q. And so was she trying to prove a hypothesis that -- or

23 strike that.

24 　　　So what was she using the fulvestrant for as part of

02:02PM 25 that hypothesis?

A.   So she was basically saying a fulvestrant, which is a

powerful antiestrogen, cannot stop the growth of this

particular cell line, and so it's not affected by it, proving

its independence from that agent.

02:03PM   THE COURT: But it was a hormone-independent cell

line.

    THE WITNESS: Right. She had to prove that point

before she went on with the cell line.

    THE COURT: So if you were interested in treating a

02:03PM   hormone-dependent breast cancer, what would McLeskey say to

you?

    THE WITNESS: Basically, again, all it would say to

you is that among the three agents she chose, of her time,

which was considered very powerful to test this hypothesis,

02:03PM   Faslodex® had made the grade, and so it must have been

impressive enough for ICI, AstraZeneca to supply, from the

other side, but not to supply the letrozole, and, of course,

fulvestrant -- the formestane is the third aromatase inhibitor

already in the market in Europe, so they are using that as a

02:03PM   third agent to see. Because these are all again -- the

hypothesis is that if this cell line indeed is independent,

these three powerful agents, none of them will show that the

growth of the cell line will slow down. And that's what she

was wanting to show, and that's what she ended up showing.

02:04PM   Q.   So would a person of skill in the art reading McLeskey

	1 understand that ICI 182,780 was chosen because it was
	2 recognized to be an effective antiestrogen?
	3 A. Chosen because it was novel and a powerful antiestrogen,
	4 yes.
02:04PM	5 Q. And did she prove her hypothesis?
	6 A. She did.
	7 Q. So does that mean that McLeskey's study was actually a
	8 success?
	9 A. From the viewpoint of what she was trying to prove, yes.
02:04PM	10 Q. And so do you consider McLeskey 1998 to represent a
	11 treatment failure, in your opinion?
	12 A. No.
	13 THE COURT: Were you here for Dr. Kern's testimony?
	14 THE WITNESS: Yes. No. I was here for
02:05PM	15 Dr. Robertson.
	16 THE COURT: Were you here this morning for
	17 Dr. Kern's?
	18 THE WITNESS: No.
	19 BY MS. PETERSON:
02:05PM	20 Q. So would a person -- a person of skill in the art
	21 interested in using fulvestrant to treat hormone-positive
	22 breast cancer, what would such a person learn from McLeskey?
	23 A. That if you are looking for a new powerful agent in the
	24 antiestrogen category, you had an interesting agent that
02:05PM	25 deserved attention and further studies.

1   Q.   And what would a person of skill in the art understand

2   from McLeskey with respect to the castor oil-based

3   formulation?

4   A.   So, McLeskey follows Howell, and Howell talks about a

02:05PM   5   castor oil formulation. And McLeskey gives that formulation

6   with the other fill-in-the-blanks agents. And it's around the

7   same time that Howell's results are published, subsequently

8   comes McLeskey, and to me, it would suggest that if I see ICI

9   or AstraZeneca supplied Dr. Howell his product, then the same

02:06PM   10   product was in McLeskey's article, and so that's the formula

11   of fulvestrant at that time in use.

12   Q.   And did McLeskey 1998 cite to and reference the Howell

13   1996 study?

14   A.   She does. One of the references she cites is exactly

02:06PM   15   that article, Reference 19.

16   Q.   And you are referring to your demonstrative, DDX-10-044?

17   A.   Yes.

18   Q.   Is there anything in McLeskey 1998 that would have

19   dissuaded a person of skill in the art from pursuing a

02:06PM   20   long-acting, 50 milligram per milliliter, castor oil-based

21   fulvestrant formulation to treat hormone-dependent breast

22   cancer?

23   A.   No.

24   Q.   Let's move on to the last publication from your overview.

02:07PM   25   This would be the Robertson 1999 abstract.

1   And can you just briefly tell us again what does the

2   Robertson '99 abstract teach?

3   A.   So these are the postmenopausal women. These were being

4   scheduled for surgery, and before surgery, a treatment

02:07PM   5   protocol was given. The women were given fulvestrant dose of

6   50 or 125 or 250 intramuscularly, with tamoxifen in one group,

7   and in the comparator group tamoxifen placebo. And his idea

8   was to -- that group's idea was to test this -- and he calls

9   it the most advanced of the new class of drugs. In this

02:08PM   10   particular two category, you see what happens.

11   Q.   And is this the same abstract you identified earlier in

12   your testimony?

13   A.   This is the same abstract that was presented to the

14   preliminary session of the San Antonio Breast Conference in

02:08PM   15   1999, selected out of 440 abstracts presented at that

16   particular conference.

17   Q.   And what does Robertson 1999 say about fulvestrant

18   relative to other pure antiestrogens under development at the

19   time?

02:08PM   20   A.   He goes on to call it the most advanced of the new class

21   of drugs, a non-agonist, and to quote, "pure," steroidal

22   antiestrogen.

23   Q.   Before we move off this topic of all the prior art, I do

24   want to go back and follow up on one point.

02:09PM   25   A lot of -- do you recall a lot of the papers you had

1 discussed involved research discussing anti-utertropic effects

2 of fulvestrant?

3 A.   Yes.

4 Q.   Why would that be relevant to a breast cancer researcher

02:09PM 5 looking for a new treatment?

6 A.   So, think of what was prevalent at that time. The most

7 important drug at that time was tamoxifen. And while it was

8 very useful in most of the women, where it created problems

9 was that it was not a pure estrogen blocker. In some

02:09PM 10 instances it stimulated like a estrogen.

11   And the one other it stimulated was uterus. It would

12 increase the uterine lining. There are problems with

13 menorrhagia and excessive blood loss.

14   And the worst of it was that in a small number of

02:09PM 15 women, the incidence of the lining of the uterus cancer going

16 up was noted.

17   So one of the ways you start looking at a drug is to

18 say is it efficacious, and the prior art shows in the earlier

19 preclinical phase that on the cell line, in the xenograft,

02:10PM 20 there was efficacy.

21   But, simultaneously, the second question that was

22 equally important was: Does it have any advantage in terms of

23 side effects? And it came up with this not have it being a

24 very strong anti-uterotropic agent, which basically meant that

02:10PM 25 it did not have the attribute to stimulate the lining of

1 uterus, and thereby, it was possible that the side effect of

2 uterine cancer could be prevented.

3 So you have a drug that has a promise of efficacy and a

4 promise of not having the side effects of the prevailing main

02:10PM 5 agent you are trying to find an alternative. And that's

6 probably the way this science then progressed.

7 MS. PETERSON: Your Honor, before we move into the

8 next area of Dr. Mehta's testimony, I would like to move into

9 evidence the exhibits that he has discussed thus far. The

02:11PM 10 defendants move to enter PTX-392, DTX-285, JTX-13, DTX-39,

11 DTX-48, JTX-16, DTX-49, JTX-17, JTX-15, JTX-11, JTX-14, and

12 JTX-10.

13 THE COURT: Okay. Any objections?

14 MS. PENSABENE: No objection, your Honor.

02:11PM 15 THE COURT: Okay. In evidence.

16 (DEFENDANT EXHIBITS' PTX-392, DTX-285, JTX-13, DTX-39, DTX-48,

17 JTX-16, DTX-49, JTX-17, JTX-15, JTX-11, JTX-14, and JTX-10

18 WERE RECEIVED IN EVIDENCE.)

19 BY MS. PETERSON:

02:11PM 20 Q.   Dr. Mehta, in your opinion, would a person of ordinary

21 skill in the art have been motivated to select fulvestrant to

22 treat hormonal dependent breast cancer?

23 A.   Yes.

24 Q.   Why?

02:11PM 25 A.   Because the prior art had a sort of seamless transition

1 from preclinical studies showing efficacy, safety,

2 tolerability, a definite method of administering it, which

3 would create a sustained drug level and require less frequent

4 administration, and the Phase I trial showed that it was safe,

02:12PM 5 and the Phase II trial again confirmed in human beings that it

6 was really efficacious. And so all that would basically bring

7 us to the corroborative pieces again, with Dr. Robertson and

8 other articles, that basically at that time heralded this drug

9 as the most advanced of the antiestrogen, and that would

02:12PM 10 certainly make it a very interesting subject to pursue.

11 Q.   And, in your opinion, would a person of ordinary skill in

12 the art have been motivated to select fulvestrant to treat

13 hormonal dependent breast cancer over candidates in other

14 categories of antiestrogens?

02:13PM 15 A.   So the candidates in other category were already moving

16 on. If you had a postmenopausal woman and the development was

17 for aromatase inhibitors, three agents are already on their

18 way to approval.

19   In case of the SERMs, the category where tamoxifen was

02:13PM 20 the principal agent, there were attempts to develop better

21 tamoxifen or safer tamoxifen, except really no agent came to

22 surpass or better the level of tamoxifen.

23   In some of them, which were similar to tamoxifen, but

24 not really efficacious, but they were found to have better

02:13PM 25 side-effect profile, and moved on to get approved for

1   something like preventing osteoporosis like Raloxifene.

2   But in the third category of pure antiestrogen, which

3   was a novel mechanism category, the most promising compound

4   was fulvestrant. And somebody who is interested in developing

02:14PM   5   something at that stage would say, okay, I realize they are on

6   their way to approval and are already doing very well.

7   Tamoxifen is the centerpiece of this particular mechanism.

8   This is interesting because a different mechanism, not likely

9   to be cross-resistant, and I'm interested. And the prior art

02:14PM   10   would lead you then to develop that further.

11   Q.   In your opinion, would a person of ordinary skill in the

12   art have been motivated to develop a long-acting

13   fulvestrant-based breast cancer therapy before 2000?

14   A.   Yes.

02:14PM   15   MS. PETERSON: Chris, if you could pull back up again

16   Dr. Mehta's demonstrative DDX-10-09.

17   BY MS. PETERSON:

18   Q.   So, if you could just explain your opinion.

19   A.   So, basically, that is a seamless transition in terms of

02:14PM   20   time and evidence. The Wakeling and Dukes data tells us that

21   on cell lines of MCF-7, this product was efficacious.

22   It tells us that on rats and monkeys, the side effect

23   of stimulating uterine lining was not present.

24   It takes us to a Phase I study in DeFriend where before

02:15PM   25   surgery, given every day for seven days, the product was seen

1 to be safe and had efficacy in terms of reducing estrogen

2 receptors.

3   In Howell, in Phase II, it proved that it was

4 efficacious in actual patients who have resistance to

02:15PM 5 tamoxifen, were postmenopausal, and produced 69 percent

6 improvement in a fairly impressive duration of response.

7   And, to go on, if that evidence is not enough, there

8 were evidence and praise coming in from some of the principal

9 authors of the preceding papers who were now saying this is

02:15PM 10 the most advanced of the antiestrogens. And they were already

11 trying it in their own patients for further trials with

12 standard of care, megestrol, or further trials where they were

13 saying preoperatively, let's look at the product, plus

14 tamoxifen which is a product, plus placebo, and see where we

02:16PM 15 go.

16   So not only did it impress these investigators, but

17 they are proceeding with further studies and clinical studies

18 which were on their way to Phase III trials.

19 Q.   And, in your opinion, would a person of ordinary skill in

02:16PM 20 the art have had a reasonable expectation of success that a

21 fulvestrant formulation would work to treat hormonal dependent

22 breast cancer?

23 A.   Yes.

24   Again, same argument. The preclinical, clinical

02:16PM 25 studies progressed in a logical lockstep, and come to Howell,

1 where you see the efficacy of 69 percent in this population,

2 which was resistant to tamoxifen, and you have other evidence

3 that suggests that it will basically be a product of promise.

4 Q.   And would your opinion be the same for a person of

02:17PM 5 ordinary skill in the art having a reasonable expectation of

6 success that a castor oil-based formulation would work to

7 treat hormonal dependent breast cancer?

8 A.   So Howell used a castor oil-based formulation once every

9 month and showed his results, and, yes, I would expect that to

02:17PM 10 be the principal formulation of interest.

11 Q.   And what does the teaching of McLeskey 1998 add to your

12 opinion?

13 A.   It basically tells me that that group also considered

14 Faslodex® as a principal representative of the antiestrogens

02:17PM 15 to test their hypothesis that the estrogen therapies do not

16 work in that independent cell line.

17   THE COURT: Which would be more valuable to someone

18 who was looking for a treatment for hormonal independent

19 breast cancer, correct?

02:18PM 20   THE WITNESS: That, and if somebody was saying, okay,

21 I have enough evidence about fulvestrant that it seems

22 interesting from Howell, here was another proof that another

23 group of investigators chose that drug to test their

24 hypothesis that such a powerful drug would not modulate this

02:18PM 25 cell line. So it sort of identifies and stamps the product

1   with approval from another set of investigators.

2   And McLeskey was not part of the AstraZeneca ICI

3   complex. She was an independent investigator. So her group,

4   having brought this product for their experiment, sort of

02:18PM   5   created one more impression which, in my mind, is

6   corroborative, saying okay, it's a front runner with letrozole

7   and with the formestane, that this is the product she chose.

8   So even though the cell lines didn't respond to them, they

9   were not supposed to. The fact that she chose that, it

02:18PM 10   basically tells you that she also evaluated the prior art that

11   was assisting them and said, okay, of the antiestrogens, I'm

12   going to use this to prove my hypothesis.

13   THE COURT: When you said earlier that it was not a

14   treatment failure, is that what you meant?

02:19PM 15   THE WITNESS: I meant that it is not a treatment

16   failure because she was not looking for treating

17   estrogen-positive breast cancer.

18   Her study had a hypothesis that these are independent

19   cell lines, and she was successful in proving it. And so it's

02:19PM 20   a positive study. She would report as a positive study. And

21   you can't go and say it's a treatment failure because she

22   wasn't treating estrogen-positive hormone cancer.

23   THE COURT: So let me see if I can summarize what

24   you're saying. It was a success, her study was a success

02:19PM 25   because it proved her hypothesis that the line that she was

1 developing was hormonally independent.

2   THE WITNESS: Right.

3   THE COURT: And she proved that hypothesis by

4 treating it with Faslodex® and powerful, to use your word,

02:19PM 5 antiestrogen.

6   THE WITNESS: Yes.

7   THE COURT: But it did not deal with treating the

8 disease itself.

9   THE WITNESS: No.

02:20PM 10   THE COURT: Okay. Thank you.

11 BY MS. PETERSON:

12 Q.   Dr. Mehta, just to make the record clear, the hypothesis

13 that Dr. McLeskey was teaching, did that relate to a method of

14 treatment or was it just -- or was it related to establishing

02:20PM 15 whether a cell line was independent?

16 A.   So I think what it basically established is that this

17 powerful product would not have any effect on her independent

18 cell line, but the fact that she used that particular

19 formulation means that she thought that if she had to test

02:20PM 20 with the best working formulation of that time, that the

21 AstraZeneca supplied, then she would use the formulation that

22 had shown success in Howell which came before her. So why

23 would she use something else?

24 Q.   Was it unexpected that an antiestrogen like fulvestrant

02:21PM 25 would not work on her estrogen-independent cell line?

	1	A. So, if it was truly independent, then it should not work.
	2	Q. And that's why she successfully proved her hypothesis?
	3	A. She did.
	4	Q. Do you recall Dr. Robertson's testimony about several
02:21PM	5	hormonal therapies from the 1990s that failed to receive
	6	approval?
	7	A. Yes, I do.
	8	Q. In your opinion, does the fact that a drug fails to
	9	receive FDA approval indicate that it was not efficacious?
02:21PM	10	A. No.
	11	Q. Why not?
	12	A. Because so many drugs don't reach FDA approval. Some are
	13	effective but may not complete all the trials. Some, the
	14	pharmaceutical industry that's sponsoring it may lose
02:21PM	15	interest. There are a lot of products that don't complete the
	16	entire journey, but they may be otherwise quite relevant.
	17	Q. Now, Dr. Mehta, you're familiar with the patents-in-suit,
	18	right?
	19	A. Yes.
02:22PM	20	Q. Can we put up demonstrative DDX-10-46.
	21	Do you recognize this claim from the '122 patent,
	22	generally representative of the claims asserted in this case?
	23	A. Yes, I do.
	24	MS. PENSABENE: Your Honor, this claim is not at
02:22PM	25	issue in this case.

1   THE COURT: Okay.

2   MS. PETERSON: I'm only trying to establish --

3   THE COURT: Background?

4   MS. PETERSON: Yes, just background. I'm only trying

02:22PM   5   to establish what elements of the claim, in general,

6   Dr. Mehta's testifying to.

7   MS. PENSABENE: Your Honor, it's not representative.

8   The assertion that's being made is that this claim is

9   representative of the claims at issue in this case and that's

02:23PM   10 just not true.

11   MS. PETERSON: And, your Honor, we provided notice of

12 this demonstrative to AstraZeneca I think two days ago, and

13 they did not indicate that they had any objection to us using

14 it. We could have prepared a different demonstrative using

02:23PM   15 one of the asserted claims. But --

16   THE COURT: What is the question? Let me hear the

17 question.

18 BY MS. PETERSON:

19 Q.   Within these claim elements, which portion are you

02:23PM   20 opining on?

21 A.   Method of treatment.

22   THE COURT: "Method of treatment" he said. Okay.

23   MS. PETERSON: And that's it.

24   THE COURT: Okay. Are you going to show him the

02:23PM   25 relevant claim?

1   MS. PETERSON: I can, sure.

2   THE COURT: Okay.

3   BY MS. PETERSON:

4   Q.   Can you pull up JTX-1? Actually, pull up JTX-4, please.

02:24PM   5   Go to the claims. If you could go in on -- go to Claim 1,

6   which is the original independent claim on which one of the

7   asserted claims-in-suit depends from.

8   Dr. Mehta, looking at Claim 1, can you tell me what

9   element of the claim you're primarily opining on?

02:25PM   10   A.   The one where it says the method for treating hormonal

11   dependent benign or malignant disease of the breast or

12   reproductive tract comprising administering intramuscularly to

13   a human in need of such a treatment a formulation comprising

14   of 50 milligrams of fulvestrant, and then the description of

02:25PM   15   ethanol benzyl alcohol, benzyl benzoate, and sufficient amount

16   of castor oil vehicle.

17   Q.   Okay. And you just read the entire claim.

18   A.   Right.

19   Q.   I was just asking you which portion of the claim are you

02:25PM   20   opining on?

21   A.   The method.

22   Q.   And then if we could go down to Claim 10 now.

23   THE COURT: Ms. Peterson, if you want to use your

24   prior chart, that's fine. I just didn't know if you were

02:25PM   25   going to get to it but -- what was the number?

1   MS. PETERSON: The demonstrative?

2   THE COURT: Yes.

3   MS. PETERSON: It was Number 46.

4   THE COURT: Yes, I don't see any harm in using it.

02:26PM   5 BY MS. PETERSON:

6 Q.   Dr. Mehta, you're not -- oh, excuse me.

7   THE COURT: Yes, okay. Go ahead.

8 BY MS. PETERSON:

9 Q.   So you're primarily responding -- you're primarily

02:26PM 10 opining on the method-of-treatment aspects of the claims,

11 right?

12 A.   Yes.

13 Q.   Are you offering opinions as to the formulation or

14 pharmacokinetic aspects of the claims?

02:26PM 15 A.   No, I am not.

16 Q.   Okay. You could take that down.

17   If you could pull back up Demonstrative Number 47.

18   Dr. Mehta, can you summarize for us the patient

19 populations and animal models that were used in the studies of

02:26PM 20 fulvestrant that you described earlier today?

21 A.   So, all the studies except one basically looked at either

22 ovariectomized animal systems or postmenopausal women.

23 Q.   And, again, what are the ovariectomized animals?

24 A.   So they are the physiological model for a postmenopausal

02:27PM 25 woman.

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1 Q.   And is there a study in this group of studies that is a

2 different patient population?

3 A.   So Dukes 93 had intact ovaries and similar testing to

4 other hypothesis was done.

02:27PM 5 Q.   And what does that patient population represent?

6 A.   So, that patient population refers to the premenopausal

7 women.

8 Q.   Now, do the postmenopausal women and ovariectomized

9 animal populations in your demonstrative reflect the

02:27PM 10 indication for which Faslodex® was originally approved to

11 treat?

12 A.   Yes.

13 Q.   Now, switching back to the patents in the case, you have

14 reviewed the specification of the patents?

02:28PM 15 A.   Yes.

16 Q.   And, in your opinion, does the specification of the

17 patents-in-suit inform a person of ordinary skill in the art

18 that the inventors were in possession of a method for treating

19 hormonal dependent breast cancer in premenopausal women?

02:28PM 20 A.   No.

21 Q.   Why not?

22 A.   Because there's no data. The data that you have on the

23 chart there, the only particular group that even simulates the

24 premenopausal women were Dukes 93, and there the outcome was

02:28PM 25 that the -- when the drug was used, the results were variable

1 and unpredictable, so really you can't translate that into

2 clinical efficacy in any way.

3 Q.   Limiting your analysis just to the patent, does the

4 specification of the patent inform a person of skill in the

02:29PM 5 art that the inventors were in possession of a method for

6 treating hormonal dependent breast cancer in premenopausal

7 women?

8 A.   No.

9 Q.   Why not?

02:29PM 10 A.   There is no -- no evidence or data supporting that

11 contention.

12 Q.   There is no evidence or data supporting that contention

13 where?

14 A.   In these patients.

02:29PM 15 Q.   Do you agree or disagree that once a scientific rationale

16 for a drug has been demonstrated in postmenopausal women, that

17 could be applied to premenopausal women? Do you agree with

18 that?

19 A.   No, I don't.

02:29PM 20 Q.   Why not?

21 A.   These are two different models in terms of what's

22 happening in their systems.

23   The premenopausal hormonal system is a tsunami of

24 estrogen hormone. So throughout the menstrual periods, the

02:30PM 25 estrogens rise and fall; throughout lactation, they rise and

1 fall; throughout pregnancies, there is a very sustained surge,

2 and the ovaries produce a very large number of -- amount of

3 estrogen.

4   Compared to that, in a postmenopausal woman, the

02:30PM 5 ovaries are gone. In terms of functionality, estrogen levels

6 have dropped. Slowly, the ovarian function is starting to

7 diminish to the point where all of the menopausal symptoms and

8 signs are taking over.

9   And these two -- these two models are -- when breast

02:30PM 10 cancer happens have totally different applicability.

11   So, for example, a postmenopausal woman will respond

12 even to a tiny amount of estrogen, that is converted from

13 androgen by enzyme aromatase.

14   But in the case of premenopausal woman, these surges of

02:30PM 15 estrogen are high, and hence, the same system, same idea of

16 control, does not usually work.

17   So these are -- for all the times we have treated them,

18 the premenopausal milieu, M-I-L-I-E-U, is a totally different

19 entity, and has different efficacy for different drugs.

02:31PM 20 Q.   Now, in your opinion, could a person of ordinary skill in

21 the art use fulvestrant to treat hormonal dependent breast

22 cancer in premenopausal women without undue experimentation?

23 A.   No.

24 Q.   Why not?

02:31PM 25 A.   Because, again, there is no data to suggest how it is to

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1   be used or whether it will be useful, and so it would require

2   a new experimentation to prove that point.

3   Q.   Does the patent provide any examples of how to treat

4   premenopausal women?

02:31PM   5   A.   No, it does not.

6   Q.   And what does the prior art say about treating

7   premenopausal women with hormone dependent breast cancer?

8   A.   Until that time, nothing. And the only report that we

9   have is from Dukes 93, which sort of suggests that it probably

02:32PM   10   is not a good idea because the results are variable and

11   unpredictable.

12   Q.   In your opinion, does the specification, the patent

13   specification, inform a person of ordinary skill in the art

14   that the inventors were in possession of a method for treating

02:32PM   15   hormone dependent breast cancer in men?

16   A.   No.

17   Q.   Why not?

18   A.   So, male breast cancer arises in a totally different

19   environment. While it is a cancer in the breast as a

02:32PM   20   location, the male's predominate hormone is estrogen -- is

21   androgen, the ogesterone, and these tumors have arise in a

22   testosterone resistant manner. While they are ER/PR positive,

23   they also express androgens. Just because there are no trials

24   in men, you can't automatically presume that everything that

02:33PM   25   has been proven for postmenopausal women would automatically

1 apply to men. These are different characteristics, they have

2 different prognoses, different sensitivity, even the hormones,

3 even the estrogen receptors in the male breast are taught not

4 to be functional. They express proteins in a different way.

02:33PM 5 The presence of estrogen receptor makes them a different kind

6 of a hormonal model and I would say that there is nothing to

7 suggest that male breast cancer has similar treatment outcomes

8 as female breast cancers.

9 Q.   And does the patent provide any guidance on using

02:33PM 10 fulvestrant to treat breast cancer in men?

11 A.   No, it doesn't.

12 Q.   And does the prior art say anything about using

13 fulvestrant to treat hormone-dependent breast cancer in men?

14 A.   No.

02:34PM 15 Q.   Dr. Mehta, before we move on, if we could go back to

16 demonstrative 48. So, I just wanted to ask you again, I think

17 you had already explained about the teachings of Dukes with

18 respect to premenopausal women, were there any other teachings

19 that you are aware of in the art with respect to the use of

02:35PM 20 fulvestrant in premenopausal women?

21 A.   So, one of the important voices of that time was Mitch

22 Dowsett and he says in 1995 that all the same -- it will be of

23 value to determined the effect of fulvestrant on ER/PR of

24 premenopausal breast cancer. And if you go on to Dr.

02:36PM 25 Robinson's opinion in 2007, he goes on to say that fulvestrant

1 250 mg has no effect, zero, on hormone sensitivity and

2 proliferation in premenopausal women with primary breast

3 cancer measured at 14 to 21 days. So, the prevailing wisdom

4 from the mid nineties and beyond, and even today, is that it's

02:36PM   5 a different animal requiring different kinds of treatment

6 programs.

7 Q.   In support of your opinion, are you relying on Dowsett

8 DTX-433 and Robinson DTX-881?

9 A.   Yes, I am.

02:36PM 10 Q.   Are you also relying on the DTX-309 Potter reference, the

11 DTX-320 Clark reference and the DTX-311 Wittliff reference?

12 A.   Yes, I am.

13   MS. PETERSON: Your Honor, we would move to enter

14 those exhibits into evidence.

02:37PM 15   MS. PENSABENE: No objection, your Honor.

16   THE COURT: Okay. In evidence.

17 (DEFENDANT EXHIBITS DTX-433, 881, 309, 320 AND 311 WERE

18 RECEIVED IN EVIDENCE)

19 BY MS. PETERSON:

02:37PM 20 Q.   If we could move forward to DTX-49. Dr. Mehta, can you

21 confirm you were relying on DTX-317 and DTX-318 in support of

22 your opinions concerning treatment of breast cancer in men?

23 A.   Yes, I was.

24   MS. PETERSON: Defendants move into evidence DTX-317

02:37PM 25 and DTX-318.

1   MS. PENSABENE: No objection.

2   THE COURT: In evidence.

3 (DEFENDANT EXHIBITS DTX-317 AND DTX-318 WERE RECEIVED IN

4 EVIDENCE)

02:38PM   5 BY MS. PETERSON:

6 Q. Now, Dr. Mehta, you also provided opinions in this case

7 responding to Dr. Robinson's testimony concerning certain

8 secondary considerations. Do you recall that?

9 A. Yes.

02:38PM   10 Q. And one of those secondary considerations that Dr.

11 Robinson has relied on is that Faslodex® has received acclaim

12 and praise from the industry based on certain industry

13 articles. Do you agree with Dr. Robinson's opinion?

14 A. I don't.

02:39PM   15 Q. Why not?

16 A. Around the launch of products, as well as when there is a

17 label change and the company needs to bring it again to the

18 attention the oncologists, a lot of pharma newsletters,

19 announcement at meetings, press releases start to talk about

02:39PM   20 the drug. Also review articles start to appear. I see that

21 more as part of marketing than actually sort of industry

22 praise. And a lot of things that are appearing in pharma

23 newsletters about the new product or a new indication are put

24 there to basically bring it to the attention of the treating

02:39PM   25 community that such a change is happening and in case they

1 have missed it.

2 Q. So, in your opinion are reports from practitioners better

3 indicators of industry recognition?

4 A. They are.

02:39PM 5 Q. Now, earlier we talked a lot about Dr. Howell and his

6 clinical study in the nineteen nineties. Right?

7 A. Yes.

8 Q. Has Dr. Howell commented on the performance of

9 fulvestrant compared to other hormonal therapies since it was

02:40PM 10 launched in the two thousands?

11 A. Howell's opinion was compared with other hormonal

12 therapies, the performance of Faslodex® was equivalent,

13 nothing better.

14 Q. Now, Dr. Robinson also testified that Faslodex® has

02:40PM 15 received acclaim and praise from those in the industry based

16 on the inclusion of Faslodex® in clinical guidelines. Do you

17 agree with that?

18 A. No, I don't.

19 Q. Why do you not agree with that?

02:40PM 20 A. So, let's take the most formidable American guidelines of

21 NCCN. NCCN is staffed by oncologists from all major NCI

22 designated cancer centers, and these are the leading experts

23 in their area of interest, and they look at all the evidence

24 and add new indications or new drugs as they see fit. But

02:41PM 25 they are obligated to add an agent to the list of agents

1   approved for that indication if FDA gives an approval.

2   Because FDA approval is one of the stamps saying okay, for

3   this particular paradigm you can use this particular drug.

4   So, it's almost automatic that guidelines will adopt

02:41PM   5   a drug into their algorithm of treatment when it receives FDA

6   approval, because when a physician opens up those guidelines,

7   he needs to know the drugs listed there have been approved by

8   FDA for the disease.

9   Q.   Are you aware of any instances where a guideline has

02:42PM 10   failed to recommend Faslodex®?

11   A.   There is a British guideline which is very well respected

12   in the industry which ruled otherwise.

13   Q.   And which guideline was that?

14   A.   The NICE one. I think it's the next one. That's

02:42PM 15   correct.

16   Q.   And what is NICE?

17   A.   So, this is the National Institute of Health and Care

18   Excellence, it's based in the UK. And drugs, as they enter

19   the treatment formulation in the National Health Service and

02:42PM 20   otherwise, the NICE takes a position on whether a new drug

21   with all its claims of improvement, etcetera, is something

22   they recommend for their patients. And as late as 2011 NICE

23   basically said that fulvestrant is not recommended within its

24   licensed indication as an alternative to aromatase inhibitors

02:43PM 25   for treatment of estrogen in a separate positive, locally

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1 advanced or metastatic diseases in postmenopausal women.

2 Q.   One other opinion that Dr. Robinson offered was that

3 Faslodex® has received acclaim and praise from the industry

4 based on its use as a control arm of a clinical trial. Do you

02:43PM 5 agree with that opinion?

6 A.   No, I don't.

7 Q.   Why not?

8 A.   So, I think one has to understand why a drug gets into

9 the control arm. A drug company wants to bring in a new

02:43PM 10 product and they basically are looking at saying okay, this is

11 a product and we're going to compare it against something

12 else. And they would choose a drug -- sometimes if they can

13 help it they will choose a drug where the company that is

14 marketing the competitor arm, a drug that is used as control,

02:44PM 15 joins into the research, joins into the expenditure, because

16 these are very expensive trials. And the fact that Faslodex®

17 was used as a control arm is largely recognition of the fact

18 that AstraZeneca was pretty forward in making sure that it

19 used their control arm in this trial. And that's a -- my take

02:44PM 20 on that is that that basically is largely because these then

21 become trials where the drugs are supplied free to the

22 patients, and these are expensive drugs, still under patent,

23 and the drug companies try to find partners where the

24 competitor drug is supplied.

02:44PM 25 Q.   Is your testimony based on DTX-10-53?

1 A. The NCCN, yes.

2 Q. I'm sorry. Did we have the wrong slide up? Okay, go

3 back. So the DTX-10-53.

4 A. 10-53.

02:45PM 5 Q. And if we could go back to DTX-10-52. Your testimony

6 about whether Faslodex® was included in the NICE guideline,

7 was that reference to DTX-10-52?

8 A. Yes.

9 Q. And the opinions that you've just offered with respect to

02:45PM 10 whether Faslodex® has received industry praise, were your

11 opinions from a perspective of a person of skill in the art

12 prior to 2000?

13 A. Yes.

14 Q. Just so I didn't -- I don't want to make anything

02:46PM 15 confusing, I wasn't meaning just your opinions relating to

16 secondary considerations were from the perspective of one of

17 skill in the art of 2000, and that applies to all of your

18 opinions, correct?

19 A. Yes.

02:46PM 20 Q. Now, Dr. Robinson has also offered opinions regarding

21 unexpected results as well, right?

22 A. Yes.

23 Q. Do you agree with Dr. Robinson's opinion that Faslodex®

24 has unexpectedly improved side effects profiles?

02:47PM 25 A. No.

1   Q.   Why not?

2   A.   So, if you are looking at the prior art before

3   January 2000, the prevailing works, the major research are

4   summarized on this slide. Howell is again saying that the

02:47PM   5   long-acting administration of 4 mL was tolerated locally

6   without any problems.

7   THE COURT: Was tolerated locally?

8   THE WITNESS: Without any problems.

9   A.   Howell again said that the greater exposure was not

02:47PM   10   associated with any increased side effects or efficacy.

11   Howell again stated that the product was associated with high

12   response rate and long experienced duration in patients

13   previously treated with tamoxifen. But even down to -- and

14   then I quote Wakeling, who basically went on to say that

02:47PM   15   analysis of bone density in rats on Faslodex® did not reveal

16   any deleterious effects.

17   So, all of the prior art we have looked at that comes

18   to Howell and beyond, one of the remarkable things everybody

19   notes is that its side effect profile is very good and that

02:48PM   20   then should not come as a surprise now.

21   Q.   And, for the record, is your testimony in relation to

22   DTX-10-054?

23   A.   Yes.

24   Q.   And is it based on JTX-11 and DTX-49?

02:48PM   25   A.   Yes.

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 1  Q.  Dr. Mehta, just going back to a topic one more time that

 2  we covered before.  Would there have been a motivation to use

 3  a long-acting castor oil-based formulation of fulvestrant to

 4  treat hormone dependent breast cancer before 2000?

 5  A.  Yes.

 6  Q.  And can you explain why?

 7  A.  So, the linear progression of preclinical to clinical

 8  studies which showed that there was efficacy, there was

 9  safety, there was a method of delivery.  The method of

10  delivery was a once a month type of injectability possible.

11  The Phase I studies showing safety and efficacy in terms of

12  estrogen receptors, Phase II showing efficacy and again

13  safety, all the 19 women had hardly any side effects, all

14  these things lead you to the point where you say okay, the

15  drug has promise and a person of skill in ordinary art would

16  basically consider it as something that would be interesting

17  enough to explore further.

18  Q.  And likewise, would there have been motivation to use a

19  long-acting castor oil-based formulation of fulvestrant to

20  treat hormone-dependent breast cancer before 2000 as

21  administered intramuscular by 5 mL injections?

22  A.  Yes.

23  Q.  And why is that?

24  A.  So, again, Howell uses that formulation and brings his

25  results.  And that's a formulation that is --
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02:49PM (line 5)
02:49PM (line 10)
02:49PM (line 15)
02:50PM (line 20)
02:50PM (line 25)

1   THE COURT: He uses that formulation and brings his

2 what?

3   THE WITNESS: Brings his efficacy that we have

4 described. And he basically brings up the possibility of

02:50PM 5 having a therapeutic agent that can be administered monthly by

6 intramuscular depot progressions and reducing the need for

7 more frequent injections.

8   MS. PETERSON: Defendants also move to enter the

9 following exhibits into evidence: JTX-1, JTX-3, JTX-4,

02:51PM 10 PTX-432, DTX-282, DTX-287, DTX-306 and DTX-307.

11   THE COURT: Any objection?

12   MS. PENSABENE: Let me just ask, are these the

13 exhibits that were discussed here?

14   MS. PETERSON: They were discussed in the last

02:51PM 15 section on secondary considerations plus the patents.

16   MS. PENSABENE: No objection, your Honor.

17   THE COURT: Okay, in evidence.

18 (DEFENDANT EXHIBITS JTX-1, JTX-3, JTX-4, PTX-432, DTX-282,

19 DTX-287, DTX-306 and DTX-307 WERE RECEIVED IN EVIDENCE)

02:51PM 20   MS. PETERSON: Pass the witness.

21   THE COURT: Okay. So this is a good time to take our

22 break. So I was in the middle of a sentencing. I don't think

23 it will go maybe 20 minutes. So if I can ask you to just --

24 we'll take about a 20-minute break, okay? You can sort of pop

02:52PM 25 in and see in we're done. So, don't get too comfortable.

1 Okay. We'll pick right back up. All right?

2   THE DEPUTY CLERK: All rise.

3   (Brief Recess at 2:52 p.m.)

4   THE COURT: Whenever you're all ready. Sorry for the

03:37PM 5 delay.

6   Ms. Peterson, can I give you back the reply report?

7   MS. PENSABENE: Thank you, your Honor.

8   THE COURT: As I indicated, counsel, we'll go to

9 about 5:00.

03:40PM 10   MS. PENSABENE: Thank you, your Honor.

11   THE COURT: Okay?

12   MS. PENSABENE: Thank you, your Honor.

13 (CROSS-EXAMINATION OF DR. MEHTA BY MS. PENSABENE:)

14 Q. Good afternoon, Dr. Mehta.

03:40PM 15 A. Good afternoon, counselor.

16 Q. It's nice to see you again.

17 A. Same here.

18 Q. Dr. Mehta, you said that McLeskey had a very unique idea,

19 right? You remember that?

03:40PM 20 A. Yes.

21 Q. And you said she had success from the viewpoint she was

22 trying to prove. And that's hormonal independence, right?

23 A. That's correct.

24 Q. Now, you used the term "powerful antiestrogen agent"

03:41PM 25 several times during the discussion of McLeskey. She never

1   used those words, right?

2   A.   No, subsequent and proceeding prior art had used

3   terminology saying the most advanced. And the evidence also

4   had suggested that this was powerful enough to be used in

03:41PM   5   tamoxifen resistant breast cancer patients, it was a powerful

6   new agent.

7   Q.   That's your interpretation?

8   A.   Yes, it is.

9   Q.   That's not the interpretation of Dr. McLeskey's paper, is

03:41PM 10   that right?

11   A.   No.

12   Q.   Now, you talked about Dr. McLeskey's paper using a

13   particular formulation. So to be clear, there were two

14   formulations of fulvestrant in that paper, isn't that right,

03:41PM 15   and she used both of them?

16   A.   Yes, she did.

17   Q.   And she doesn't distinguish between them, does she?

18   A.   No.

19   Q.   And so your point is -- I want to make sure I'm getting

03:42PM 20   this right.

21   Your point is that she selected the compound for study

22   not the formulation, right?

23   A.   I think she selected the formulation.

24   Q.   You agree that she used two formulations interchangeably,

03:42PM 25   don't you?

1 A.   She has mentioned both formulations, yes.

2 Q.   And you agree she used then interchangeably, right?

3 A.   I'm not sure what you mean by "interchangeably."

4 Q.   She doesn't distinguish between one from another?

03:42PM 5 A.   She used both phrases, yes.

6 Q.   And you'd agree with me there's nothing in the paper --

7 no data in the paper that compares the two formulations, no

8 data in the paper that says that one -- or statement in the

9 paper that says one formulation is better than the other

03:43PM 10 that's right?

11 A.   That is correct.

12 Q.   And you would also agree with me that all of the

13 formulations in that McLeskey paper are animal formulations,

14 right? You'd agree with me on that?

03:43PM 15 A.   Yes.

16   MS. PENSABENE: Okay. And let's put --

17 BY MS. PENSABENE:

18 Q.   So you'd agree with me --

19   MS. PENSABENE: Let's put up that McLeskey methods

03:43PM 20 section.

21   Thank you, Mr. Hoy.

22 BY MS. PENSABENE:

23 Q.   So you'd agree with me that McLeskey's is four different

24 antiestrogen compounds. And for the letrozole formulation,

03:43PM 25 that's not a commercial formulation, right?

1 A.   No.

2 Q.   That's a research formulation for use in animals, right?

3 A.   That's correct.

4 Q.   And for her experiments with tamoxifen, McLeskey used a

03:43PM 5 preformulated pellet that's only sold for animal research and

6 that's not the formulation for humans either, right?

7 A.   That's correct.

8 Q.   Okay. That's an animal formulation, right?

9 A.   Yes.

03:44PM 10 Q.   Okay. And you would agree with me that the peanut oil

11 formulation that McLeskey uses similarly is the animal

12 research formulation that's used in the early preclinical

13 research that you discussed during your direct testimony,

14 right?

03:44PM 15 A.   Yes.

16 Q.   And I think you already agreed with me, let me just be

17 sure, McLeskey is about hormone independent pathway?

18 A.   That is correct.

19   MS. PENSABENE: You know what, I just want to keep

03:44PM 20 track of stuff, so do you mind if I write some things down on

21 the board?

22   Your Honor, may I approach and use that chart?

23   THE COURT: You may.

24 BY MS. PENSABENE:

03:44PM 25 Q.   I hope you will indulge my handwriting. I apologize.

1   It's -- I'll try to be neat.

2   So I've written here McLeskey and under it hormone

3   independent. You'd agree with that?

4   A.   Yes, I would.

03:45PM 5   Q.   Okay. Now, if you could take a look, please, at the

6   method section for the formulations that were used of

7   fulvestrant, you would agree with me that both of those

8   formulations were administered subcutaneously, is that

9   correct?

03:45PM 10   A.   That is correct.

11   Q.   Okay. I'm just going to write that down here on this

12   chart then.

13   And you'd also agree with me, right, Dr. Mehta, that

14   the fulvestrant formulations, the two fulvestrant formulations

03:45PM 15   were both administered once weekly?

16   A.   That is correct.

17   Q.   So if I write "weekly" on the chart, that expresses what

18   we just agreed upon?

19   A.   Agreed.

03:46PM 20   Q.   You would also agree with me that in the McLeskey system,

21   the fulvestrant formulations were cross-resistant with

22   tamoxifen, is that right?

23   A.   Say that again?

24   Q.   In the McLeskey system --

03:46PM 25   MS. PENSABENE: We can pull up the title, perhaps,

1 Mr. Hoy?

2   THE WITNESS: That's okay. Go ahead.

3   Can you repeat the question?

4 BY MS. PENSABENE:

03:46PM 5 Q.   In the McLeskey system the fulvestrant formulations were

6 cross-resistant with tamoxifen, is that right?

7   I'll just read the title for you, Dr. Mehta, and maybe

8 that will help.

9   THE COURT: Were the formulations that she used

03:46PM 10 cross-resistant with tamoxifen?

11   THE WITNESS: I think basically says the cell line is

12 cross-resistant. Where does it say it is cross-resistant to

13 tamoxifen?

14 BY MS. PENSABENE:

03:47PM 15 Q.   Let's read the title together. Okay?

16 A.   So I read for you.

17   Tamoxifen resistant FGF-transfected MCF-7 cells are

18 cross-resistant *in vivo* to the -- Faslodex is the other

19 approach. So that means they don't respond to these products

03:47PM 20 not tamoxifen. It's a fancy way of saying this is a hormone

21 independent cell line, that's how I interpret this particular

22 title.

23 Q.   Okay. So you don't interpret this title to mean that the

24 cells are resistant to both ICI 182,780 and tamoxifen?

03:48PM 25 A.   Basically she's talking about cell lines being

1 cross-resistant in terms of these three products she used,

2 which is another way of saying these are independent of these

3 three hormonal manipulator drugs.

4 Q. So I can write here on my chart cross-resistant? I just

03:48PM 5 want to be accurate in what your opinion is.

6 A. Yes.

7 Q. Okay. I'll go back over here so I'm not leaning over

8 your shoulder, Dr. Mehta. Sorry about that.

9 Okay. Now, you would agree with me that the McLeskey

03:48PM 10 paper doesn't give any data on the extent of estrogen pathway

11 suppression for any of the compounds that were used in any of

12 the formulations, correct?

13 A. Correct. Yes.

14 Q. And you would agree with me, too, that the McLeskey paper

03:49PM 15 doesn't gave any pharmacokinetic data for any of the

16 treatments that were used, right?

17 A. That is correct.

18 Q. Also the McLeskey paper doesn't give any data on

19 antiestrogen effect for any compound used, right?

03:49PM 20 A. Yes.

21 Q. Now, the only results that are given for the formulations

22 with ICI 182,780 for fulvestrant is that it is a treatment

23 failure, right?

24 A. No.

03:49PM 25 Q. Do you disagree with me that McLeskey describes the

1 results with ICI 182,780 as a treatment failure?

2 A.   Basically it's one way of saying that these are

3 independent cells that are not possible to be manipulated by

4 three powerful antiestrogens. And if that's what you mean by

03:50PM 5 the question, I agree.

6 Q.   And those are the words that were used by Dr. McLeskey in

7 her paper is "treatment failure," you'd agree with that,

8 right?

9 A.   Yes.

03:50PM 10 Q.   And you'd also agree that Dr. McLeskey in her paper says

11 that treatment with fulvestrant does not inhibit tumor growth,

12 right?

13 A.   That is correct.

14 Q.   And you'd also agree that Dr. McLeskey says in her paper

03:50PM 15 these treatments did not slow estrogen independent growth or

16 prevent metastasis of tumors, right?

17 A.   That is correct.

18 Q.   And your goal in treating a patient with hormonal

19 dependent breast cancer is indeed to slow growth and prevent

03:51PM 20 metastasis, is that right?

21 A.   By and large, yes.

22 Q.   And I think you used the term "successful." But McLeskey

23 doesn't use the word "successful" about the use of any of the

24 fulvestrant formulations within her paper, does she?

03:51PM 25 A.   What it basically means is she was testing that these are

1   hormone independent cell lines, which normally are hormone

2   sensitive because of MCF-7, and she has created a cell line

3   which are totally independent than using these drugs and

4   showing that they are hormone independent is a successful

03:51PM   5   experiment because that's what she was trying to show. So

6   success is basically proving the hypothesis.

7   Q.   And you agree there's no data about an estrogenic effect

8   of these compounds, right?

9   We'll move on. I'll withdraw.

03:52PM   10   Okay. I think you cited a connection with the Howell

11   paper from McLeskey, right?

12   A.   Yes.

13   Q.   Okay. And you included a footnote that cites to Howell

14   but you didn't include what that citation was for. So can we

03:52PM   15   look together as to what that citation was for?

16   A.   Yes.

17   Q.   What I did, I took your slide and put that together, and

18   you should check it and make sure it's right.

19   MS. PENSABENE: Can you pop that up, Mr. Hoy? I

03:52PM   20   think it's -- we put it together with Dr. Mehta's slide.

21   BY MS. PENSABENE:

22   Q.   Just so we're on the same page. Okay?

23   A.   Right.

24   Q.   Here we go. Sorry about that.

03:53PM   25   Okay. So you had cited to Footnote 19, and that's a

1   Howell paper. So let's look first at what McLeskey says in

2   the abstract. She says that only 30 to 40 percent of patients

3   have a positive response to second hormonal therapies, and

4   then she calls that a lack of response. Do you see that?

03:53PM 5   A. Yes.

6   Q. Okay. And then she goes on to explain within the body of

7   the paper, and there she says that, early results for small

8   numbers of tamoxifen resistant patients have shown that only

9   about 30 to 40 percent of such patients have a positive

03:53PM 10   response to subsequent ICI 182,780 or aromatase inhibitor

11   therapy. Do you see that?

12   A. Yes.

13   Q. And that's where she cites Howell, isn't that right?

14   A. Yes.

03:54PM 15   Q. She cites it as one of a series of papers about endocrine

16   therapy, right?

17   A. Right.

18   Q. And her point being endocrine therapy doesn't work all

19   that well so we're looking for another pathway to work on,

03:54PM 20   isn't that what she's saying?

21   A. Yes.

22   Q. She's distinguishing what she's doing from endocrine

23   therapy, right?

24   A. Right.

03:54PM 25   Q. Okay. And I think that's been some of your point, right,

1 Dr. Mehta?

2 A.   Yes.

3 Q.   That this is different, totally different from endocrine

4 therapy.

03:54PM 5 A.   That's correct.

6 Q.   I'm sorry, let me make sure I'm clear.

7   This is totally different from hormonal dependent

8 pathways, right?

9 A.   That is correct.

03:54PM 10 Q.   Okay. All right. And now in thinking about the McLeskey

11 paper and sort of where it fits into this time line, you had

12 noted several times I think today the names of some well-known

13 researchers, and you noted Dr. Robertson and Dr. Howell, and

14 some people also from AstraZeneca.

03:55PM 15 A.   Yes.

16 Q.   Dr. Wakeling and Dr. Dukes. So let's take a look at the

17 McLeskey paper.

18   MS. PENSABENE: Can you pull up the front of the

19 paper, please, Mr. Hoy? And that's JTX-10. Great. There we

03:55PM 20 go.

21 BY MS. PENSABENE:

22 Q.   Okay. You would agree with me, right, Dr. Mehta that

23 none of these folks that are authors on this paper or any of

24 those researchers that you've been naming and none of them are

03:55PM 25 from AstraZeneca, right?

03:56PM 1 A.   That is true. This is the Lombardi Cancer Center, which

2 was independent of the research going on in the UK.

3 Q.   Okay. And you would agree with me, right, that there

4 were other researchers who had used fulvestrant as a research

03:56PM 5 tool in their work with animals, right?

6 A.   Yes.

7 Q.   Okay. So you would agree with me, like, for example, the

8 Al-Matsubi reference, I think you and I talked about that at

9 your deposition.

03:56PM 10 A.   Yes.

11 Q.   You would agree with me that that reference was looking

12 at the estrogenic cycle in sheep also used fulvestrant and

13 that used it for basic animal research and injected it

14 intramuscularly, right?

03:56PM 15 A.   I would have a look at it.

16 Q.   I can show that to you and see if you agree.

17 A.   Please.

18 Q.   I want to make sure we're right on the same page.

19   MS. PENSABENE: May I approach, your Honor?

03:57PM 20   THE COURT: Yes.

21   MS. PENSABENE: May I hand you one?

22   THE COURT: Yes. Thank you.

23 BY MS. PENSABENE:

24 Q.   And, Dr. Mehta, this work is just also basic animal --

03:57PM 25   Let me just clarify. This is PTX-693. So the record

1 will be clear, it's the Al-Matsubi paper.

2 BY MS. PENSABENE:

3 Q. And this is just talking about the compound fulvestrant,

4 its using it in animal research. This time it's injecting the

03:57PM 5 compound intramuscularly into sheep and it's the same kind of

6 situation, some basic animal research, right?

7 A. Yes.

8 Q. Okay. And here also they, to the last page, the

9 researchers thanked ICI Pharmaceuticals for their gift of the

03:58PM 10 compound, right?

11   MS. PETERSON: Your Honor, we object to this line of

12 testimony on the Al-Matsubi reference. Dr. Mehta did not

13 provide any opinion about this on direct testimony and I think

14 it's not in the scope of his expert reports as well.

03:58PM 15   MS. PENSABENE: Actually, it's in the scope of his

16 report.

17   That was the last question, anyway. The point being

18 the compound was used for basic animal research and in a

19 number of different --

03:58PM 20   THE COURT: That's for the general proposition?

21   MS. PENSABENE: I'm sorry?

22   THE COURT: For the general proposition?

23   MS. PENSABENE: Yes, exactly, your Honor. No

24 specifics about that.

03:58PM 25   THE COURT: Okay. For that purpose I'll permit it.

1 BY MS. PENSABENE:

2 Q. Now, just to finish off talking a little bit about

3 McLeskey here. I want to just get an idea where McLeskey

4 falls on this picture we've got here to understand where it is

03:59PM 5 in the pathways if you don't mind.

6 So you'd agree with me, Dr. Mehta, that McLeskey is

7 looking at FGF, one of these growth factors, right?

8 A. Right.

9 Q. As a possible pathway for hormone independent breast

03:59PM 10 cancer, is that correct?

11 A. Yes.

12 Q. Okay. So if I put this up here, that's correct that

13 McLeskey is FGF hormone independent. And I've circled the FGF

14 receptor in these growth factor pathways.

03:59PM 15 A. Yes.

16 Q. And that's different from the estrogen receptor and the

17 hormonal dependent pathways, is that right?

18 A. That's correct.

19 Q. And I think that was your point, right?

04:00PM 20 A. Yes.

21 Q. Okay. Let's go back a little bit and talk about options

22 for active ingredients for treatment for hormonal dependent

23 breast cancer. Okay?

24 You would agree with me, right, that by 2000 treatment

04:00PM 25 that had been used for hormonal dependent breast cancer

1   included tamoxifen, other SERMs, third generation aromatase

2   inhibitors and other aromatase inhibitors, progestin,

3   androgen, hydro estrogen. Do I have it right?

4   A.   Yes.

04:00PM 5   Q.   Okay. And so the SERMs, those were a proven mechanism,

6   right?

7   A.   That's correct.

8   Q.   And aromatase inhibitors also proven mechanism, right?

9   A.   Yes.

04:01PM 10   Q.   And the progestin, also proven mechanism?

11   I think you have to answer audibly so we get it on the

12   record.

13   A.   Yes. Yes.

14   Q.   Thank you.

04:01PM 15   And the androgen, those are also a proven mechanism?

16   A.   Yes.

17   Q.   And the hydro estrogens, also a proven mechanism?

18   A.   Old fashion but, yes.

19   Q.   All right. And all those categories are still being

04:01PM 20   investigated for improvements?

21   A.   I would disagree. The hydro estrogens, the megestrol

22   type of categories, the agents that target the progestins,

23   they're becoming less of an interest because the direct drugs

24   that were evolving for estrogen related pathways were far more

04:02PM 25   interesting and powerful. So you're right, in general these

1   were the options available at that time.

2   Q.   And in fact antiprogestins were being researched at this

3   time as promising options, is that correct?

4   A.   Yes.

04:02PM 5   Q.   And I think you'd agree lots of ideas about approaching

6   the estrogen receptor positive breast cancer, right?

7   A.   Correct.

8   Q.   And probably every group considered their idea the best

9   and touted it in their papers, right?

04:02PM 10   A.   I would suppose so, yes.

11   MS. PENSABENE: And, Neil, can you put up our chart,

12   of some of these promising compounds, please?

13   BY MS. PENSABENE:

14   Q.   And so you would agree with me that there was research

04:02PM 15   and promising compounds being -- being researched in all of

16   these categories, the aromatase inhibitors, the SERMs, the

17   androgens, the antiprogestins, the pure antiestrogen, the

18   progestins?

19   A.   Yes.

04:03PM 20   Q.   And in your direct, you didn't talk about any of these

21   specific compounds, right? Like, you didn't talk about

22   Vorozole, for example, right?

23   A.   No, I didn't.

24   Q.   And you didn't compare what was known about any of these

04:03PM 25   compounds --

1   A.   No.

2   Q.   -- to fulvestrant, right?

3   A.   That's correct.

4   Q.   Okay. Now, let's just look at those pure antiestrogens

04:03PM   5   if we could for a second.

6   There were -- this was a small -- a small class, right?

7   A.   That's correct.

8   Q.   At the time in 2000, right? There's only -- there's only

9   five of them and two of them are related, the EM compounds,

04:03PM   10   right?

11   A.   Yes.

12   Q.   In your direct, you didn't address EM 800 which is a pure

13   antiestrogen that had some promising Phase II results that had

14   been published and were currently in Phase III, right?

04:04PM   15   A.   No, I didn't, no.

16   Q.   So you didn't consider that in your thoughts about

17   fulvestrant. Now --

18   A.   I would take exception to that statement. The issue here

19   is that, yes, these products at that time were also being

04:04PM   20   worked on. But if you look at the team from ICI and

21   subsequently AstraZeneca that had been currently developed

22   tamoxifen, and then subsequently anastrozole, a very reputable

23   group of doctors who were focused on, mid-1980s, '90s, or even

24   earlier on one product, because national interest in meetings,

04:04PM   25   they pronounced as the most advanced antiestrogen and had a

1 clear track record in the research proceeding seamlessly from

2 preclinical data of efficacy and toxicity to clinical efficacy

3 and safety clinical data and corroborative presentations all

4 the way up to Dr. Robertson in 1999 in San Antonio.

04:05PM 5   So while these other products were certainly around, it

6 is not unreasonable that based on that kind of testimony, I

7 would pick fulvestrant as a drug development.

8 Q.   You would agree with me, wouldn't you, Dr. Mehta, that

9 Dr. Howell and Dr. Robertson and Dr. Dowsett all worked on

04:05PM 10 aromatase inhibitors, on SERMs, on antiprogestins. You would

11 agree with that, right?

12 A.   I would agree with that, yes.

13 Q.   Okay. So those groups have worked on all these different

14 options?

04:05PM 15 A.   I have a clarification.

16   THE COURT: You had a clarification, but let her

17 finish the question first and then you can clarify.

18   What was your question?

19 BY MS. PENSABENE:

04:06PM 20 Q.   Okay. So let me rephrase -- because now, I have totally

21 forgotten my question, I'm sorry.

22   THE COURT: That's okay.

23 BY MS. PENSABENE:

24 Q.   So you would agree with me, right, that you started with

04:06PM 25 fulvestrant because that's what the patent is about, right,

1   Dr. Mehta?

2   A.   No.   I -- a hypothetical POSA would find this product of

3   interest is what we're talking about here.

4   THE COURT: Okay.   I think I might be confused now.

04:06PM   5   What is it that you wanted to clarify earlier?   I don't want

6   the record to not be complete.   What is it?

7   THE WITNESS: So while the team that was mentioned as

8   the team working on other products, the same team basically

9   was not only mentoring this product into clinical studies, but

04:06PM   10   at every national forum and international forum was talking

11   about it, so if one was -- there were already great products

12   coming in, aromatase inhibitors, such as anastrozole,

13   letrozole, exemestane, and that if somebody is interested in

14   developing a new product with a new mechanism of action, there

04:07PM   15   was no sense going there.

16   All the competitors of the SERMs, were again not

17   proving to be either better than tamoxifen or safer than

18   tamoxifen.   And so one category that stood out to be novel,

19   with a new mechanism of action, with lack of cross-resistance

04:07PM   20   with tamoxifen, that was again by this team that had been

21   heralding all these important drugs, had been touting it as

22   the new major advance, that is probably the reason why it

23   would be reasonable to expect that a POSA would find that

24   product ahead of others and develop it.

04:07PM   25   BY MS. PENSABENE:

1 Q. Okay. So, Dr. Mehta, your opinion doesn't address the

2 data or literature from any of those other compounds. It's

3 looking at the -- you're just looking at the team that had

4 worked on fulvestrant, right?

04:08PM 5 A. Looking at the team and the massive amount of prior art

6 that is accumulating basically in support of this particular

7 product.

8 Q. Okay.

9   THE COURT: But it sounds -- I'm sorry.

04:08PM 10   MS. PENSABENE: Oh, I'm sorry, Your Honor.

11   THE COURT: But it sounds like your opinion includes

12 an assessment that given the prior success that the team at

13 AstraZeneca had, that you would expect fulvestrant to be

14 further developed. Does that sound --

04:08PM 15   THE WITNESS: Absolutely.

16   THE COURT: That's what you're saying.

17   THE WITNESS: I am.

18   THE COURT: Okay.

19 BY MS. PENSABENE:

04:09PM 20 Q. Dr. Mehta, you would agree with me, wouldn't you, that

21 there is another AstraZeneca pure antiestrogen on this list,

22 too, right?

23 A. Yes.

24 Q. Okay. And that one was ultimately not successful, right?

04:09PM 25 A. That is correct.

1   Q.   And you would agree with me that the Howell and Robertson

2   and Dowsett team have worked on many of these compounds and,

3   in fact, many of them were -- all -- in fact, all of then,

4   except for fulvestrant, were unsuccessful, isn't that right?

04:09PM   5   A.   That is correct.

6   Q.   Okay. Now during your direct today, you discussed the

7   1999 San Antonio Breast Cancer Symposium. Do you remember

8   that?

9   A.   Yes.

04:09PM   10   Q.   Okay. And you would agree that the '99 San Antonio

11   abstract book contained over 440 abstracts, right?

12   A.   Yes, that's correct.

13   Q.   Now, you used a methodology to sort of narrow that down,

14   and in that methodology, you excluded the growth factor

04:10PM   15   treatments, right, because you considered them to be not

16   relevant to the question here, right?

17   A.   So I just considered the hormone-related treatments of

18   breast cancer.

19   Q.   And I think you said, and correct me if I'm wrong --

04:10PM   20   THE COURT: Excuse me, treatments of breast cancer.

21   BY MS. PENSABENE:

22   Q.   I think you said what was recommending the Robertson '99

23   abstract to you, was that it was the only one that was about a

24   novel agent, is that right?

04:10PM   25   A.   By and large, yes.

1 Q. I'm sorry?

2 A. By and large, yes.

3 Q. Oh, okay. I just want to take a look at the page that

4 the Robertson abstract is on.

04:10PM 5 That's at -- it's not JTX-13.

6 MS. PENSABENE: And I'll ask Mr. Hoy, would you mind

7 popping that up on the screen.

8 BY MS. PENSABENE:

9 Q. And this is in your book, too --

04:11PM 10 A. Yes.

11 Q. -- Dr. Mehta, that's over there on the side from your

12 direct. So what I'd like to do, this is -- this is the --

13 this is the abstract that you were talking about, about

14 Dr. Robertson, but I'd like to look up on the same page, if I

04:11PM 15 could, up at an abstract in the -- catty-corner to this. It's

16 Abstract No. 25.

17 So you would agree with me, Dr. Mehta, that this is

18 talking also about a hormone-dependent endocrine -- also about

19 an endocrine therapy, right?

04:11PM 20 A. Yes.

21 Q. It's about a SERM, right?

22 A. Yes.

23 Q. And this is also about a novel compound, right?

24 A. Yes, it is.

04:12PM 25 Q. It's about a novel SERM. This one is about LY 353381.

1 A. Yes.

2 Q. That's correct, right?

3   Okay. So there were a lot of novel compounds -- there

4 were other novel compounds. Let me be more accurate. There

04:12PM 5 are other novel compounds, weren't there, other novel

6 endocrine therapies that were being discussed in the general

7 session at San Antonio, right?

8 A. So this particular paper was discussed in the general

9 session? Can we confirm that?

04:12PM 10 Q. Mm-hmm. Yes, yes, it's part of that --

11 A. Okay.

12 Q. It's part of those general session discussions.

13 A. So I stand corrected. There might have been more than

14 one.

04:12PM 15 Q. Okay. And then looking on this same page, this page also

16 talks about Raloxifene and discusses Arimidex, right? And

17 those are also endocrine therapies, right?

18 A. Arimidex has already been approved by that time and so

19 it's not an oral therapy. It's already on its way to becoming

04:13PM 20 a standard of care for postmenopausal women. Raloxifene, the

21 data is basically moving it towards a treatment for

22 osteoporosis and prevention of breast cancer. The data for

23 treating breast cancer itself in hormone-dependent category

24 for Raloxifene is five, three years at the most, it doesn't

04:13PM 25 really stand out -- it's being moved towards treatment of

1 osteoporosis, because it improves the bone health, but in

2 terms of comparing it to the anticancer properties of

3 tamoxifen, it was proven to be not equivalent.

4 Q.   Okay. Then you would agree with me, right here on the

04:13PM 5 same page as the Robertson 1999 abstract, there are at --

6 there's an abstract for a novel SERM, another SERM, and a

7 aromatase inhibitor, is that correct?

8 A.   True.

9 Q.   In the general session --

04:14PM 10 A.   Yes.

11 Q.   -- of San Antonio. And that's just a snapshot, right?

12   So -- and you would agree with me that EM 800, which

13 was another pure antiestrogen was -- had reported high

14 response rates in Phase II trials by 2000 and was currently in

04:14PM 15 Phase III trials, right?

16   MS. PETERSON: Your Honor, I object to this line of

17 questioning. I don't think this has anything to do with the

18 abstract from the San Antonio Breast Cancer Conference.

19 That's outside the scope of his direct testimony.

04:14PM 20   MS. PENSABENE: Your Honor, this goes directly to

21 credibility, because this witness has testified -- is

22 testifying that one would choose fulvestrant as the most

23 advanced of all the anti -- pure antiestrogens, EM 800, as an

24 antiestrogen. This was published before 2000.

04:15PM 25   It is phase -- it's in Phase III trials and it has

1   promising Phase II data. It directly goes to the -- to the

2   witness's opinion about fulvestrant.

3   THE COURT: To his opinion that fulvestrant is the --

4   what --

04:15PM   5   MS. PENSABENE: His opinion was that fulvestrant was

6   the most advanced of all of -- if you could put the chart back

7   up, just so I can -- I know there's a lot of names, sir,

8   floating about.

9   THE COURT: Why would you quarrel with that?

04:15PM   10   MS. PENSABENE: I'm sorry?

11   THE COURT: Why would you quarrel with that?

12   MS. PENSABENE: That fulvestrant was the most

13   advanced at this time in 2000?

14   THE COURT: Yes.

04:15PM   15   MS. PENSABENE: I would quarrel with it because I

16   don't -- I disagree that fulvestrant was the most advanced and

17   the clear choice here.

18   MS. PETERSON: And we would also disagree with her

19   characterization of Dr. Mehta's testimony. I don't believe

04:15PM   20   that he's offered an opinion that it was the most advanced.

21   He was simply reporting what others in the literature reported

22   and described it as including Dr. Robertson and other people.

23   I believe Dr. Mehta's testimony was limited to

24   expressing reasons why people would be interested in pursuing

04:16PM   25   tamox -- in pursuing fulvestrant, but not necessarily that it

1 was the most advanced.

2   THE COURT: So the dispute is the words "most

3 advanced."

4   MS. PETERSON: Well, and also the line of questioning

04:16PM 5 asking Dr. Mehta about other compounds that he did not discuss

6 within his direct testimony.

7   THE COURT: Well, do you agree with what

8 Ms. Pensabene said that at the time that fulvestrant was the

9 most advanced of these pure antiestrogens?

04:16PM 10   THE WITNESS: So if you're looking at --

11   THE COURT: Can you just answer that with a yes or

12 no? And if you don't understand the question, then you have

13 to tell me.

14   THE WITNESS: Yeah, please repeat the question.

04:16PM 15   THE COURT: Yeah. Do you agree that at the time, in

16 2000 -- 2000, is that the question?

17   THE WITNESS: Right, 1999, 2000, yeah.

18   THE COURT: That fulvestrant was the most advanced?

19   THE WITNESS: That is correct. That was --

04:17PM 20   THE COURT: In terms -- of the purest antiestrogens,

21 you agree with that.

22   THE WITNESS: Yes.

23   THE COURT: So then if Ms. Pensabene wants to impeach

24 that statement, she may, despite the fact that he did or did

04:17PM 25 not -- well, I don't recall that he testified about EM 800,

1   but it's subject to impeachment, go ahead.

2   BY MS. PENSABENE:

3   Q.   So Dr. Mehta, you would agree with me, right, that there

4   had been promising Phase II data published on EM 800?

04:17PM   5   A.   Yes.

6   Q.   And EM 800 was also by 2000 in Phase III clinical trials?

7   A.   That is true.

8   THE COURT: It almost sounds as if you are saying,

9   and correct me if I'm wrong, that Dr. Robertson shouldn't have

04:17PM   10   been surprised by the results --

11   THE WITNESS: Yes.

12   THE COURT: -- that he achieved. So his testimony

13   that he was, you --

14   THE WITNESS: I don't agree, yeah, right.

04:18PM   15   THE COURT: You don't agree that he was surprised?

16   THE WITNESS: So I think, basically, in the

17   preclinical phase and the clinical phase and before '99, there

18   was already -- they, themselves, were saying that this was the

19   most advanced product. They were mentoring it into clinical

04:18PM   20   trials which happened right around this time, and it went on

21   to receive approvals, an FDA approval.

22   So to subsequently say that this was not a -- you know,

23   there was no surprise about it or people were surprised the

24   drug was doing very well, is exactly contrary to what they

04:18PM   25   presented at San Antonio, that this is the most advanced and

1   they want -- the further studies will continue. So I think

2   there's a dichotomy there.

3   The same group that was developing this compound was

4   very positive at that time and they would not have been

04:18PM   5   shepherding it into further trials and presenting it to

6   international audiences such as San Antonio, if they didn't

7   believe that it was a compound with major potential and

8   interest for them, and that's all I'm saying is that in

9   looking at those options in that frame of time, if I'm looking

04:19PM   10   for antiestrogen as one of the agents I want to use, it is

11   reasonable that I would put this product for development.

12   THE COURT: Okay.

13   BY MS. PENSABENE:

14   Q.   Dr. Mehta, you would agree with me, right, that there

04:19PM   15   were prominent researchers who were looking at Vorozole for

16   example, and touting its promise, is that correct?

17   A.   Yes.

18   Q.   And there were prominent researchers who -- at -- in

19   2000, were looking at ORG 33201 and touting its promise,

04:19PM   20   right?

21   A.   I have not seen any touting of promise by any of those,

22   so I really have to generically agree, saying yes, everybody

23   must be proud of what drugs they were working on. But as

24   Dr. Robertson also indicated, some of these drugs were killed

04:20PM   25   because they didn't seem to work. And so just because you

1   were working on it, doesn't mean they were touting it.

2   Here was a team very consistently saying they're a new

3   product with promise, and they were calling it most advanced

4   and advancing it in their clinical trials and using it on

04:20PM 5   their patients in clinical trials. So I think that's

6   basically the direction in which my mind would go when I'm

7   looking at a possible product for development.

8   Q.   Okay. Let me just see if I'm understanding you.

9   So your point is that because of this -- because this

04:20PM 10   team was behind this product, it really didn't matter what the

11   other choices were, or what the data on the other

12   possibilities is, that you would pick whatever compound they

13   were working on and saying was promising?

14   A.   Again, that is a mischaracterization of what I'm trying

04:20PM 15   to say.

16   THE COURT: Let me -- let me see if I understand what

17   your testimony is.

18   Were you here when Dr. Robertson testified about the RU

19   compound?

04:21PM 20   THE WITNESS: Yes.

21   THE COURT: Which, at the time was -- appeared to be

22   promising. Do you agree with that?

23   THE WITNESS: Yes.

24   THE COURT: So are you saying that at the time that

04:21PM 25   the ICI 182 appeared to be promising, the RU 58668 compound

1   appeared to be promising, but you have Team A and Team B and

2   Team A sort of -- they hold the gold --

3   THE WITNESS: Mm-hmm.

4   THE COURT: -- medal?

04:21PM   5   THE WITNESS: Yes.

6   THE COURT: And the RU team sort of holds the bronze

7   medal. So are you saying, then, that all bets were on the ICI

8   team? Is that what you're saying?

9   THE WITNESS: Something similar to that, but I would

04:21PM   10   basically say it's not all based on one product. It's simply

11   that you can look at the clinical evidence, the clinical

12   evidence. The mounting body of evidence that suggest there's

13   going to be a successful product and you look at the people

14   who are developing it, their track record.

04:22PM   15   THE COURT: The gold -- the gold medalist.

16   THE WITNESS: Right. So you basically both give the

17   weight to the product and say, okay, this is the team, this is

18   the body of data, why would I not go develop it.

19   BY MS. PENSABENE:

04:22PM   20   Q.   Dr. Mehta, you included in that team Michael Dukes, is

21   that right?

22   A.   He was one of the presenters, yes.

23   Q.   And you looked at -- when you were talking about

24   preclinical research, the two Dukes' papers?

04:22PM   25   A.   Right.

1 Q.   Right? And you would agree, I think from what you're

2 saying that Michael Dukes is a well-respected researcher in

3 this field?

4 A.   Yes.

04:22PM 5 Q.   Okay. And you would agree that Dukes has a very

6 respectable track of work that led to the paper that you

7 quoted?

8 A.   Yes.

9 Q.   Now, the Dukes works that you were -- the Dukes work that

04:23PM 10 you were talking about earlier today was a valuation of

11 fulvestrant in primates, right?

12 A.   Yes.

13 Q.   There were two papers, right?

14 A.   Yes.

04:23PM 15 Q.   Now, in your timeline here, you don't include the Dukes

16 '814 patent, do you?

17 A.   No, I don't.

18   MS. PENSABENE: May I approach, Your Honor?

19   THE COURT: Yes.

04:24PM 20 BY MS. PENSABENE:

21 Q.   Now, the inventor of this patent, this is the Dukes '814

22 patent, right? It's JTX-18 for the record.

23   This patent is assigned to AstraZeneca, is that

24 correct?

04:24PM 25 A.   Yes.

1 Q.   And the inventor is the same Michael Dukes who we had

2 been talking about and you had been looking at his work during

3 your direct testimony, right?

4 A.   That is correct.

04:24PM   5 Q.   Okay.

6   MS. PENSABENE: And can you pull up Example 3 of this

7 patent, please?

8 BY MS. PENSABENE:

9 Q.   And you would agree with me that this patent to Dr. Dukes

04:24PM   10 is -- includes examples of formulations of fulvestrant, right?

11 A.   Yes.

12 Q.   And here, in Example 3, the patent describes a castor

13 oil-based intramuscular injection that is 50-milligrams per

14 milliliter and it has -- the composition is given, right?

04:25PM   15 It's 40 percent benzyl alcohol, right?

16 A.   Right.

17 Q.   Okay. Now, that's not the same composition as in the

18 formulation you were talking about earlier in the McLeskey --

19 A.   It's not.

04:25PM   20 Q.   -- paper.

21   And the Dukes patent --

22   MS. PENSABENE: If we can go down a little further to

23 the table.

24 BY MS. PENSABENE:

04:25PM   25 Q.   This patent -- the patent includes some data, too, on

1   antiestrogen activity, right?

2   A.   Yes.

3   Q.   So if we look at our timeline of AstraZeneca work and we

4   can actually look at our timeline, that's back -- that's back

04:26PM   5   behind us. You could see that Dukes patent is on there,

6   right?

7   A.   Yes, it is.

8   Q.   Okay. Because that's part of the AstraZeneca work that

9   was on fulvestrant, right?

04:26PM   10   A.   That is correct.

11   Q.   Okay. But you didn't consider the dukes patent, right?

12   MS. PETERSON: Your Honor, we object to this line of

13   questioning as well, and Dr. Mehta did not opine on the '814

14   patent or offer any opinions during his direct testimony.

04:26PM   15   MS. PENSABENE: And, Your Honor, that's the point.

16   THE COURT: No, but it goes to the weight of his

17   opinions.

18   THE WITNESS: So is this a yes or no answer, or is

19   there any chance or elaborating what I mean by yes or no?

04:26PM   20   THE COURT: What you mean by what --

21   THE WITNESS: I mean, almost all of the questions are

22   yes or no, but I do need to -- and I would love to agree with

23   everything, you know, but I can't.

24   THE COURT: So in cross-examination, that is quite

04:27PM   25   typical.

1   THE WITNESS: I know that.

2   THE COURT: So Ms. Peterson will get up on redirect,

3   if there's anything you need to explain, she will ask if

4   there's --

04:27PM 5   THE WITNESS: I get that, all right.

6   THE COURT: Okay. However, if a truthful answer to

7   the question can't be answered with yes or no, then you have

8   to tell Ms. Pensabene that you can't answer it with a yes or

9   no. Okay?

04:27PM 10   THE WITNESS: So I can't answer it with yes or no,

11   the last question.

12   THE COURT: What, that you didn't consider the Dukes

13   '814 patent?

14   THE WITNESS: No, that -- the answer to that is yes,

04:27PM 15   but I can't do the last part. All right. Proceed.

16   BY MS. PENSABENE:

17   Q.   Okay. And you -- in forming your opinions, you didn't

18   consider whether the Howell paper that you talked about might

19   have used the Dukes patent formulation, right?

04:28PM 20   A.   Look at the timeline. If Howell is being published in

21   '95, '96, and McLeskey around that time is being supplied by

22   AstraZeneca, Mr. Vose, with a castor oil-based intramuscular

23   preparation or injectable preparation, why would AstraZeneca

24   that is trying to test this product in clinical lines, as well

04:28PM 25   as other investigators who requested, why would they supply a

1   product that was available from '80s and obviously was

2   undergoing further development, because what McLeskey got

3   supplied was a different formula.

4   So I basically would think that in terms of the

04:28PM   5   timeline, what Howell got in his reserve were attributable to,

6   must be the same product or similar one supplied by

7   AstraZeneca in that timeline, because they were testing that

8   product. Why would they pull out the product from the prior

9   decade?

04:29PM   10   Q.   You have no idea, right, you whether -- what formulations

11   Howell used, right?

12   A.   I don't have that idea, no. I'm just making logical

13   conclusions.

14   Q.   Okay.

04:29PM   15   THE COURT: Excuse me. Are you speculating?

16   THE WITNESS: I am. There is nothing in the

17   literature to confirm my speculation.

18   BY MS. PENSABENE:

19   Q.   If we could stay with your preclinical work. Looking at

04:29PM   20   your slide DTX- 019, you would agree with me -- this is the

21   Wakeling '91 paper. You would agree with me, wouldn't you,

22   that what Wakeling is saying here is he wants to use

23   fulvestrant to explore the possibilities of this unproven

24   mechanism, right?

04:30PM   25   A.   That is correct.

1 Q.   Okay. Because it's an unproven mechanism. You don't

2 even know how it's going to work, what's going to be the

3 mechanism of action. So there is a lot of research to be

4 done, right?

04:30PM 5 A.   That is correct.

6 Q.   Let's take a look at your slide DTX-1-030. That's also

7 in your preclinical work.

8 A.   Yes.

9 Q.   This is Wakeling 93. And I think here with this slide

04:31PM 10 you did a dose conversion, right, from monkeys to humans from

11 this paper. Do you remember that during your direct?

12 A.   Yes.

13 Q.   And your dose conversion from this paper was that the

14 monkey dose used in discussing Wakeling 1993 was equivalent to

04:31PM 15 a 250 mg dose for a woman, right?

16 A.   Yes.

17 Q.   And your opinion was that that dose, that 250 mg dose

18 sustained 100 percent estrogen receptor blockade, right?

19 A.   I was quoting the article, yes.

04:32PM 20 Q.   So, there is nowhere to go. You can't go up from there,

21 right?

22 A.   No.

23 Q.   Now, let's turn our attention to the early clinical work,

24 okay, in your timeline. All right?

04:32PM 25 A.   Yes.

1 Q. And let's talk about DeFriend. That's at JTX-15. Maybe

2 we can pull up your Slide 38. Now, I just want to make sure

3 we're on the same page here because I see that you have some

4 highlighting in the authors and highlighting in the

04:33PM 5 institutions that they are with. Dr. DeFriend and Dr. Howell

6 and Dr. Robinson, they are not with Zeneca, right?

7 A. No.

8 Q. So you are just highlighting Zeneca to --

9 A. There is a separate highlight in the names that are

04:33PM 10 recognized and seem consistent through research papers, I

11 highlighted simply to point out the commonality.

12 Q. In your view someone of skill in the art could not start

13 with the DeFriend formulation as being one that had been used

14 with success, right?

04:33PM 15 A. That is correct.

16 Q. And one wouldn't take from the DeFriend study a teaching

17 of once-daily dose, right?

18 A. DeFriend was basically looking for side effects. It's --

19 but one would not take that dose as a dose one wants to double

04:34PM 20 up in a once a month depot injection, it's that's just the

21 data, that's how they used it over their 7-day period.

22 Q. So, DeFriend is -- in your view DeFriend is looking at

23 side effects not at --

24 A. And efficacy.

04:34PM 25 Q. Okay. But not on the issue of daily dose, right?

1 A.   That's what he uses so that's the -- that's one of the

2 features of that particular trial, is that 7 days before

3 surgery they give them a -- non daily doses.

4 Q.   Dr. Mehta, you are familiar with the experience with

04:34PM 5 endocrine therapies that greater doses even without toxicity

6 did not lead to increased efficacy, right?

7 A.   I'm familiar with that.

8 Q.   And, for example, anastrozole was tolerated at 10 mg and

9 1 mg, but there is no additional clinical benefit for the

04:35PM 10 higher dose, right?

11 A.   That is correct.

12 Q.   And that was known in 2000?

13   MS. PETERSON: This is outside the scope of his

14 testimony as well.

04:35PM 15   THE COURT: Sustained.

16   MS. PENSABENE: Your Honor, he testified about dosing

17 and he testified and he did multiplication from DeFriend and

18 said you could come to a different -- and he talked about

19 maximum tolerated dose. This is directly relevant to that

04:35PM 20 testimony.

21   THE COURT: But I don't think he talked about

22 efficacy.

23   MS. PENSABENE: That's exactly what he was talking

24 about, your Honor. He was talking about maximum tolerated

04:35PM 25 dose, that there would be a reason to increase dose. And he

1 said you would go to a maximum tolerated dose, that would be

2 the theory that would apply. Not so. And now testing that

3 theory because the endocrine agents do not fit in that theory,

4 that is not how dosing is done -- was done with the endocrine

04:35PM 5 agent at this time.

6   MS. PETERSON: We would disagree. Dr. Mehta was not

7 drawing an opinion based on -- drawing an opinion of efficacy

8 based on the dosing.

9   THE COURT: Did you render an opinion about the

04:36PM 10 dosage and the correlation between dosing and efficacy?

11   THE WITNESS: No, ma'am.

12   THE COURT: What were you talking about when you

13 talked about the maximum dose?

14   THE WITNESS: It sort of points out that if you look

04:36PM 15 at this dose, it gives you some idea of how -- if you were to

16 take this on a daily basis for 28 days, how it might actually

17 calculate to a different dose level than 250. So, it's

18 possible that that dose could enter the calculations in

19 future. But beyond that, you can't make any other

04:36PM 20 assumptions.

21   THE COURT: Yes. I don't think he was correlating it

22 with efficacy.

23   THE WITNESS: Not at all.

24   THE COURT: I think he was saying that -- looking at

04:36PM 25 DeFriend was during a short period of time, but if you did the

1   math or some -- I don't remember --

2   THE WITNESS: So it's 28 times 18.

3   THE COURT: Did the math, you would come out at

4   approximately 250 monthly. I thought that's what he was

04:37PM 5   discussing.

6   MS. PENSABENE: That you would come out with 250?

7   THE WITNESS: 500.

8   THE COURT: 500.

9   MS. PENSABENE: And as long as Dr. Mehta is not

04:37PM 10   talking about efficacy related to that dose or is not talking

11   about a reason to go to an increased dose from 250, if

12   that's -- as long as he's not testifying about that, then

13   we'll move on. But our point being we should have the

14   opportunity to question that opinion if he is testifying that

04:37PM 15   that was a reason to go to a higher dose.

16   THE COURT: I understood, correct me if I'm wrong,

17   the import of your testimony was with respect to that

18   publication that you can't necessarily discount the value of

19   that publication because of the lower doses because that was a

04:38PM 20   7-day dosage.

21   THE WITNESS: Right.

22   THE COURT: But if you did the math you would come

23   close on a monthly basis to 500.

24   THE WITNESS: Yes.

04:38PM 25   THE COURT: And you did that simply -- did you do it

1 because you correlated it to efficacy?

2   THE WITNESS: Not at all.

3   THE COURT: Okay. Does that resolve the issue?

4   MS. PENSABENE: As long as DeFriend is not going to

04:38PM 5 be used as an argument for going to a higher dose.

6   THE COURT: Well --

7   MS. PETERSON: Well, I think that -- you know, if

8 DeFriend, if the data can be extrapolated to convert it to a

9 once monthly dose of 500 mg, that's what it is.

04:38PM 10   MS. PENSABENE: In that case, your Honor, I think we

11 should have the opportunity to test that hypoposias.

12   THE COURT: I think that you can. Go ahead.

13   MS. PENSABENE: Okay.

14 BY MS. PENSABENE:

04:38PM 15 Q.   And, Dr. Mehta, you would agree that in fact anastrozole,

16 aminoglutethimide and fadrozole studies all showed that higher

17 tolerated doses did not provide greater efficacy?

18 A.   That is correct.

19 Q.   And all of that was known prior to 2000, correct?

04:39PM 20 A.   That is correct.

21   THE COURT: So, would it be somewhat of a leap to use

22 DeFriend for the proposition that you are positing?

23   THE WITNESS: Somewhat of a leap, yes. And I think,

24 on the other hand, the 250 dose as Howell successfully uses

04:39PM 25 it, if I were a developer at that time you finally found a

1 dose that has brought 69 percent response rate with good

2 duration of response, you found a safety profile that is

3 completely acceptable. Going forward into Phase III trial, I

4 would not monkey with the dose bringing it down because I

04:39PM 5 don't know if I would be hurting those women saying -- that's

6 the whole idea of Phase II trials, you are setting efficacy

7 and it's set on the doses which are set by the Phase I trial.

8   So, I think that at the end of the Phase II as you

9 are beginning randomized trial where you tell women this is

04:40PM 10 the standard of care, but half of you are not going to get it,

11 you are going to get this new drug, why would you lower the

12 dose of something that just worked? And what would be the

13 justification to say I'm going to try 25 or 50 mg and see what

14 happens why those women don't get controlled. You should have

04:40PM 15 known that's probably not a very scientific way of doing

16 research clinically.

17   So there is an awesome amount of responsibility to

18 getting a dose that has actually given you safety and efficacy

19 into the next set, and that's exactly what happened. 250

04:40PM 20 was -- went through their Phase III trials, it's just that

21 subsequently it was realized that that was not as efficacious

22 as they would have hoped and then 500 was cleared. So, yeah,

23 the 500 is simply a leap of faith in terms of it's interesting

24 that this 7-day dose actually translated to 500. But Howell,

04:41PM 25 did they know that? I don't know. I wasn't part of that

1   discussion. But to take Howell 250 mg, which is efficacy and

2   safety data, the only Phase II then, which everybody's now

3   saying, so now we test it further, how would I assure a women

4   saying I'm going to try a little lower on you because that

04:41PM   5   might work? It's not a good idea. It's a new compound and

6   laws about SERMs and AIs may not work there.

7   Q.   Dr. Mehta, you would agree with me that the gold metal

8   team that you talked about --

9   A.   Yes.

04:41PM   10   Q.   -- went down in dose after Howell following the Howell

11   teachings, right?

12   A.   Yes.

13   Q.   Okay, let's take a look at Howell, if we could. That's

14   at JTX-11. You'd agree with me that you selected Howell to

04:42PM   15   consider because it related to hormone-dependent breast

16   cancer?

17   A.   Yes.

18   MS. PENSABENE: Your Honor, if I could, I'd like to

19   just fill in the rest of our chart over here --

04:42PM   20   THE COURT: Okay.

21   MS. PENSABENE: I'm going to fill in the rest of our

22   chart over here that's nearest Dr. Mehta.

23   BY MS. PENSABENE:

24   Q.   So, let's fill in for Howell. I'm accurate if I put here

04:42PM   25   under Howell "hormone-dependent," right?

1 A.   Postmenopausal hormone-dependent, yes.

2 Q.   And the Howell formulation was given intramuscularly?

3 A.   That is correct.

4 Q.   So I can fill that with intramuscularly, correct?

04:43PM 5 A.   Yes.

6 Q.   And the Howell formulation is given every 4 weeks, once

7 monthly, right?

8 A.   That is correct.

9 Q.   Okay. And in Howell the fulvestrant was not

04:43PM 10 cross-resistant?

11 A.   That's correct.

12 Q.   So, you would agree with me that this chart, that

13 McLeskey and Howell don't match in four areas that we've

14 discussed, right?

04:44PM 15 A.   Yes.

16 Q.   Okay. So they don't, McLeskey and Howell don't match on

17 hormone dependence. McLeskey is hormone-independent, Howell

18 is hormone-dependent, right?

19 A.   Which is not a surprise, right.

04:44PM 20 Q.   And McLeskey, the formulations of fulvestrant were

21 subcutaneous and in Howell the formulations were

22 intramuscular?

23 A.   Yes.

24 Q.   So, they do not match on that either, the route of

04:44PM 25 administration, right?

1   A.   True.

2   Q.   And in McLeskey the formulations were administered once

3   weekly and in Howell the fulvestrant formulations were

4   administered once monthly, so they do not much on dosage

04:44PM   5   frequency, right?

6   A.   Yes.

7   Q.   And McLeskey found that the fulvestrant formulation to be

8   cross-resistant and Howell not cross-resistant, so they do not

9   match on cross-resistance, right?

04:45PM   10   A.   Yes.

11   Q.   Let's talk a bit more about Howell, if we could. Now,

12   reading the Howell paper, Howell says in the paper that the

13   patients were highly selected. Is that right?

14   A.   Yes.

04:45PM   15   Q.   And Howell also says in the paper that tamoxifen

16   withdrawal may have accounted for the response seen in up to

17   one third of the patients. Do you remember that?

18   A.   He does say that, yes.

19   Q.   Now, you just disagree with both of those things; is that

04:46PM   20   right?

21   A.   So, I have my own interpretation of that data, yes.

22   Q.   But your interpretation is different from the

23   interpretation of the paper?

24   A.   Yes.

04:46PM   25   Q.   And you are familiar with the fact that researchers at

1 the time cautioned that the Howell response rate should be

2 interpreted with care.

3 A.   That's always true for Phase II studies, so yes, that was

4 said.

04:46PM 5 Q.   And you are familiar, aren't you, with the paper that Dr.

6 Dowsett published in the Lancet about the Howell study?

7 A.   I'm familiar with that.

8 Q.   And let's just talk for a moment. The Lancet, that's one

9 of the premier medical journals, right?

04:46PM 10 A.   Yes.

11 Q.   It's like sort of the gold standard medical journal,

12 right?

13 A.   Yes.

14 Q.   And Dr. Dowsett, he was one of the people that you

04:47PM 15 mentioned as being on this gold metal team, right?

16 A.   Yes.

17 Q.   And what Dr. Dowsett said was, he criticized -- he said

18 it should be -- Howell should be viewed with caution for two

19 reasons, and one of those reasons was that Howell had included

04:47PM 20 the no change patients in the response rate, and the second

21 reason was that the patients were highly selected. Did I get

22 that description of Dowsett's criticisms correct?

23 A.   That description is correct.

24 Q.   But you disagree with both of those criticisms by Dr.

04:47PM 25 Dowsett that he made in the Lancet in 1995 at the time of the

1 Howell research?

2 A.   I do.

3 Q.   Dr. Mehta, you'd agree with me that the Howell study in

4 the papers published, that Howell published in 1995 and 1996,

04:48PM 5 he indicated that further research was needed to confirm the

6 response rate?

7 A.   That is true.

8 Q.   And the Howell papers also indicated that further

9 research was required to see long-term effects on bone because

04:48PM 10 that was a concern, right?

11 A.   That is true, yes.

12 Q.   And Howell also indicated that further research was

13 required on amount on dose, right?

14 A.   Yes.

04:48PM 15 Q.   So, those were all open questions according to the Howell

16 paper, right --

17 A.   Yes.

18 Q.   -- in 1996, right?

19 A.   Yes.

04:48PM 20   THE COURT: Excuse me. Remind me again why it's

21 significant to you that Howell viewed no change -- why you

22 view that to be a response?

23   THE WITNESS: So, there is a body of thought that --

24 and they were being honest, so basically said okay, we are

04:49PM 25 bunching the no responses with the responses, but that may or

1 not be true. But the prevailing wisdom then and prevailing

2 wisdom now is that if you have rapidly progressive disease or

3 metabolic disease and a patient stabilizes and you have stable

4 disease, that is counted as response. Today, drugs are

04:49PM 5 approved based on a result that says patient stabilized. So

6 it's become -- so my basic take is that while they were being

7 very cautious in interpreting their data, I interpreted it

8 differently. I interpreted that only progression was

9 progression, deaths were deaths, either a woman stabilized and

04:49PM 10 there was stable disease and a woman responded, they were all

11 in the same basket.

12 THE COURT: And so, my question is would a person

13 skilled in the art -- was that how a person skilled in the art

14 would interpret those results? And, if so, then why did

04:50PM 15 Howell break it down?

16 THE WITNESS: He's the one who reports the 69 percent

17 response rate. By being an honest investigator, he's also

18 listing caveats. And listing caveats in terms of this may be

19 the reason why these results are this good is a good way of

04:50PM 20 doing it because subsequent studies will basically look at

21 that option. And if that's the reason why this happened, then

22 that drug would probably start to lose its support. So, all

23 Phase II studies that are at times these thoughts expressed

24 which basically -- may look at the results and look at the --

04:50PM 25 look at the population and come up with what they may honestly

1 feel might have resulted in the results that were described,

2 but in my opinion the stable disease was counted and should be

3 counted as part of those who responded.

4 Q.   Dr. Mehta, your interpretation is today, is that correct?

04:51PM 5 A.   That was my interpretation then.

6   MS. PENSABENE: Can you put up the Howell paper for

7 me, please? If you could just enlarge that a little so we can

8 see it.

9 BY MS. PENSABENE:

04:51PM 10 Q.   And what Dr. Dowsett is saying here is that the approach

11 of including no change patients is uncommon. And that was in

12 1995?

13 A.   Right.

14 Q.   That's his statement here in 1995, right?

04:51PM 15 A.   Yes. It's uncommon but it's not unheard of. And it

16 became over the next 15 years a dictum that everybody accepts

17 that stable disease is good news. We tell our patients no

18 news is good news and that's exactly what this is.

19 Q.   Dr. Mehta, in your timeline in your pre --

04:52PM 20   THE COURT: Excuse me. What is the exhibit number

21 that was just up on the screen?

22   MS. PENSABENE: I'm sorry. That is Dowsett, it's

23 been admitted into evidence, it's PTX-421, your Honor.

24   THE COURT: Thank you.

04:52PM 25 BY MS. PENSABENE:

1 Q. Dr. Mehta, there's a couple other things I just want to

2 talk about that aren't included in your timeline.

3   So right after Howell, you understand that four oral

4 clinical trials with fulvestrant were conducted from 1994 to

04:53PM 5 1997?

6 A. Yes.

7 Q. Okay. But you didn't include that in your analysis --

8 A. No.

9 Q. -- right?

04:53PM 10   Another thing that's not in your timeline is the early

11 clinical work for Thomas.

12 A. Yes.

13 Q. Now, that publication by Thomas came to the conclusion

14 that fulvestrant showed activity in premenopausal women, isn't

04:53PM 15 that right?

16 A. Can I see the publication?

17 Q. Oh, certainly.

18 A. Because there was a mixed conclusion from Thomas.

19   MR. O'BOYLE: Your Honor, may I approach?

04:54PM 20   MS. PENSABENE: May my colleague approach?

21   THE COURT: Yes.

22 BY MS. PENSABENE:

23 Q. This is PTX-249. And, Dr. Mehta, you'd agree with me

24 that PTX-249, the Thomas study, that's not on your timeline.

04:54PM 25 It's another seven day study, like DeFriend, that looked at

1 fulvestrant in premenopausal patients?

2 A.   Yes.

3 Q.   And Thomas concludes that the compound may be able to be

4 used in premenopausal women based on biological activity,

04:54PM 5 right?

6 A.   Yes. If I read his conclusion, in going to the last

7 page, the last paragraph, he basically says that fulvestrant

8 was well tolerated during short-term use. It did not cause an

9 increase in LH or FSH secretion and may suppress LH surge.

04:55PM 10 There was no evidence of ovarian hyperstimulation although

11 follicular growth continued.

12   And so he basically confirmed that in premenopausal

13 woman using of this product would not stimulate the lining of

14 the uterus, which we already know from other prior art. I

04:55PM 15 don't interpret this article to say that there was a

16 therapeutic response that he was basically talking about in

17 terms of not having uterus vehicle side effects is what he's

18 talking about. If response in terms of how hormones were

19 affected in a premenopausal woman was something he was talking

04:56PM 20 about, but there's no mention of treating premenopausal women

21 without looks that improved because of this particular study.

22 Q.   Dr. Mehta, do you remember having your deposition taken

23 in this action?

24 A.   Yes.

04:56PM 25   MS. PENSABENE: And if you could put up Mehta

1 transcript 163, Lines 10, I think, to 17.

2 BY MS. PENSABENE:

3 Q.   Do you remember that we talked about the Thomas paper at

4 your deposition Dr. Mehta?

04:57PM 5 A.   Yes, I do.

6 Q.   And I asked you the following question and you gave the

7 following answer:

8   QUESTION: And Thomas concludes, right, that the

9 absence of adverse events or of evidence of ovarian

04:57PM 10 hyperstimulation suggests that this compound may be able to be

11 used for the treatment of estrogen dependent diseases in

12 premenopausal women, right?

13   And there was an objection.

14   And your answer was:

04:57PM 15   ANSWER: That's what he concludes.

16   Correct?

17 A.   Right.

18 Q.   Okay. So in terms of treatment of premenopausal women,

19 if you could just look at your slide DDX-1-10 -- I'm sorry.

04:57PM 20 No, 1-11. I apologize.

21 A.   Yes.

22 Q.   On the right-hand side of this slide you would agree with

23 me this shows how to treat premenopausal women with endocrine

24 therapy?

04:58PM 25 A.   It shows options available at that time.

1 Q.   So one could treat premenopausal women with fulvestrant

2 after using an LHRH agonist and that was known? The use of

3 LHRH agonists were known?

4 A.   So the understanding was that because it does not work in

04:58PM **5** premenopausal women you had to convert the premenopausal woman

6 into a menopausal female by some means so that now you will

7 have physiology which is similar to postmenopausal and then

8 this product would be used. So the option of using

9 fulvestrant was always possible if the woman agreed to go into

04:59PM **10** menopause.

11   THE COURT: Ms. Pensabene, do you have much more?

12   MS. PENSABENE: I don't -- of course it depends on

13 the witness.

14   THE COURT: Let me ask this, were you planning on

04:59PM **15** coming back in the second phase of the trial?

16   THE WITNESS: No. I could.

17   MS. PENSABENE: I can hurry up and maybe we can

18 finish redirect.

19   THE WITNESS: I could come back if that's what it

04:59PM **20** takes.

21   MS. PETERSON: He does have plans to return home and

22 was not planning on coming back for the second week of trial.

23 So if we could accommodate the witness, we would like to try

24 to finish today if that's okay.

04:59PM **25**   MS. PENSABENE: That's fine.

United States District Court
Camden, New Jersey

1   MS. PETERSON: I appreciate you volunteering but we

2   would like to finish.

3   THE WITNESS: I'll speed up my answers.

4   THE COURT: Well, don't talk any faster.

04:59PM   5   So let's see if we can finish him up as a curtesy to

6   the witness.

7   MS. PENSABENE: Absolutely, your Honor. We'll cross

8   a bunch of things out, Dr. Mehta.

9   BY MS. PENSABENE:

04:59PM   10   Q.   Dr. Mehta, you'd agree with me that in 2000, as well as

11   today, treatment of male breast cancer follows the same

12   principles as treatment of female breast cancer, right?

13   A.   That's the treatment we offer, yes.

14   Q.   And in your practice you offer hormone therapy for male

05:00PM   15   breast cancer?

16   A.   Yes, I do.

17   Q.   And the paradigm for treatment of women's breast cancer

18   just transfers to men's breast cancer, right?

19   A.   Yes.

05:00PM   20   Q.   You know, just going back to your thoughts about this

21   gold medal team, Dukes was on the gold medal team, right?

22   A.   Yes.

23   Q.   And McLeskey was not on the gold medal team, right?

24   A.   Yes, McLeskey was an independent investigator in the

05:00PM   25   United States, she was not part of AstraZeneca's stable of

1 investigators.

2 Q.   Dr. Mehta, your focus has been on treating patients, I

3 understand from when we've talked before, and not on

4 researching new treatments, right?

05:01PM 5 A.   I have been involved in human research. And there is no

6 oncology practice or person in this country that in some way

7 or other would not participate in research because so many

8 questions need answering.

9 Q.   And you're not an expert on pharmacokinetics, right?

05:01PM 10 A.   No, I'm not.

11 Q.   And you've never been involved in preclinical research,

12 right?

13 A.   So the American Society of Oncology 2011 presentation in

14 Chicago was a big clinical research on a Phase I molecule

05:02PM 15 called B28, so that's the molecule that was shepherded and

16 subsequently it was now in Phase II trial. So in my time in

17 the academic world I have participated in clinical studies.

18 Q.   Let me be more precise then. Prior to 2000 you were

19 never involved in preclinical research?

05:02PM 20 A.   During my fellowship, I was. But once I left for India,

21 no.

22 Q.   And you've never formulated any compounds, right?

23 A.   No.

24 Q.   And you don't have any experience using breast cancer

05:02PM 25 animal models, right?

1 A. No.

2 Q. And you've never advised a pharmaceutical company on

3 whether to select a drug for development, continue

4 development, or abandoned development, right?

05:03PM 5 A. No.

6 Q. And you've never served on a scientific advisory board on

7 drug development, right?

8 A. No.

9 Q. And you did not publish any scientific papers prior to

05:03PM 10 2005, right?

11 A. That's correct.

12 Q. And you've never been involved in the selection of

13 clinical end points for a breast cancer trial, right?

14 A. Yes, that is correct.

05:03PM 15 Q. Okay. You would agree with me that breast cancer is a

16 very complicated disease?

17 A. It is.

18 Q. And the ability to extend endocrine therapy was important

19 because that means patients have a better chance of survival,

05:04PM 20 right?

21 A. That is correct.

22 Q. And if you had a patient with expected life survival of

23 six months and adding one month to survival becomes very

24 relevant, right?

05:04PM 25 A. True.

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 1  Q.   And if you have a choice between two treatments, all else

 2  being equal, in your view that additional time to progression

 3  would be a factor in choosing between those treatments?

 4  A.   Yes.

 5  Q.   Now, I think you and I both agree that the development of

 6  treatment for breast cancer is very difficult, right?

 7  A.   Yes.

 8  Q.   And tamoxifen, as an example, almost didn't get to the

 9  market, right?

10  A.   Yes.

11  Q.   And tamoxifen took decades actually to develop into a

12  breast cancer treatment, right?

13  A.   That is correct.

14  Q.   But tamoxifen saved millions of lives, right?

15  A.   Yes.  It did, yes.

16  Q.   So suffice it to say it was important to patients to

17  spend that time and effort on development, right?

18  A.   Yes.

19       MS. PENSABENE:  I have nothing further, your Honor.

20  I'll pass the witness.

21       THE COURT:  Redirect.

22       MS. PETERSON:  Yes, Your Honor.

23  (REDIRECT EXAMINATION OF DR. MEHTA BY MS. PETERSON:)

24       MS. PENSABENE:  I'm sorry, so sorry.

25  BY MS. PETERSON:
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Time stamps: 05:04PM (line 5), 05:04PM (line 10), 05:05PM (line 15), 05:05PM (line 20), 05:05PM (line 25)

1 Q.   Dr. Mehta, looking at the board over there that

2 Ms. Pensabene wrote on describing Howell and McLeskey, the

3 studies in Howell and McLeskey, were they for a different

4 purpose?

05:06PM 5 A.   They were for different purpose, yes.

6 Q.   And the purpose in Howell, was that to treat humans?

7 A.   Purpose in Howell was to treat postmenopausal women with

8 metastatic disease.

9 Q.   And was the purpose in McLeskey to test a hypothesis

05:06PM 10 about estrogen independent cell lines?

11 A.   That is correct.

12 Q.   Are there any similarities between McLeskey and Howell,

13 in terms of the formulation that was administered?

14 A.   The only similarities that involved castor oil base and

05:06PM 15 they are drawn from the same source around the same time.

16 Q.   What do you mean, drawn from the same source at the same

17 time?

18 A.   Most were supplied by AstraZeneca in -- around the same

19 time, so one would feel that AstraZeneca at that time was

05:06PM 20 testing same iteration of the product.

21 Q.   And are there any similarities in the concentration of

22 the drug that was delivered?

23 A.   Similarities with what?

24 Q.   Or the concentration of the drug that was administered.

05:07PM 25 A.   In Howell?

1 Q. Yes, and McLeskey.

2   THE COURT: Are there any similarities in the

3 concentrations between the two?

4   THE WITNESS: 15-milligrams per mL was the reigning

05:07PM 5 principle, so...

6 BY MS. PETERSON:

7 Q. Now, Ms. Pensabene asked you if the formulation in

8 McLeskey was an animal formulation.

9   Do you recall that?

05:07PM 10 A. Yes.

11 Q. And, of course, the formulation in McLeskey, was that

12 administered to animals in her study?

13 A. Yes.

14 Q. Now, would that fact dissuade a person of skill in the

05:07PM 15 art from using that formulation in humans if it contained the

16 same components?

17   MS. PENSABENE: Objection. Leading.

18   THE WITNESS: It would not.

19   THE COURT: Wait, wait, wait. No, I'll allow it.

05:08PM 20   THE WITNESS: It -- it would not detract from using

21 it.

22 BY MS. PETERSON:

23 Q. Now, Ms. Pensabene also referenced the Robertson 19 --

24 I'm sorry, strike that. I'll start again.

05:08PM 25   Ms. Pensabene mentioned that Howell had instructed or

1   told people to go down in dose.

2   Do you recall that?

3   A.   Yes.

4   MS. PETERSON: If we could pull up JTX-13, please,

05:08PM   5   and go to Abstract No. 28 on the bottom right?

6   BY MS. PETERSON:

7   Q.   And do you recognize this?

8   A.   Yes.

9   Q.   What is this?

05:08PM   10   A.   This is the Robertson abstract on Faslodex versus

11   tamoxifen.

12   Q.   And this came after in time after -- did this come after

13   in time after Howell?

14   A.   Yes.

05:08PM   15   Q.   At what point in time?

16   A.   This was '99, so many years later.

17   Q.   And what doses were being tested in Robertson?

18   A.   50, 125 and 250 milligrams of fulvestrant.

19   Q.   So even after Howell, the researchers were continuing to

05:09PM   20   test the 250-milligram dose, correct?

21   A.   They were.

22   Q.   And I wasn't sure, when Ms. Pensabene was asking about

23   the Dukes patents, I didn't know if there was something that

24   you wanted to clarify about your answer or if you understood.

05:09PM   25   Was there something you wanted to clarify?

1 A.   So I think again, it's my common sense that tells me that

2 if Duke patent, the product was available from '80s, got

3 patients in early '90s, but subsequently if McLeskey is

4 supplying a product in the time frame of '95, '96 by

05:09PM 5 AstraZeneca's executives for testing it, then that's the

6 product they actually been giving others who are trying to

7 test it in humans.

8   And so it makes sense that that's exactly the product

9 that brought the results that Howell describes. Why would

05:10PM 10 something else be tried at two times because the results would

11 then not make any sense.

12   So while it is possible that you couldn't have any

13 product because we don't have information, common sense

14 suggests that what formulation McLeskey lists in that time

05:10PM 15 frame supplied by AstraZeneca, was the product AstraZeneca

16 supplied its team of researchers that did the most important

17 phase through trial for a very important product the company

18 was in the process of developing.

19   So I think I would basically, as a POSA, feel that

05:10PM 20 that's the leap of faith I was willing to take.

21   THE COURT: I was just going to ask that -- it sounds

22 as if you have questions in your mind and you are wondering

23 and you're speculating and -- but you're saying it could be.

24   THE WITNESS: Yes.

05:11PM 25   THE COURT: Okay.

1   THE WITNESS: It is reasonable to expect that these

2   two products are the same. Beyond that, we don't have any

3   data.

4   THE COURT: And do you agree that other POSAs may not

05:11PM   5   view it quite the way you do.

6   THE WITNESS: It's possible.

7   BY MS. PETERSON:

8   Q.   Just to clarify your answer there.

9   Was your answer -- was your opinion that that was what

05:11PM   10 a person of skill in the art would understand?

11 A.   Yes.

12   MS. PETERSON: If we could pull up defendant's

13 demonstrative DDX-10-019.

14 BY MS. PETERSON:

05:11PM   15 Q.   I recall during Ms. Pensabene's cross-examination, she

16 may have -- or she referred to -- she pulled up this

17 demonstrative, DDX-10-019, and asked you to confirm that you

18 agreed with her that Wakeling 1993 was telling people to

19 conduct further tests for this unproven mechanism.

05:12PM   20   Do you recall that?

21 A.   Yes.

22 Q.   Are those words "unproven mechanism," here on your

23 demonstrative?

24 A.   No. Those were her words.

05:12PM   25 Q.   So you do not agree with that?

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 1   A.   No.

 2            MS. PETERSON:  No further questions.

 3            THE COURT:  Okay.  You get to go home.

 4            THE WITNESS:  Thank you, Your Honor.

 5            THE COURT:  Very nice to meet you, safe travels home.

 6   Please be careful stepping down.  Thank you.

 7            MR. PRUGO:  Your Honor, just one question about the

 8   boards.

 9            THE COURT:  Yes.

10            MR. PRUGO:  I think it's probably clear from the

11   transcript and we don't need the boards necessarily, but do

12   you want us to take a picture of it.  How would you like us to

13   handle a couple of the demonstratives here.

14            THE COURT:  Well, you have the smaller versions.

15            MS. PENSABENE:  Of this one and --

16            MR. PRUGO:  Well --

17            MS. PENSABENE:  I'm sorry.

18            MR. PRUGO:  No, go ahead, please.

19            THE COURT:  On the chart here?

20            MR. PRUGO:  Yeah, exactly.

21            THE COURT:  I think that was okay.  I don't think we

22   need a copy of that.

23            MR. PRUGO:  And I think this verbally came out.

24            THE COURT:  Yes, I think so, yeah.

25        So a question has arisen as to the exhibits.  So you
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05:12PM (line 5)
05:12PM (line 10)
05:13PM (line 15)
05:13PM (line 20)
05:13PM (line 25)

	folks are welcome to leave the exhibits in the attorney
1	folks are welcome to leave the exhibits in the attorney
2	conference rooms. I think Mr. Roney has checked and they are
3	available. So you can just somehow secure them, okay?
4	So are we on schedule? Is it going as the parties had
5	anticipated?

1 folks are welcome to leave the exhibits in the attorney

2 conference rooms. I think Mr. Roney has checked and they are

3 available. So you can just somehow secure them, okay?

4   So are we on schedule? Is it going as the parties had

05:13PM 5 anticipated?

6   MS. PENSABENE: Yes, Your Honor, I think we will be

7 able to complete on schedule.

8   THE COURT: Yes. Do the defendants agree, Mr. Rizzi,

9 do you agree?

05:13PM 10   MR. RIZZI: I would say more or less, Your Honor. I

11 guess one question in terms of the week of August 1st.

12   THE COURT: Yes.

13   MR. RIZZI: Is it your expectation that we would --

14 well, let me ask this, would you like closings?

05:14PM 15   THE COURT: Yes.

16   MR. RIZZI: In addition to post-trial briefing.

17   THE COURT: Yes.

18   MR. RIZZI: So would the closings be deferred, then,

19 until we complete the trial on the extra couple of days?

05:14PM 20   THE COURT: I would like to have closings as to this

21 portion of the trial.

22   MR. RIZZI: Okay.

23   THE COURT: And I would like to have post-trial

24 briefing as to this portion of the trial, because we don't

05:14PM 25 have the date for the, quote, third portion yet, right?

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1   MR. RIZZI: That's correct, Your Honor.

2   THE COURT: And so --

3   MR. RIZZI: But the issues do overlap.

4   THE COURT: They do, they do. I'm not suggesting it

05:14PM 5 one way or the other that they don't, but it's all up here and

6 I want to keep it up here as long as I possibly can. So the

7 more that it -- that we can get much of this -- is there a

8 reason why you couldn't do the briefing?

9   Is there a reason why a party might be prejudiced if I

05:14PM 10 required briefing now as to all of the issues, except for the

11 inequitable conduct?

12   MR. RIZZI: I guess it's hard to say in terms -- we

13 don't know obviously what testimony will be elicited from the

14 witnesses who haven't been deposed yet.

05:15PM 15   THE COURT: Right.

16   MR. RIZZI: Obviously, that's geared towards

17 inequitable conduct.

18   THE COURT: Right.

19   MR. RIZZI: It may also be relevant to invalidity.

05:15PM 20   THE COURT: Right.

21   MR. RIZZI: And I can see some logic to deferring at

22 least on invalidity and doing that together with inequitable

23 conduct.

24   MS. PENSABENE: It seems to us, Your Honor, that it

05:15PM 25 makes sense to do the invalidity and infringement briefing now

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 1  that we're presenting in this portion of the case, and it also

 2  could be helpful in narrowing whatever issues there might be

 3  left for inequitable conduct.

 4          So we would think that briefing now while everything is

 5  fresh is best.  One other suggestion is to do briefing and

 6  then have a short closing at a later date after the briefing,

 7  if that makes sense to Your Honor to have a time to ask

 8  questions based on the briefing.  I know we've done that in

 9  some other cases.

10          THE COURT:  Yeah, I mean, we could do that.  I

11  mean --

12          MR. RIZZI:  Would it make sense to --

13          THE COURT:  Mr. Rizzi.

14          MR. RIZZI:  Would it make sense to do the briefing

15  after August 4th and then defer --

16          THE COURT:  The closings?

17          MR. RIZZI:  -- closings?

18          THE COURT:  Yeah.  We can defer the closings, but I

19  would like the briefing and so we can talk about dates for the

20  briefing, but we can defer the closings and so the parties

21  won't need to be prepared for the closings.

22          MR. RIZZI:  And then, I mean, if -- depending on time

23  the additional testimony that might come in may allow for

24  supplemental briefing, if that's --

25          THE COURT:  Right.  Well, see, do the parties have a
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Timestamps in left margin: 05:15PM (line 5), 05:16PM (line 10), 05:16PM (line 15), 05:16PM (line 20), 05:16PM (line 25)

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	1	sense as to when the third phase might occur? Because then
	2	you need --
	3	MR. RIZZI: I think we're in the process of trying to
	4	schedule depositions in the U.K.
05:17PM	5	THE COURT: Yeah, has that gone well?
	6	MR. RIZZI: I don't think we have dates. We're
	7	trying to do them in September.
	8	THE COURT: Okay. In September. Yeah. So --
	9	MR. RIZZI: Obviously sometime --
05:17PM	10	THE COURT: -- what we could do is maybe do the
	11	closings at that stage as well.
	12	MR. RIZZI: Yes. I mean, assuming the depositions
	13	happen in September, what was Your Honor thinking about
	14	scheduling the last part of trial?
05:17PM	15	THE COURT: Sometime in October, because I have a
	16	very long criminal trial in November which will go into
	17	December. So I would want to get this done, again, if the
	18	testimony is secured by then, I'd want to get this done in
	19	October.
05:17PM	20	MR. RIZZI: Understood.
	21	THE COURT: That's my hope. Okay.
	22	So we will pick up on the week of August 1st. There
	23	won't be closings, and then I will talk to you folks about
	24	post-trial briefing then, okay?
05:18PM	25	MR. RIZZI: Thank you, Your Honor.

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1   THE COURT: Okay. So everyone enjoy some of their

2   summer until I see you back, okay?

3   MS. PENSABENE: You also, Your Honor.

4   THE COURT: All right. Thank you.

05:18PM   5   THE DEPUTY CLERK: All rise.

6   (5:18 p.m.)

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