

1
2 UNITED STATES DISTRICT COURT
3 FOR THE DISTRICT OF DELAWARE

4 -----X
ALCON RESEARCH, LTD.,

5 Plaintiff, Civil Action No.

6 v. 16-129 (LPS) (SRF)

7 WATSON LABORATORIES, INC.,

8 Defendant.

9 -----X

10 VIDEOTAPED DEPOSITION

11 OF

12 MAUREEN DONOVAN, PH.D.

13 New York, New York

14 Friday, August 24, 2018

15
16
17
18
19
20
21
22
23 Reported by:

24 ANNETTE ARLEQUIN, CCR, RPR, CRR, CLR

25 JOB NO. 145678

1 M. Donovan, Ph.D.

2 And, again, nearly every product in
3 the armamentarium of all drug products could
4 have something done to it that would make
5 somebody happier with it.

6 Q. In the course of your work in this
7 case, did you consider what options were
8 available to the person of ordinary skill in the
9 art in 2009 who wanted to improve the Nevanac
10 product?

11 A. Yes. I looked at, you know, what was
12 known about ophthalmic formulations in 2009 and
13 preceding that, or at least refreshed my memory
14 regarding the specific date 2009 and what was
15 already being done in the art; investigated
16 regarding ophthalmic delivery; and, you know,
17 looked at a little bit of information in
18 specific about Nevanac.

19 Q. And in your view, what options would
20 the person of ordinary skill have considered in
21 2009 if they wanted to improve the Nevanac
22 product?

23 A. Can you specify what improvement
24 the --

25 Q. Well, you said that, if I understood

1 M. Donovan, Ph.D.

2 you correctly, that the person of ordinary skill
3 would have thought there was room for
4 improvement in the Nevanac product like there is
5 room for improvement in many products.

6 A. Um-hmm.

7 Q. Fair?

8 A. Right. Yes.

9 Q. And the question I have is: Looking
10 at the Nevanac product and thinking there may be
11 ways to improve this product, what sorts of
12 options would the person of ordinary skill have
13 thought of as ways it could be improved,
14 formulation steps that could be taken to improve
15 it?

16 A. Right. But I mean, each of those
17 formulations steps is directed at improving an
18 aspect --

19 Q. Okay.

20 A. -- or maybe a group of aspects or
21 something. So I think I need a little bit more
22 definition in the question of what aspect would
23 you like me to focus on.

24 Q. I'm asking you about -- let's ask
25 this: What aspects do you think the person of

1 M. Donovan, Ph.D.

2 ordinary skill would have focused on in order to
3 improve Nevanac?

4 MR. JAGOE: Objection to form.

5 A. So you're asking me to identify what
6 I -- if I -- as a POSA, if I were to look at
7 Nevanac and be asked to improve Nevanac, what
8 approach would I use?

9 Q. Yes. Or what options of approaches
10 would be available to you?

11 A. Well, there is a myriad of options,
12 some of them already available in the commercial
13 space and some of them that were research-based.

14 So if my goal as a POSA was to bring
15 another commercial product into the marketplace
16 in a reasonable time period, there are many of
17 the -- especially the things that were in the
18 research realm that probably wouldn't be
19 seriously considered.

20 Q. And why is that?

21 A. Well, they are just -- the
22 understanding of how they work is probably
23 underdeveloped, and the actual basic research
24 effort to understand whether they apply to
25 Nevanac would take a longer period of research

1 M. Donovan, Ph.D.

2 and development time. And there would be other
3 approaches that, again, were well-known in the
4 art that could be brought forward that would get
5 an additional product or an improved product
6 into the marketplace in a faster way without
7 having to do an excessive -- or not an
8 excessive, but even just a battery of more R&D
9 regarding a more unique formulation.

10 So to go back to the question I think
11 you asked, I'll identify it, so we were talking
12 about maybe it would make sense to try to
13 identify formulations that could be administered
14 less than three times a day. That would be one
15 potential improvement to the Nevanac product
16 that a person of ordinary skill that is a
17 formulator would be able to identify and would
18 understand that there were known methods to
19 bring forward to do that.

20 Q. Okay. And let's back up for one
21 second.

22 You drew a distinction in your answer
23 between the commercial space and what I think
24 you called the research area or the research
25 space.

1 M. Donovan, Ph.D.

2 Q. Okay.

3 Okay. And based on that, what is the
4 answer to the question?

5 A. Well, Figure 2 actually is a
6 graphical depiction of how someone calculates
7 the AUC and demonstrates the area under the
8 curve.

9 The bioavailability of a -- and we'll
10 do this -- might as well stay -- well, the
11 bioavailability of a drug product is a measure
12 or a description of the amount of drug that the
13 body was exposed to following administration of
14 that formulation or dosage form.

15 Okay. So the initial comparator is
16 an intravenous or interarterial administration
17 typically because you don't have absorption
18 effects. You don't have other dosage form
19 effects.

20 So that is your baseline that you
21 compare against is what were the distribution
22 parameters when you gave something
23 intravenously. And then when you added a
24 formulation, delivery system, whatever, to that,
25 how much drug, what time course and so forth as

1 M. Donovan, Ph.D.

2 a comparison, you either -- either you
3 understand that all of the drug you gave, the
4 body was exposed to the same amount of drug and
5 gave the same area under the curve, or it was
6 not exposed to the same amount of drug, or it
7 was exposed in a different time frame, which you
8 may tease out of your data or whatever.

9 So the bioavailability is a
10 description relative to a well-understood
11 control of what you're willing to represent as
12 100 percent. It may not be 100 percent. And
13 that's where relative bioavailability -- in my
14 report, I chose to include that because whatever
15 your reference is, whatever you're using as 100
16 percent, what's your fractional comparison to
17 that is the, is the bioavailability.

18 But if you're using blood as a
19 measure, for example, the built-in assumption to
20 that is that blood represents the rest of the
21 body, which it may or may not.

22 So there's always assumptions on what
23 your sampling matrix means regarding the rest of
24 the systems exposure.

25 Q. Okay. So let's go back to page 52.

1 M. Donovan, Ph.D.

2 (Witness complies.)

3 Q. You say, "Although AUC is generally
4 an indicator of bioavailability, formulations
5 with different bioavailabilities can achieve the
6 same efficacy results in clinical endpoint
7 studies higher bioavailability may not produce
8 any additional benefit."

9 Do you see that?

10 A. I see that.

11 Q. Can you explain to me how it is that
12 higher bioavailability may not produce any
13 additional benefit?

14 A. Well, because for the actual clinical
15 results, and for a drug that has a receptor, a
16 known receptor or a know ligand in the body
17 where you're targeting the drug to go to have an
18 effect, the standard or the understanding in
19 pharmacology is that the dose response
20 relationship is not linear and it doesn't go on
21 forever. So that is you increase the dose, you
22 don't necessarily get a proportional increase in
23 response.

24 And at some point in dosing or
25 exposure concentration to the receptor that you

1 M. Donovan, Ph.D.

2 don't have any more receptors to accept the
3 drug, it can't have any more response regardless
4 of how much more drug is in the system. And so
5 you can have more drug in the system, it -- that
6 more drug doesn't elicit more response.

7 Q. I see.

8 You say, "That appears to be the case
9 for Nevanac and in Ilevro since these
10 formulations have nearly the same effectiveness
11 in clinical studies even when both are
12 administered once a day."

13 Is what you're saying there is that
14 Ilevro has higher bioavailability than Nevanac,
15 but it doesn't produce any additional clinical
16 benefit?

17 Am I understanding that correctly?

18 A. That's not what I intended to
19 communicate when I wrote this.

20 Q. What did you intend?

21 A. Well, the intention was, it's in the
22 description in the paragraph about some of the
23 clinical data that I was reviewing and that
24 clinical data has -- some of the charts have
25 information about concentration in various

1 M. Donovan, Ph.D.

2 A. No, I didn't.

3 Q. And since 1991, am I correct that you
4 haven't worked as an employee for any
5 pharmaceutical company?

6 A. No, I haven't.

7 Q. And have you ever the developed an
8 ophthalmic suspension?

9 A. I've worked on formulations in my
10 laboratory that could have or, you know, even
11 were applied in an experimental sense as -- I
12 think they were suspensions. I don't even --
13 the issue at hand that I'm thinking of was
14 something that was a multi-component formulation
15 that we were looking at. I don't remember
16 whether all of the components were in suspension
17 or whether one was in solution. But we've
18 certainly looked at formulations that could have
19 been used ophthalmically. I don't recall since
20 I've been at Iowa actually personally being the
21 principal investigator at least of a formulation
22 development activity where we've actually tested
23 anything even in an animal model for ophthalmic
24 use.

25 Q. Would it be fair to say, then, that

1 M. Donovan, Ph.D.

2 you've never worked on an ophthalmic suspension
3 formulation that had been administered to a
4 human, at least to your knowledge?

5 A. So "worked on" is -- that I've never
6 developed a formulation for an ophthalmic
7 suspension that was administered to a human?

8 Q. Correct. That's the question.

9 A. Yes, that's true.

10 Q. And have you ever developed an
11 FDA-approved product of any kind?

12 A. No. My work is not focused on trying
13 to develop FDA-approved products.

14 Q. Now your CV is at the end of your
15 opening report, but you may not need it for this
16 question.

17 Am I correct over the years you've
18 published a number of articles and abstracts in
19 professional scientific journals; is that
20 correct?

21 A. Yes.

22 Q. Would it be fair to say that you have
23 published many articles related to the nasal
24 administration of drugs?

25 A. Yes, I think it's fair to say.

1 M. Donovan, Ph.D.

2 Q. How many articles have you published
3 that are focused on ophthalmic administration?

4 A. That's probably one article out of
5 what I've published.

6 Q. And can you identify for me which
7 article that is?

8 A. It's the first article on the
9 publication list and it's -- the pages are not
10 numbered on Exhibit A, but it's page 2 of
11 Exhibit A.

12 Q. And it's the Miller & Donovan --

13 A. Yes.

14 Q. -- effect of poloxamer gels
15 article --

16 A. Yes.

17 Q. -- from International Journal of
18 Pharmaceutics in 1982?

19 A. Yes.

20 Q. And was that about ophthalmic
21 suspensions?

22 A. The test agent we were using in that
23 formulation, the drug was in solution I believe
24 in those products.

25 MR. PERLMAN: Okay. Should we take a

1 M. Donovan, Ph.D.

2 short break?

3 MR. JAGOE: Sounds good.

4 THE VIDEOGRAPHER: The time is
5 9:12 a.m. We are off the record.

6 (Recess is taken.)

7 THE VIDEOGRAPHER: The time is
8 9:24 a.m. We are on the record.

9 BY MR. PERLMAN:

10 Q. Doctor, before the break, we had
11 spoken about how in an ophthalmic suspension,
12 some of the API is dissolved in solution and the
13 rest is in the form of undissolved particles in
14 the suspension.

15 Do you recall that?

16 A. Yes.

17 Q. And am I correct that in order for
18 the undissolved particles to be absorbed and
19 used by the eye, they have to first dissolve
20 into the solution?

21 A. That's the general understanding of
22 things unless they're really small and there is
23 another biological mechanism that's actually
24 taking them into the body.

25 Q. As a general matter?

1 INDEX OF EXHIBITS(Cont'd.)
2 DESCRIPTION PAGE
3 Plaintiff's Donovan Exhibit 6, U.S. 131
4 Patent No. 6,486,138
5
6 Plaintiff's Donovan Exhibit 7, U.S. 170
7 Patent No. 7,128,928
8
9 Plaintiff's Donovan Exhibit 8,
10 Chowhan Patent Application 219
11 Publication
12
13 Plaintiff's Donovan Exhibit 9,
14 Supplemental Report of Maureen
15 Donovan, Ph.D. 237
16
17 Plaintiff's Donovan Exhibit 10, U.S. 245
18 Patent No. 5,145,684
19
20 Plaintiff's Donovan Exhibit 11, U.S. 253
21 Patent No. 5,429,824
22
23 Plaintiff's Donovan Exhibit 12,
24 Printed FDA website to the inactive
25 ingredients database as of 2009 261

Plaintiff's Donovan Exhibit 13, 285
Article published in International
Journal of Pharmaceutics entitled
"Pharmaceutical Nanotechnology -
Nanosuspension as an ophthalmic
delivery system for certain
glucocorticoid drugs

Plaintiff's Donovan Exhibit 14, 297
International Application -
Publication No. WO 02/05815

ERRATA SHEET

1 Case Name:
2 Deposition Date:
3 Deponent:
4
5 Pg. No. Now Reads Should Read Reason
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20

21 _____
22 Signature of Deponent
23 SUBSCRIBED AND SWORN BEFORE ME
24 THIS ____ DAY OF _____, 2018.
25 _____
(Notary Public) MY COMMISSION EXPIRES: _____