

1 IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
2 BEFORE THE PATENT TRIAL AND APPEAL BOARD

3 SAMSUNG BIOEPIS CO.,)
4 LTD.,)
5 Petitioner,)
6 v.)
7 REGENERON) Patent No.
8 PHARMACEUTICALS, INC.,) 10,888,601
9 Patent Owner.) Iter Partes
10) Review No.
11) IPR2023-00739
12)
13)
14)

15 VIDEOTAPED DEPOSITION OF:

16 EDWARD CHAUM, M.D., Ph.D. (Volume II)

17 Taken on behalf of the Patent Owner

18 February 2, 2024
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EXHIBITS

EXHIBIT 2062 315

Deposition Transcript Volume I of Dr. Chaum

EXHIBIT 1002 318

Declaration (Previously marked)

EXHIBIT 1016 341

Chapter in Vol. 2 Remington: A Science and Practice
of Pharmacy (Previously marked)

EXHIBIT 1002 368

Patent 11253572 (Previously marked)

EXHIBIT 10 399

2006 Press release (Previously marked)

1 The videotaped deposition of EDWARD
2 CHAUM, M.D., Ph.D., taken on behalf of Patent
3 Owner, on the 2nd day of February, 2024,
4 commencing at 9:00 a.m., in the offices of
5 Dickinson & Wright, 242 Church Street, Suite
6 1401, Nashville, Tennessee, for all purposes
7 under the Federal Rules of Civil Procedure.

8 The formalities as to notice, caption,
9 certificate, et cetera, are waived. All
10 objections, except as to the form of the
11 questions, are reserved to the hearing.

12 It is agreed that Jennifer Haynie, being
13 a Notary Public and Court Reporter for the State
14 of Tennessee, may swear the witness, and that
15 the reading and signing of the completed
16 deposition by the witness are not waived.

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1 THE VIDEOGRAPHER: This is the video
2 deposition of Dr. Edward Chaum --

3 THE WITNESS: Chaum.

4 THE VIDEOGRAPHER: Chaum, sorry.

5 -- on 2/2/2024 at the time indicated
6 on the video screen which is 9:25 a.m.

7 Full introduction has been waived.
8 Will the court reporter please swear in the
9 witness, and counsel introduce themselves.

10 MR. SUMMERS: And I'm Zach Summers
11 for -- of Quinn Emanuel for Samsung Bioepis, the
12 petitioner and the witness.

13 MR. BRAUSA: My name's Adam Brausa.
14 I'm from the Morrison Foerster Firm on behalf of
15 patent owner, Regeneron.

16 EDWARD CHAUM, Ph.D.,
17 Having been sworn to tell the truth,
the whole truth and nothing but the
18 truth, testified as follows:

19 DIRECT EXAMINATION

20 BY MR. BRAUSA:

21 Q. Great. Good morning, Dr. Chaum. Good to
22 see you again.

23 A. Good morning.

24 Q. We spoke at a deposition last month,
25 correct?

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1 A. Yes.

2 Q. It was on January 5th. I asked you some
3 questions; you provided answers. Do you
4 remember that?

5 A. I do.

6 Q. Okay. And at the time that was not your
7 first deposition relating to patent matters.
8 You've been deposed in prior IPRs too, correct?

9 A. Yes.

10 Q. Okay. Since we spoke in January, on
11 January 5th, have you gone back and reviewed the
12 transcript from that deposition?

13 A. I have not.

14 Q. Okay. I want to go ahead and mark what I
15 can represent is the official copy of that
16 transcript as Exhibit 2062.

17 MR. BRAUSA: We can go off the
18 record briefly.

19 THE VIDEOGRAPHER: The time is 9:.
20 We're off the record.

21 (Exhibit Number 2062 was marked.)

22 THE VIDEOGRAPHER: The time is 9:.
23 We're back on the record.

24 BY MR. BRAUSA:

25 Q. Okay. And Exhibit 2062 in front of you,

1 Dr. Chaum, is -- I can represent is a copy of
2 your deposition transcript from IPR 2023-739,
3 and you see on the face of it, it bears a date
4 of January 5, 2024?

5 A. Yes.

6 Q. Do you have any plans to review this
7 transcript in the next couple of days?

8 A. If I'm asked by my counsel to do, I
9 certainly will.

10 Q. Okay. Sitting here today, do you have
11 any corrections that you'd like to make to your
12 deposition testimony that you provided on
13 January 5, 2024?

14 A. I have not read it, so I can't provide
15 you with any corrections that I might see until
16 I read it.

17 Q. Okay. But sitting here today, you don't
18 recall anything that you felt like you need to
19 correct or that was inaccurate?

20 A. Not that I recall, no.

21 Q. Okay. And when I asked you questions on
22 January 5th in that I proceed -- IPR
23 proceedings, you testified truthfully and
24 accurately, correct?

25 A. Yes.

1 Q. Okay. We can put that to one side.

2 A. Sure.

3 Q. In this proceeding, the patent that we're
4 dealing with is US patent number 11253572. Does
5 that sound right to you?

6 A. Yes.

7 Q. And if I refer to that as the 572 patent,
8 you'll understand what I mean?

9 A. Yes.

10 Q. And previously we were talking about US
11 patent 10888601 or the 601 patent.

12 A. Yes.

13 Q. Okay. And so I'll try and very precise
14 because I know there are a lot of patent
15 numbers. If it's ever unclear what patent I'm
16 referring to, just ask for me to clarify, and
17 I'll do my -- my best to do that.

18 A. Okay.

19 Q. Okay. Great. So in this proceeding,
20 you've offered a declaration with respect to all
21 the claims of the 572 patent, correct?

22 A. Yes.

23 Q. And it's your opinion that based on the
24 prior art that you discussed in the declaration,
25 all of these claims are either anticipated or

1 obvious in view of the prior art, correct?

2 A. Yes.

3 Q. And let me go ahead and mark your -- or
4 provide you with a copy of your declaration.
5 This is Exhibit 1002.

6 (Exhibit Number 1002 was marked.)

7 MR. SUMMERS: Thank you, Counsel.

8 BY MR. BRAUSA:

9 Q. And I would ask that you turn to the
10 table of contents, romanette 3 and 4, it's in a
11 section called Invalidity under section 103, and
12 then there's an analysis section, and it has D 1
13 through 11. Let me know when you're there.

14 A. I'm not sure where you're directing me.

15 Q. So if you could go to the table of
16 contents of Exhibit 1002 --

17 A. Okay.

18 Q. And actually, why I don't just use the
19 bold page numbers in the lower right-hand
20 corner.

21 A. Okay.

22 Q. So page 3.

23 A. Okay.

24 Q. And you see there's a subsection called
25 Analysis, and then underneath that there are 11

1 different headings?

2 A. Yes.

3 Q. And am I correct that these 11 different
4 headings represent each of the bases you opine
5 on in your report for why, in your view, the
6 claims of the 572 patent are invalid?

7 A. Yes.

8 Q. And so if we go to, for example, heading
9 5 referring to claims 16 through 17 and 20
10 through 21. Do you see that?

11 A. Yes.

12 Q. There are multiple references listed
13 there, correct?

14 A. Yes.

15 Q. Could you explain to me for, again,
16 heading 5, claims 16 through 17 and 20 through
17 21, which references or combinations of
18 references are you relying on for your opinion
19 that these claims are obvious?

20 A. As -- as it states in the section
21 heading, I am relying on the 2009 press release
22 alone.

23 Q. Uh-huh.

24 A. And I am relying on the 2000 press
25 release alone or in connection with or in

1 consideration of both the 2007 ARVO abstract,
2 the Disk -- Dickson reference, and the 2010 ARVO
3 abstract. So both singly, alone, and in
4 combination with those other references.

5 Q. Okay. And so I understand what you said
6 with respect to the 2009 press release alone. I
7 want to talk a little bit about combination.

8 Is there a specific combination of the
9 2009 press release that you're relying on in
10 heading 5 with respect to claims 16 through 17
11 and 20 through 21 in your opinion that those
12 claims are obvious?

13 A. Well, Counsel, I have to go to that
14 section and review it, and we can discuss it.

15 Q. Okay. I think we can do that in a little
16 bit. I wanted to -- before we get there, turn
17 to page 16 and 17 of Exhibit 1002. Again, I'm
18 going to use the bold page numbers in the lower
19 right-hand corner for reference.

20 A. Okay.

21 Q. And there's an Information Relied Upon
22 section that goes from paragraphs 14 through 18.
23 Do you see that section?

24 A. Yes.

25 Q. And this lists various documents,

1 including some documents from other IPR
2 proceedings, right?

3 A. Yes.

4 Q. And in addition to these documents, are
5 you aware that there have been additional
6 developments in IPR proceedings since you
7 authored and provided this report?

8 A. I understand that there may be some new
9 developments related to a case in West Virginia.

10 Q. Okay.

11 A. But that's all I know about.

12 Q. And -- and what's your understanding of
13 the developments with respect to that case in
14 West Virginia?

15 MR. SUMMERS: Objection.

16 I'll caution witness not to reveal
17 the substance of any attorney-client
18 communication.

19 THE WITNESS: Only that there's new
20 developments.

21 BY MR. BRAUSA:

22 Q. Okay. Do you know what the developments
23 are?

24 A. I do not.

25 Q. Okay. Have you read any opinions or

1 papers from the Western District? Or the
2 District of West Virginia? Excuse me.

3 A. I have not.

4 Q. In this particular IPR that we're here
5 talking about today, IPR 2023-884, are you aware
6 that there's been institution decision authored
7 by the board?

8 A. I am not aware, no.

9 Q. Okay. And so you haven't read any
10 institution decision by the board?

11 A. Related to which specific patent?

12 Q. Relating to the 572 patent.

13 A. I'm not aware of, no.

14 Q. Okay. And so you're not aware of whether
15 the board has excreck -- expressed skepticism
16 with respect to any of your opinions?

17 A. I am not aware of -- of that.

18 Q. Okay. In paragraph 16, you refer to IPR
19 2022-012 relating to the 601 patent. Do you
20 see that?

21 A. Yes.

22 Q. Do you know whether there's been a final
23 written decision in that proceeding?

24 A. I'm not aware if there has been one or
25 not.

1 Q. Okay. And since we spoke in January at
2 your deposition, beyond preparing for this
3 deposition, have you gone back and looked at any
4 materials relating to the 601 patent?

5 A. I have not.

6 Q. Okay. What did you do to prepare for
7 today's deposition?

8 A. I reviewed the materials that are listed
9 in the table of contents, and I reviewed my
10 declaration, which was previously provided.

11 Q. Okay. And are there any corrections or
12 clarifications you'd like to make to any
13 portions of your declaration, Exhibit 1002?

14 A. Not at this time, no.

15 Q. And when you say not at this time, are
16 you aware of any clarifications that you'd like
17 to make at this point?

18 A. I am not.

19 Q. Okay. If we can go to paragraphs 91
20 through 103 of your report, this spans pages 44
21 through 48 of Exhibit 1002.

22 This is under a section 9 entitled
23 Priority Date. Do you see that?

24 A. I do.

25 Q. And in this section, you offer your

1 opinion that claim 25 of the 572 patent has an
2 earliest effective filing date of July 12, 2013,
3 correct?

4 A. So as I state here, I was asked to assume
5 the earliest priority date for the 572 patent is
6 January 2011 for all claims other than claim 25.

7 Q. Right. And with respect to 25 -- claim
8 25, you offer an opinion starting at paragraph
9 95 of your view that it has an earliest
10 effective filing date July 12, 2013, correct?

11 A. That is the date that I have been asked
12 to assume as its effective filing date, yes.

13 Q. Okay. And do you recall in January when
14 you were deposed I asked you some questions
15 about the analysis you did of the priority date
16 for certain claims of the 601 patent?

17 A. Vaguely.

18 Q. Okay. Do you recall whether you did any
19 independent analysis of the prior art date or
20 priority date -- excuse me -- for the 572 patent
21 as compared to the 601 patent?

22 A. I'm not quite sure I understand exactly
23 what you're asking.

24 Q. Did you -- do you recall whether you
25 conducted a priority analysis for the 601 patent

1 we talked about in January?

2 A. No. I didn't perform an independent
3 analysis. I was asked to assume specific
4 priority dates by counsel and I did.

5 Q. Okay. And in this case too you were just
6 asked to assume certain priority dates by
7 counsel, correct?

8 A. That is correct.

9 Q. You haven't conducted any independent
10 analysis of the priority dates of any claims of
11 the 572 patent?

12 A. I have not.

13 Q. Okay. I think when we last spoke, you
14 had mentioned that in the 2010, 2011 timeframe,
15 you were primarily prescribing Avastin off-label
16 for angiogenic eye disorders; is that fair?

17 A. That's correct, yes.

18 Q. Okay. And from time to time, you might
19 prescribe Lucentis if one of your colleagues was
20 prescribing it, but your practice was primarily
21 to prescribe Avastin off-label?

22 A. That's correct.

23 Q. And I think in that timeframe, if my
24 memory is correct, you were -- your practice was
25 to use a PRN or pro re nata strategy; is that

1 fair?

2 A. At that time that was part of my practice
3 pattern, yes. If not, all patients that
4 received a PRN dosing, but to the extent that I
5 could extend patients and modify the injection
6 regimen to reduce the burden, I attempted to do
7 so.

8 Q. Okay. And -- and the goal for those
9 patients that you were using PRN dosing with was
10 to dose as needed, but the goal is to administer
11 less frequently than monthly, fair?

12 A. No. The goal is really to treat the
13 disease, so the goal is to identify the status
14 of the disease, whether it's quiescent, and to
15 the extent possible, then extend to minimize the
16 burden.

17 The goal wasn't to establish a particular
18 regimen, but rather to treat as needed, as
19 frequently or infrequently, based upon the
20 patient's response to treatment.

21 Q. Okay. Was there any -- do you recall,
22 did you have a lot of patients or did you have
23 any patients where you use PRN dosing strategy
24 and administer more frequently than monthly?

25 A. Well, PRN means as needed, so are you

1 asking specifically about more frequently than
2 monthly?

3 Q. Yes.

4 A. Typically not, no.

5 Q. Okay. And so it's -- well, the treatment
6 is the ultimate goal. One aspect of PRN that's
7 desirable from the patient's perspective is the
8 potential for the less frequent than monthly
9 injections into their eyes, correct?

10 A. Yes.

11 Q. When you're treating patients, when you
12 have patients that you're treating using a PRN
13 strategy, were there any comparisons that you
14 would do to determine whether that treatment was
15 effective?

16 A. I'm not sure I'm understanding your
17 question.

18 Q. So in the 2010, 2011 timeframe, I think
19 you previously testified that there was data
20 available showing the efficacy of Avastin and
21 Lucentis on a monthly basis, right?

22 A. Yes.

23 Q. Were those -- or was that data used as a
24 point of comparison in your practice for
25 determining whether your PRN dosing strategy was

1 effective?

2 A. If I understand your question, I think
3 the answer is probably, yes. So the monthly
4 strategy was shown to be effective and an
5 effective strategy for managing neurovascular
6 eye disease, for example, macular degeneration.

7 And so the initial course for patient
8 treatment was to initiate a monthly dosing
9 schedule. And so as a reference, if you will,
10 maintenance of the monthly dosing schedule would
11 be that reference. My goal and the goal of
12 other practitioners at that time who were
13 looking at -- who were attempting to reduce the
14 treatment burden, both for the patient and the
15 clinical practice, was to determine if that
16 patient could be extended beyond that monthly
17 dosing regimen.

18 So if you're asking is a month -- was the
19 monthly regimen the reference upon which we then
20 made a decision to extend beyond one month, the
21 answer is yes.

22 Q. Okay. And if there were patients that
23 you used a PRN dosing strategy with that you
24 observed them to be performing or -- or have
25 less effective treatment than the monthly dosing

1 regimen, would you continue on an extended
2 dosing regimen?

3 A. No. Again, the goal is to effectively
4 treat the patient's disease. So in those cases
5 where the extension of the duration of treatment
6 was not showing equivalent efficacy or sustained
7 efficacy, then I would make a decision to reduce
8 that duration in some form or other.

9 And it would depend upon where that
10 patient was in the PRN regimen, if you were --
11 if you would, how long they had been effectively
12 treated at a certain dosing regimen and the
13 nature extent of the reactivation of the
14 disease.

15 So all of those things would play a role
16 in my decision about how to change from PRN to a
17 different strategy or to a more regimented
18 strategy.

19 Q. Okay. When you saying you're evaluating
20 whether they were -- had equivalent or sustained
21 efficacy, that was compared to monthly Avastin,
22 right?

23 A. I'm not -- I'm not sure I understand
24 exactly what you're asking because my answer to
25 that question would be no. Again, I'm treating

1 a patient individually. I'm looking at their
2 response, so if they're -- for example -- let me
3 give you an example.

4 I've got a patient who I've now extended
5 to every ten weeks for an injection, and they
6 been successfully maintained at a ten-week
7 schedule for, say, six months, eight months, and
8 they're doing well. And they come back and now
9 they new leakage when I've seen them for their
10 ten-week injection schedule.

11 What that tells me is that the disease
12 has reactivated in advance of that ten-week
13 window. So to answer -- to answer your
14 question, would I then take that patient who had
15 been at ten weeks reproducibly, reliably, and
16 effectively managed and take that patient back
17 to a monthly regimen to reinduce that patient on
18 a monthly schedule, not necessarily.

19 It would depend on the level of leakage,
20 the nature of the patient's previous response.
21 So I might take that patient back to an
22 eight-week schedule, or I might take that
23 patient back to a six-week schedule and then try
24 and extend again on a PRN basis.

25 Q. In -- in your practice, would you ever be

1 satisfied with less efficacy than you thought
2 was possible in exchange for less frequent
3 dosing?

4 MR. SUMMERS: Objection. Form.

5 THE WITNESS: Maybe you can rephrase
6 the question for me.

7 BY MR. BRAUSA:

8 Q. Sure. Would you ever extend and maintain
9 an extended dosing interval for patients if you
10 thought that that extended interval was less
11 effective than a shorter interval will be?

12 A. It depends on your definition of
13 effectiveness. In general, obviously as a
14 physician taking care of a patient, trying to
15 preserve and maintain their vision, I certainly
16 wouldn't want to manage that patient in a way
17 that I thought was at -- would put their vision
18 at risk or in which they would lose vision.
19 That would make no sense.

20 Q. Sure.

21 A. So the question is more, is the decision
22 regarding the dosing effic- -- or dosing
23 frequency, it kind of depends on what -- what
24 your definition of -- of efficacy is in the
25 sense that you -- for example, you know, I could

1 see a patient who might have some new leakage
2 for a disease that I'm treating, but their
3 vision hasn't changed.

4 So am I obligated to treat that patient
5 knowing that there's a little bit less efficacy
6 there at that time? Am I obligated to treat
7 that patient based upon an image that I'm
8 seeing? Or do I have a conversation with that
9 patient to say, hey, we're seeing some changes
10 here. This may indicate a new activity in your
11 disease. We have to come to a decision about
12 whether or not to treat it or not.

13 Also understand that decisions aren't
14 100 percent in the hands of the physician. The
15 patient is a partner in this process. In
16 particular, if receiving treatment means that I
17 have to stick a needle in her eye. That's
18 something that that patient needs to be part of
19 that conversation and that decision making.

20 And so I might be in a situation where
21 I'm seeing less efficacy than I would like, but
22 the patient doesn't want to get an injection in
23 their eye every month because of the burden and
24 the discomfort.

25 And so it -- it's -- it's -- it's more

1 nuanced and complex answer to your question.
2 And I'm sure if I answered your question, but
3 that's my response.

4 Q. You referred to a making a decision
5 whether to treat in a patient receiving
6 treatment in your prior answer. When we're
7 talking about treatment, does that involve
8 anything, in your view, beyond administering a
9 drug?

10 A. No, treatment is for the benefit of --
11 treatment is to administer the drug for the
12 benefit to -- to achieve a -- a benefit for the
13 patient.

14 Q. Okay.

15 A. That's how I would define it.

16 Q. And if you don't observe any benefit,
17 have you treated the patient?

18 A. Your question doesn't make any sense to
19 me.

20 Q. Let's say you administer Avastin into a
21 patient and their vision worsens. Have you
22 treated that patient?

23 MR. SUMMERS: Objection. Form.

24 THE WITNESS: Well, I've -- I've
25 given them a treatment.

1 BY MR. BRAUSA:

2 Q. Uh-huh.

3 A. The response to the treatment may not be
4 what I had anticipated or expected or predicted,
5 and therefore, I make a decision, treatment
6 decision, based upon that new information.

7 Q. Okay. And would you consider that to be,
8 if their vision worsens, an effective treatment?

9 MR. SUMMERS: Objection. Form.

10 THE WITNESS: Well, typically not.
11 The goal of treatment is to, ideally, stabilize
12 the patient's vision or, if possible, in certain
13 circumstances, to be able to improve that
14 patient's vision.

15 BY MR. BRAUSA:

16 Q. In your practice as of 2010 and 2011, did
17 you have a particular standard for yourself to
18 consider a treatment to be effective when we're
19 talking about these angiogenic eye disorders?

20 MR. SUMMERS: Objection. Form.

21 THE WITNESS: Well, it's -- again,
22 it's -- the definition of effectiveness is -- is
23 complex. So if we're talking about an
24 angiogenic eye disease, efficacy can be
25 demonstrated in a number of different ways.

1 Efficacy can be demonstrated by
2 stabilization or improvement in visual acuity.
3 Efficacy of the drug can be demonstrated by a
4 reduction in the thickness of -- the maximal
5 thickness of retinal swelling. Efficacy can be
6 demonstrated in the form of reduction in central
7 retinal subfield thickness, which is a -- a
8 metric that's part of our optical coherence
9 tomography imaging units.

10 Efficacy can be considered or can be
11 related also to the patient's subjective sense
12 of -- of quality of vision. There are a number
13 of different metrics that can and are used to
14 determine efficacy. It's not one thing that
15 says did this treatment work? Yes or no? There
16 are complex physiologic and anatomical issues
17 that are evaluated for every patient in -- in
18 the clinic to determine what's the status of the
19 disease? How are they responding? Are we
20 getting the efficacy that we are seeking? And
21 what's the nature of that efficacy, and how does
22 the patient want to move forward with their
23 treatment regimen?

24 BY MR. BRAUSA:

25 Q. Of the various forms of efficacy or

1 methods of determining and evaluating efficacy
2 you mentioned, were there any in particular that
3 you focused on in your practice in the 2010,
4 2011 timeframe?

5 MR. SUMMERS: Objection. Form.

6 THE WITNESS: Well, I think I
7 answered that question. So I utilize all of
8 those features and metrics to arrive at a
9 decision regarding whether or not or what the
10 status of that patient's disease was and the
11 efficacy, if you will, of treatment.

12 BY MR. BRAUSA:

13 Q. Do you have any training in formulating
14 drug substances?

15 A. No.

16 Q. Have you ever developed a formulation for
17 a fusion protein like aflibercept?

18 A. No.

19 Q. Have you ever developed a protein
20 formulation for an antibody like Avastin or
21 Lucentis?

22 A. No.

23 Q. Are you familiar with the term
24 excipients?

25 A. I'm not sure how you're using it. I'm...

1 Q. Have you ever heard that word?

2 A. I have. I'm not familiar with the
3 context in which you're using it.

4 Q. Okay. What context have you used that or
5 heard that word in?

6 A. I'm not familiar with it. I'd have to
7 look it up.

8 Q. Okay. So sitting here today, you don't
9 have any understanding of what the term
10 excipients means?

11 A. Well, if I looked it up, I would
12 understand what it meant, yes.

13 Q. Okay. But you'd have to consult a
14 dictionary or other resource to understand?

15 A. Yeah, I -- I've seen -- I've seen the
16 word. I'm just -- in this context, I'm not
17 familiar with its use.

18 Q. Okay. Have you ever looked at what the
19 ingredients of the Avastin formulation are?

20 A. I -- I certainly know the molecule
21 itself.

22 Q. Okay. But the Avastin that you
23 administer to your patients, it has other
24 ingredients in the formulation that gets
25 injected into their eye, right?

1 A. Yes.

2 Q. Do you know what those other ingredients
3 are?

4 A. Not offhand, no.

5 Q. Okay. Do you know what the other
6 ingredients are in the Lucentis formulation?

7 A. Not offhand, no.

8 Q. Okay. Do you know what the ingredients
9 are in the Eylea formulation?

10 A. Not offhand, no.

11 Q. Do you know whether there are any certain
12 types of ingredients in any of those
13 formulations that would present safety concerns?

14 A. If those formulations had been created
15 for use for intravitreal injection and had been
16 approved by the FDA for that purpose, then I
17 would not predict that there would be specific
18 safety issues related to the formulation.

19 There are safety issues related to the
20 activity of the molecule in the eye, but if
21 you're asking specifically about the
22 formulations, I would not predict that there
23 would be safety issues.

24 Q. Do you know what a surfactant is?

25 A. Yes.

1 Q. What is it?

2 A. Surfactant is a molecule that reduces the
3 surface tension between two liquids.

4 Q. Okay. And do you know whether those are
5 used in drug formulations?

6 A. They are.

7 Q. Do you know why?

8 A. Excuse me.

9 Q. Do you know why they're used?

10 A. Yes.

11 Q. Why?

12 A. Because they enhance the solubility of
13 molecules. So, for example, if we're talking
14 about a drug, for example, an anti-VEGF agent is
15 a protein solution that has an aqueous component
16 and a protein solution -- and a protein
17 component to it. The protein is not necessarily
18 freely admissible in an aqueous environment, and
19 so the surfactant acts to solubilize the protein
20 in that aqueous environment. Also adds -- acts
21 to maintain the clarity of that solution that's
22 used in the drug.

23 Q. Do you know what a nonionic surfactant
24 is?

25 A. Surfactants have a particular type of

1 structure that allows them to act in the way
2 that they do. They have a -- basically, a
3 hydrophilic portion of that molecule which
4 interacts with the aqueous part of the
5 molecule -- of the solution, and they have a
6 hydrophobic part of the solution, sometimes a
7 long hydrophobic tail which acts -- which
8 interacts with the polar organic or other types
9 of molecules within the -- within the solution.
10 And so the -- that's how -- that's how the
11 surfactant functions because it adds this two
12 bipolar nature to the molecule.

13 Q. So what is an ionic surfactant, and how
14 does it function?

15 A. Well, there're different forms of
16 surfactants. So there are nonionic surfactants.
17 There are anionic surfactants. There are
18 cationic surfactants. The nature of that
19 anionic, non-ionic, or cationic is a function of
20 the electrical charge in the hydrophilic head of
21 the molecule.

22 Q. And just to confirm: You don't have any
23 experience deciding whether a surfactant should
24 or should not be included in any given drug
25 formulation, correct?

1 A. I don't have any specific experience, no.

2 Q. Okay. And you don't have any direct
3 experience deciding whether to use an ionic
4 surfactant or a nonionic surfactant?

5 A. Well, as I say in my declaration and
6 looking at Hecht as a reference, Hecht -- and
7 let me -- let me track it down for you. I want
8 to be clear.

9 (Exhibit Number 1016 was marked.)

10 BY MR. BRAUSA:

11 Q. Yeah, we can go ahead and introduce it as
12 Exhibit 1016. And so just for the record,
13 Exhibit 1016 is volume 2 or the chapter in
14 volume 2 of something called Remington: A
15 Science and Practice of Pharmacy, correct?

16 A. Yes.

17 Q. Was this a reference you were familiar
18 with prior to your retention in this case?

19 A. I was asked to review this reference.

20 Q. Understood. But were you familiar with
21 it before you were asked to review it?

22 A. Not this specific chapter in this
23 specific book, no.

24 Q. Okay. Were there you familiar with this
25 specific book at all?

1 A. Not that I recall, no.

2 Q. And so this particular chapter in this

3 specific book was provided to you by counsel?

4 A. It was.

5 Q. And did you review the entire chapter?

6 A. I did.

7 Q. Did you ask to look at any other chapters

8 in the book?

9 A. No. Because I was focused on ophthalmic

10 preparations.

11 Q. Okay.

12 A. So if I might answer your question.

13 Q. Sure.

14 A. So in my declaration -- and we can go

15 back to where that in the Hecht reference if you

16 want, but I state from the Hecht reference that

17 Hecht teaches that non-ionic surfactants should

18 be used in ophthalmic solutions because they are

19 the least toxic to ophthalmic tissues and can

20 act as aides in achieving solution clarity or as

21 cosolvents to increase solubility.

22 Q. And you're reading from paragraph 115 of

23 your expert declaration at 1002?

24 A. Yes. Yes.

25 Q. Okay. And did you review any other

1 portions of the Hecht reference beyond those
2 that you quoted?

3 A. I did. I looked the issue of
4 isotonicity.

5 Q. What's isotonicity?

6 A. Isotonicity refers to the osmotic
7 pressure in a solution that contains solutes.

8 Q. And the other options, as I understand
9 it, in terms of tonicity are hypertonic or
10 hypotonic?

11 A. That -- again, those terms refer to
12 concepts regarding the relative level of
13 tonicity with respect to a particular other, if
14 you will.

15 Q. Okay. And my understanding is that you
16 unit for tonicity is osmolality; is that fair?

17 A. That's -- osmolarity and osmolality are
18 both used, but osmolality is more correct.

19 Q. Okay. Just so I'm correct: Osmolality
20 with an "L" or osmolarity with an "R"?

21 A. Osmolality --

22 Q. Okay.

23 A. -- is more precise.

24 Q. Okay. Now, I'll try and be precise.
25 Have you done any osmolality calculations

1 yourself?

2 A. I have.

3 Q. Okay. When was last time you did an
4 osmolality calculation?

5 A. To be honest, perfectly honest?

6 Q. That's why we're here.

7 A. Last night.

8 Q. Okay. And what osmolality did you
9 calculate last night?

10 A. The osmolality of .9 percent sodium
11 chloride.

12 Q. Why did you calculate the osmolality of
13 .9 percent sodium chloride the night before your
14 deposition?

15 A. So two reasons. One is .9 percent sodium
16 chloride is an isotonic solution that's commonly
17 used in clinical medicine, and it is often used
18 as a reference for comparing other solutions.
19 Are they isotonic to blood plasma or sodium .9
20 percent sodium chloride? And the other reason
21 is that I thought you might ask me the question,
22 and so I did a calculation.

23 Q. Okay. You thought I might ask you when
24 the last time you calculated osmolality was?

25 A. I thought you might ask me to calculate

1 an osmolality.

2 Q. Okay. I see.

3 A. And so I did.

4 Q. So you -- you could calculate it if I
5 gave you a formulation, sitting here today?

6 A. Yes.

7 Q. Okay. Did you calculate the osmolality
8 of any specific formulation other than one that
9 includes .9 percent sodium chloride?

10 A. No, because the calculations are similar
11 based upon understanding of the science.

12 Q. Okay. Prior to last night, did you have
13 any awareness of whether Avastin's formulation
14 was hypertonic, isotonic, or hypotonic?

15 A. Well, I'd have to -- I'd have look it up.
16 But again, according to Hecht, intravitreal
17 injection of a medication should -- that
18 solution should be isotonic.

19 Q. Okay. But that's according to Hecht,
20 which is not specific to Avastin, correct?

21 A. Again, I could -- I could look up the
22 formulation for Avastin and -- and determine if
23 it was isotonic.

24 Q. Okay. But when you prepared your report
25 in this case, you didn't know whether the

1 formulation for Avastin was isotonic or not?

2 A. I think a person of ordinary skill in the
3 art would believe that -- in medicine that is
4 formulated for injection into a patient's eye
5 would be isotonic. That would be good medicine.

6 Q. Okay. But putting aside whether it's --
7 a POSA would think it's -- or a person of
8 ordinary skill in the art would think it's good
9 medicine, do you know whether Avastin's
10 formulation, without looking it up, is actually
11 isotonic?

12 A. I would have to look it up.

13 Q. Okay. And the same question for
14 Lucentis's formulation. Do you know whether
15 it's isotonic?

16 A. I would have look it up.

17 Q. Putting aside the Eylea, Lucentis, and
18 Avastin intravitreal injections that we've been
19 talking about, are there other formulations that
20 in your practice are administered via
21 intravitreal injection?

22 A. Yes.

23 Q. And what formulations are those, or what
24 drugs are those?

25 A. Kenalog, for example.

1 Q. Okay.

2 A. It's a steroid.

3 Q. Do you know whether it's isotonic?

4 A. I would have to look it up. It is my
5 presumption that it is isotonic, yes.

6 Q. Okay. Could spell that for me, just so
7 the record's clear?

8 A. Yeah. K-E-N-A-L-O-G.

9 Q. Are there any other intravitreal
10 formulations that you administer to your
11 patients?

12 A. There are other types of formulations
13 that in terms of, sort of, biological deposes
14 that are injected into patient's eyes.

15 Q. Okay. What are some of those?

16 A. Iluvien. There are a number of them.
17 There are a number of long-acting drug delivery
18 platforms for steroids.

19 Q. Okay. And I think you said Iluvien.

20 A. Iluvien.

21 Q. Could you spell --

22 A. I-L --

23 Q. -- that for the record?

24 A. I-L-U-V-I-A-N [sic].

25 Q. Okay. And do you know if the formulation

1 of Iluvien is isotonic?

2 A. It's a hydrogel, so I don't if the -- the
3 formulation of that.

4 Q. Okay. So when you say it's a hydrogel,
5 that means it's not actually an aqueous
6 solution?

7 A. Correct.

8 Q. Okay. And it's nonetheless suitable for
9 injection into the eye?

10 A. It is.

11 Q. Okay. Can we turn to paragraph 192 of
12 your report? It's on page 87. And in the first
13 sentence of the paragraph, you're referring to
14 Dickson, and you note that it talks about
15 aflibercept being formulated so that it's
16 suitable for the comfortable nonirritating
17 direct injection into the eye. Do you see that?

18 A. Yes. I believe Dickson did refer to --
19 to formulation, yes.

20 Q. Okay. And is your testimony that from
21 this statement, a person of ordinary skill in
22 the art would understand that the formulation is
23 necessarily isotonic -- that this sentence is
24 referring to?

25 A. Actually, Counsel, can you -- we may not

1 be in the same section.

2 Q. Sure. It's page 87, paragraph 192.

3 MR. SUMMERS: If I could be helpful.

4 THE WITNESS: Oh, I'm sorry. I'm
5 looking at the wrong page.

6 MR. BRAUSA: Oh, yeah, I'm sorry.
7 I'm going to -- yep.

8 THE WITNESS: I'm sorry. I got the
9 exhibit page numbers.

10 BY MR. BRAUSA:

11 Q. And do you see in paragraph 192 where I'm
12 referring?

13 A. I do.

14 Q. Okay. And so -- just so you have it, my
15 question is whether you're relying on Dickson's
16 statement that the formulations suitable for the
17 comfortable nonirritating direct injection into
18 the eye means that the formulation is
19 necessarily isotonic, in your view?

20 A. Yeah, I'm sorry. Can you repeat the
21 question?

22 Q. Sure. Your statement that Dickson refers
23 to a formulation of aflibercept that is suitable
24 for the comfortable nonirritating direction --
25 direct injection into the eye. Do you see that

1 in paragraph 192, correct?

2 A. Yes.

3 Q. Okay. And is it your opinion that that
4 statement means the formulation Dickson is
5 referring to is necessarily isotonic?

6 A. Well, further on in paragraph 193, I go
7 on to say and refer to Hecht that Hecht says
8 isotonicity is always desirable and is
9 particularly important in intraocular solutions.

10 So in my opinion, a person of ordinary
11 skill in the art would have been motivated to
12 make aflibercept, the solution disclosed in the
13 primary reference, as isotonic to avoid
14 irritation and also to avoid toxicity to the
15 eye.

16 Q. Okay. So my question was a little
17 different, which is: Based on just the
18 statement in Dickson referring to a comfortable
19 nonirritating formulation suitable for direct
20 injection into the eye, does that type of
21 formulation have to be isotonic?

22 A. I think Dickson may actually say more
23 about that. Do -- can I refer to that Dickson
24 reference?

25 Q. Sure. Passing the witness Exhibit 1009,

1 which is the Dickson reference.

2 A. Counsel, I think the reference that I --
3 the exhibit that I want to see is the 2010 press
4 release, if I might.

5 Q. Okay. We may get to that in a moment,
6 but in Dickson, does it say anything more about
7 whether the formulation is hypertonic,
8 hypotonic, or isotonic?

9 A. It would desirable for it to be isotonic.

10 Q. Okay. Understood that it would
11 desirable. My question is whether Dickson
12 actually says that.

13 A. Dickson does not appear to address the
14 isotonicity, but also I, in my declaration,
15 indicate that I utilize both Dickson and in view
16 of Hecht.

17 Q. Okay. And in this portion of your
18 declaration, in the heading you refer to this
19 December 2010 press release, but I don't see any
20 citations to it in paragraphs 191 to 194. Do
21 you?

22 A. I did not include it, but there is
23 material in it that's relevant.

24 Q. Okay. And you didn't include that
25 relevant matter in the substance of your

1 opinions in paragraphs 191 through 194?

2 A. Well, I did say in 191 I understand the
3 claims, with respect to recite, that aflibercept
4 is formulated as an isotonic solution with a
5 nonionic surfactant as discussed in the sections
6 and are anticipated by December 2010 press
7 release.

8 Q. You're reading from paragraph 191?

9 A. Uh-huh. I -- I refer to it, but I don't
10 quote it.

11 Q. Okay. And, actually, the reference to
12 December 2010 press release is only with respect
13 to claims 3 and 10 in your opinion that it
14 anticipates those claims, right?

15 A. Yes. They're anticipated in the press
16 release and made obvious by Dickson and Hecht.

17 Q. Okay. So are -- so is the combination
18 you're rely on here Dickson and Hecht or
19 Dickson, Hecht, and the December 2010 press
20 release?

21 A. The -- if you could show me the press
22 release, I can -- I can tell my -- my thoughts
23 on it. My -- the press release, as I recall,
24 confirms this is concept of isotonicity.

25 Q. Okay. And so my question, though, is

1 just in your report there's no citation to any
2 specific portion of the December 2010 press
3 release that, in your words, confirms
4 isotonicity, right?

5 A. No, not in this report. No.

6 Q. Okay. And is there a reason you didn't
7 include that in your report?

8 A. Don't recall.

9 Q. Okay. Do you recall when you became
10 aware or formed the opinion that the
11 December 2010 press release relates to
12 isotonicity?

13 A. It's, again, and in my review of the --
14 the materials provided to me.

15 Q. Okay. Was that review before or after
16 you submitted your report?

17 A. Before.

18 Q. Okay. Do you know what other
19 considerations of formulation scientists would
20 balance when they're looking at whether to make
21 a formulation isotonic, hypertonic, or
22 hypotonic?

23 A. That's a complex question. You're going
24 to have to break that down. The answer to that
25 question is, perhaps, this large.

1 Q. Okay. Have you ever evaluated the
2 stability of any formulations?
3 A. Not personally, no.
4 Q. Okay. And do you know anything about the
5 stability of anti-VEGF formulations?
6 A. Not specifically. I understand the
7 concept of stability of formulations.
8 Q. Okay. Do you know whether Hecht contains
9 any statements that you can move away from
10 isotonicity if you need to balance it with
11 stability?
12 A. I believe it does.
13 Q. Okay. And what does it say about that?
14 A. Let's look at it.
15 Q. I'm going to direct you to page 13 in
16 right-hand column. You quoted in your report at
17 the top of the page -- this is page 13 of
18 Exhibit 1016, 1571 in the publication page
19 numbers. This is a portion where it says that
20 or where the quote you provided saying
21 isotonicity is always -- or is -- excuse me.
22 This is the portion of the reference you
23 quote saying isotonicity always is desirable,
24 right?
25 A. Yes.

1 Q. That's not actually the complete
2 sentence, is it?
3 A. And desirable and particularly is
4 important in intraocular solutions.
5 Q. What's first part of the sentence say?
6 A. That is the sentence, Counsel.
7 Q. Am I correct the sentence actually reads:
8 Given a choice, isotonicity always is desirable
9 and particularly is important in intraocular
10 solutions?
11 A. Yes.
12 Q. Okay. And then can you read for me the
13 sentence that follows that is not in your expert
14 report?
15 A. It need not, however, be an overriding
16 concern when total product stability is to be
17 considered.
18 Q. Okay. Is there a reason you didn't
19 include that sentence in your report?
20 A. Well, not that I'm aware of.
21 Q. Okay. Do you know anything about the
22 stability of aflibercept formulations?
23 A. Not specifically, no.
24 Q. Do you know anything about the stability
25 of the aflib- -- of Avastin formulations?

1 A. Not specifically, no.

2 Q. Okay. Can I direct you to page 11 of
3 Exhibit 1016, and in the upper left-hand column,
4 there's a sentence that says "The finished
5 solutions." Do you see that sentence?

6 A. Yes.

7 Q. And can you read that sentence for me?

8 A. I'm just looking at the entire section,
9 Counsel, so.

10 Q. Sure.

11 A. Sterile isotonic solutions properly
12 preserved are suitable for preparing ophthalmic
13 solutions. In most cases where the
14 concentration of active ingredients is low, less
15 than 2-1/2 to 3 percent, the drug can be
16 dissolved directly in the isotonic vehicle. The
17 finished solutions will be hypertonic somewhat,
18 but well within the comfort tolerances of the
19 eye.

20 Q. And so -- oh, go ahead.

21 A. So -- so this formulation here, as I
22 understand it, relates to topical medications.

23 Q. Okay. And so the statement in your view
24 or the statement, "The finished solutions will
25 be hypertonic somewhat" doesn't apply to

1 intravitreal injections?

2 A. It may or may not. I'd -- I'd have look
3 it up, but this particular statement in this
4 particular section refers to topical drops.

5 Q. Okay. Why don't we go back to page 13,
6 and just above the section we were talking to --
7 we're talking about in Exhibit 1016, the first
8 sentence at the top of the right-hand column
9 says "In actuality."

10 A. Yes.

11 Q. And it says: In actuality, the eye is
12 much more tolerant of tonicity variations than
13 at one time was suggest -- that at one time was
14 suggested, right?

15 A. Yes.

16 Q. What do you understand that statement to
17 mean?

18 A. Well, exactly what it says. That it is
19 possible to use somewhat non isotonic solutions
20 for the treatment of the eye because the eye has
21 some buffering capacity and can tolerate
22 variances from isotonicity.

23 But this is -- again, this is a general
24 statement regarding treatment of -- about eye
25 medications. This is not specifically about

1 intraocular medications, but the -- the point is
2 correct. There -- there is buffering capacity
3 in the tears. There's buffering capacity in the
4 vitreous, which is -- is a buffering chamber in
5 the eye and -- and has the ability to modify the
6 tonicity and the pH of medications that are
7 injected. But it is always desirable for those
8 to be as close to isotonic as possible.

9 Q. Okay. That sentence I just read, that's
10 in the same paragraph as the sentence that you
11 relied upon and quoted in your report as being
12 relevant to your opinions, right?

13 A. Again, my report indicates my opinion
14 that, given the choice, isotonicity is always
15 desirable.

16 Q. And just to confirm: We established that
17 it doesn't need to be an overriding concern when
18 total product stability is to be considered,
19 right?

20 A. Well, I'm not sure whether or not Hecht
21 refers to that with respect to eye drops or
22 intraocular solutions.

23 Q. So your statement is that the sentence
24 that follows the one you quoted and relied upon
25 in your report is referring to a different form

1 than the immediately prior sentence?

2 A. Well, again, I'm not quite sure how he is
3 referring here. He's talking about in the
4 sentence above that the eye can tolerate
5 solutions equivalent to a range of half percent
6 to 1.8 percent, which is quite a broad range,
7 and I don't think a range that would necessarily
8 be tolerated by an intraoc- -- intravitreal
9 injection into intraocular preparation. So I'm
10 not sure if he's -- if this concept is regarding
11 all formulations, topical, intravitreal, or
12 other.

13 Q. And so you wouldn't be sure whether the
14 "isotonicity always is desirable" statement
15 applies to all those formulations or specific
16 formulations either, right?

17 A. Well, no. He says specifically, given a
18 choice, isotonicity is always desirable and
19 particularly is important in intraocular
20 solutions.

21 Q. Okay.

22 A. So I would disagree with that statement.

23 Q. Okay. He doesn't say it's always
24 desirable in intraocular solutions, does he? Or
25 is that how you read that sentence?

1 A. Is always -- it always -- again, always
2 desirable for comfort to the eye, but it's
3 particularly desirable and important for
4 intraocular solutions.

5 Q. Okay. Do you know whether hypertonic
6 solutions for intravitreal injection can be
7 comfortably injected?

8 MR. SUMMERS: Objection. Form.

9 THE WITNESS: Again, it depends on
10 what your definition of hypertonicity is. So if
11 isotonicity is 308 milliosmoles, hypoton - --
12 isotonicity for blood, for example, is presumed
13 to be 308 milliosmoles. A solution that's 310
14 milliosmoles is a hypertonic solution. It's not
15 isotonic; it's hypertonic. Would that solution
16 be tolerated by the eye? Certainly. We'd
17 predict that it would.

18 So the -- the relative level of
19 hypertonicity or hypotonicity is -- is important
20 relative to answering your question.

21 BY MR. BRAUSA:

22 Q. Okay. Are there any thresholds above or
23 below that isotonic value you identified that
24 would, in your view, create discomfort for the
25 patient?

1 A. I would have to look it up.

2 Q. Okay. And -- and just so I'm aware, when
3 we're talking about comfort, the patient is
4 receiving an injection in their eye, correct?

5 A. Yes.

6 Q. And so there's a certain amount of
7 discomfort associated with this process,
8 regardless of the tonicity of the formulation
9 being administered, I take it?

10 A. I would agree with that statement, yes.

11 MR. BRAUSA: Okay. I'm going to
12 switch gears. Do you want to take a quick break
13 or keep going?

14 THE WITNESS: Why don't we give you
15 a break.

16 MR. SUMMERS: Yeah, that would be
17 appreciated.

18 THE VIDEOGRAPHER: Standby. The
19 time is 10:. We're off the record.

20 (Off-the-record discussion was held.)

21 THE VIDEOGRAPHER: The time is
22 . We're back on the record.

10:40

23 BY MR. BRAUSA:

24 Q. Welcome back, Dr. Chaum. During the
25 break did you talk with counsel at all?

1 A. We talked, but about nothing substantial.

2 Q. Okay. Let me direct you back to 1002, or
3 Exhibit 1002, your report, and let me direct you
4 to paragraph 169. It's at page 77 in the lower
5 right-hand corner designation.

6 A. Yes.

7 Q. The first sentence in paragraph 116
8 refers to a secondary endpoint of the VIEW 1
9 study. Do you see that?

10 A. Yes.

11 Q. What's a secondary endpoint of the VIEW 1
12 study?

13 A. Well, clinical trials are designed to
14 yield meaningful data with respect to the
15 potential efficacy of a drug or an intervention.
16 And the studies are typically designed to have
17 what's called a primary endpoint -- there may be
18 more than one -- and secondary endpoints.

19 The primary endpoint is important because
20 whether the trial -- for example, a drug gets
21 approved may -- is typically contingent upon a
22 primary -- the primary endpoint of the study.
23 So the study has to be designed to yield a
24 result or an expected result that demonstrates
25 some kind of a clinical benefit.

1 So typically and for studies related to
2 ophthalmic drugs, the primary endpoint is most
3 often visual acuity. So does the drug preserve
4 visual acuity, prevent vision loss? And for
5 these types of studies, those are typically the
6 primary endpoints.

7 But there's other clinical data that's
8 generated from the studies that can be useful in
9 determining whether or not the drug was
10 effective or not, and -- and those other
11 endpoints, if you will, are typically called
12 secondary endpoints.

13 So it's potentially meaningful data that
14 don't determine whether or not whether the study
15 was a successful study, but rather generate our
16 data that can be -- can -- can confirm or add
17 robustness to the results of the study based
18 upon what the outcomes are.

19 Q. Okay. And so it's fair that when we're
20 talking about the endpoints of -- in a clinical
21 study, you get a primary or a secondary
22 endpoint, those are essentially the goals that
23 the clinical investigators are hoping to achieve
24 in the study, right?

25 MR. SUMMERS: Objection. Form.

1 THE WITNESS: Yeah, I wouldn't call
2 them goals. They are objective metrics that are
3 established in advance of the study to determine
4 whether or not the study is successful.

5 BY MR. BRAUSA:

6 Q. Okay. Help me understand. Why -- why
7 wouldn't you call that a goal?

8 A. It's an outcome. So if you -- if you
9 equate potential outcome with a goal, then I
10 guess you could call it that.

11 Q. Okay. And you'd agree with me, the
12 endpoints are potential outcomes, right?

13 MR. SUMMERS: Objection. Form.

14 THE WITNESS: So the endpoints are
15 outcomes that are based upon the clinical
16 studies, objectives. And so for example, if the
17 primary endpoint is to for example, if the
18 primary endpoint is to, for example, demonstrate
19 a visual acuity preservation for a patient, then
20 the expectation for that study is that some or
21 all of the patients are going to meet that
22 primary endpoint because, if they don't, then
23 the study -- the drug won't pass and it won't
24 be -- won't be approved by the -- potentially
25 approved by the FDA.

1 So the endpoints are objectives that
2 are set in advance, but they are not
3 pie-in-the-sky objectives. They are objectives
4 that the clinical study coordinators and
5 participants who are running the study and --
6 and the companies that are participating in the
7 study, they are objectives that are expected to
8 be met so that the -- the goal -- so that drug
9 achieves its -- so that the trial in essence
10 is -- is -- is determined a success.

11 So when you talked about secondary
12 endpoints, you can have some endpoints -- those
13 endpoints that may not be goals. They may be --
14 they may be metrics to determine, you know,
15 other data related to the -- to the success of
16 the trial.

17 BY MR. BRAUSA:

18 Q. You weren't involved in setting any of
19 the primary or secondary endpoints in any of the
20 clinical trials for a aflibercept, were you?

21 A. No.

22 Q. Okay. And I think when we spoke in
23 January, you testified that you've never been
24 involved in clinical trial design?

25 A. Not in trial design. I've designed my

1 own institutional review board clinical studies,
2 so I'm familiar with it and have done so over
3 the course of my career on a couple of different
4 occasions. But I have not been involved in the
5 design of national clinical trials.

6 Q. Okay. And have you ever decided on what
7 the primary or secondary endpoints should be for
8 any clinical trial with an anti-VEGF antagonist?

9 A. No.

10 Q. Okay. And do you know how anyone at
11 Regeneron or working with Regeneron set the
12 primary or secondary endpoints for any of the
13 clinical trials involving aflibercept?

14 A. I do not.

15 Q. And it's correct that, notwithstanding
16 the a phase 3 clinical trial is initiated, not
17 all drugs with -- let me withdraw that.

18 Not every drug that goes into a phase 3
19 clinical trial meets the endpoint, correct?

20 A. Your question is confusing to me. The
21 term the endpoint doesn't make sense to me in
22 context of your question, so could you rephrase
23 the question?

24 Q. Sure. For a given clinical trial with
25 primary and secondary endpoints, not every drug

1 will meet any of those endpoints, will it?

2 A. It depends on what the endpoints are and
3 the results of the clinical trial.

4 Q. Right. Some clinical trials are
5 failures, right?

6 A. Some clinical trials do -- do not meet
7 the endpoints that are established sufficiently
8 to warrant further provable by the FDA, for
9 example.

10 Q. Okay. And when we spoke in January, I
11 think you testified that you weren't sure how
12 many drugs that enter phase 3 clinical trials
13 are approved versus those who are not pursued --
14 those that are not pursued further?

15 A. I don't know.

16 Q. In paragraph 168, just above the one we
17 were referring to in Exhibit 1002, there's a
18 sentence -- I think it's the last full sentence
19 in the paragraph that says: The described gain
20 is, quote, "within 52 weeks." Do you see that?

21 A. I see that.

22 Q. Why is that "within" in quotation marks?

23 A. So this relates to one the claims in the
24 572 patent.

25 Q. Okay. How so?

1 A. Can you provide me with a copy of the
2 claims?

3 (Exhibit Number 1002 was marked.)
4

5 BY MR. BRAUSA:

6 Q. Sure. I'm passing the witness
7 Exhibit 1001, which is a copy of US patent
8 11253572.

9 A. So the term within 52 weeks is in
10 quotations because I am providing an opinion
11 regarding claim 1 where claim 1 describes a
12 method for treating an angiogenic eye disorder
13 in a patient in need of treatment thereof.

14 It goes on to describe the method or
15 the -- the dosing regimen for that treatment at
16 2 milligrams of aflibercept followed by one or
17 more secondary doses of 2 milligrams aflibercept
18 followed by one or more tertiary doses where the
19 secondary dose is administered approximately
20 four weeks following the immediately proceeding
21 dose, and wherein each tertiary dose is
22 administered approximately eight weeks following
23 the immediate proceeding dose, wherein the
24 patient achieves a gain in visual acuity within
25 52 weeks following the initial dose.

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1 Q. Okay. And so what's your understanding
2 of what that phrase within 52 weeks means?

3 A. My understanding of that phrase and my
4 interpretation of that phrase, in my opinion, is
5 that if that gain in vision and visual acuity
6 occurs at any time during the first 52 weeks or
7 prior to 52 weeks that would satisfy the
8 definition of within 52 weeks.

9 Q. Okay. And so if the patient -- you
10 observed a patient that had a visual acuity gain
11 at two weeks, but it went away at three weeks,
12 that would nonetheless satisfy this portion of
13 the claim, in your view?

14 A. Based upon the construction of the claim,
15 yes, that's my impression, my interpretation,
16 yeah.

17 Q. When you say based upon the construction
18 of the claim, what do you mean?

19 A. Well, that's the way the claim is
20 written.

21 Q. Okay.

22 A. So I'm using the language of the claim.

23 Q. Okay.

24 A. And the claim says: Wherein the patient
25 achieves a gain in visual acuity within 52 weeks

1 following the initial dose. It doesn't say
2 anything about subsequent vision follow-up or
3 anything. It says a gain in visual acuity is
4 obtain within 52 weeks, that would satisfy that
5 claim.

6 Q. Okay. If I could direct you to claim
7 in column 24 of the 572 patent. At the end of
8 that claim, it also refers to 52 weeks, but it
9 refers to achieving a gain in visual acuity, and
10 then there's a comparison, and then it's "at" 52
11 weeks instead of "within" 52 weeks. Do you see
12 that?

13 A. I do.

14 Q. Is there any difference, in your view,
15 between a visual acuity gain observed within 52
16 weeks and a visual acuity gain observed at
17 52 weeks?

18 A. Yes.

19 MR. SUMMERS: Objection. Form.

20 BY MR. BRAUSA:

21 Q. What's the difference?

22 A. Well, as I, said, visual acuity gain
23 within 52 weeks demonstrates that that -- that
24 acuity gain occurred within that period of time
25 of 52 weeks after the treatment was initiated.

1 In the case of claim at 52 weeks, the
2 definition of that is that the gain exists at
3 52 weeks, so af- -- at -- at that point in time,
4 a gain, at least in a patient, is demonstrated.

5 Q. Okay. So for example, if a patient was
6 observed at up to week 40, but then it went away
7 by week 48 and was not present at week 52,
8 that's an example of a visual acuity gain within
9 52 weeks but not at 52 weeks; is that fair?

10 MR. SUMMERS: Objection. Form.

11 THE WITNESS: That would meet that
12 definition in my view, yes.

13 BY MR. BRAUSA:

14 Q. Okay. We were talking about the
15 comparison language in claim , and you also
16 reference that language in paragraph 177 of your
17 report and page 80, using the lower right-hand
18 corner, Exhibit 1002.

19 A. Yes, I'm here.

20 Q. And in this paragraph, you say you've
21 been asked by counsel to assume that to be as
22 effective as monthly ranibizumab, a patient must
23 achieve a mean gain of visual acuity between 8.1
24 to 9.4 letters, correct?

25 A. Yes.

1 Q. And then the basis for these numbers is
2 table 1 of the 572 patent.

3 A. Yes.

4 Q. Do you know whether this range is of
5 monthly ranibizumab visual acuity gains in terms
6 of the mean is reported in any of the prior art
7 you relied on?

8 A. I believe it might be.

9 Q. Okay. But in this paragraph of your
10 report, you relied on data in the patent as the
11 point of comparison, right?

12 A. Yes.

13 Q. Okay. On the next page, in paragraph
14 108 -- or I'm sorry. On the next page,
15 paragraph 180, page 81, there's a diagram at the
16 bottom of the page with some figures in it
17 referring to initial dose, secondary doses,
18 tertiary doses. Do you see that?

19 A. Yes.

20 Q. Can you explain to me what this diagram
21 is showing?

22 A. Let me just take a moment to review this.

23 Q. Sure.

24 A. So this graph gets to the issue of
25 expectation of results. So as disclosed in

1 Dickson, we see the -- the phase 3 and the
2 dosing regimen in the blue arrows above. So
3 there are three initial monthly dosing
4 injections given, followed by injections every
5 two months thereafter.

6 So that dosing regimen disclosed by
7 Dickson shows that, through or up to 52 weeks, a
8 patient would receive eight injections for the
9 treatment of their macular degeneration.

10 The lower graph in green shows the
11 results of the phase 2 PRN dosing regimen
12 described in Dickson. And in this regimen, the
13 patients received four injections and then were
14 treated on an as-needed basis after those four
15 injections through 52 weeks. And we know
16 from -- from Dickson that only an additional 1.6
17 doses on average were given to patients treated
18 in that regimen.

19 So the number of injections given to
20 patients in the phase 2 PRN regimen was
21 approximately 5.6; whereas, the number of
22 injections given to or proposed for the phase 3
23 regimen under a claim to 28 was 8.

24 So what this graph is demonstrating is
25 that there will be more injections given to

1 patients who undergo the phase 3 AMD trial
2 regimen than were given to patients who received
3 the dose -- the medicine under the phase 2 PRN.

4 So then the question gets to looking at
5 expectations. All right. If we look at
6 the data -- we don't know what the data is for
7 the phase 3 trial yet, but we do know the
8 results of the phase 2 trial in which the
9 patients are getting less medicine for the
10 condition.

11 And what we know is and what I say in my
12 report here is that under the PR dosing regimen,
13 the patients who achieved a mean of 9-letter
14 gains -- actually, of -- of the patients who
15 were treated, a 29 percent gained greater than
16 15 letters at 52 weeks, right? Even -- only
17 requiring 1.6 additional doses, so 5.6 doses.

18 So based upon that, what I say in my
19 opinion is that the regimen recited in claims
20 to 28 would have resulted in 8 overall doses
21 during the year, at least two more than was
22 demonstrated in the PRN dosing schedule, right?

23 But we know that the patients in the PRN
24 dosing schedule had an increase in 15 letters --
25 an improvement of 15 letters in almost 1 in 5

1 patients through or by 52 weeks.

2 And so, in my opinion, given that
3 29 percent of patients following the PRN regimen
4 had greater than 15-letter gain by 52 weeks, a
5 person of ordinary skill in the art would have a
6 reasonable expectation that at least similar
7 gains and substantially higher gains than the
8 8.1- to 9.4-letter gain achieved by ranibizumab
9 would be achieved in that study.

10 BY MR. BRAUSA:

11 Q. Okay. Thank you for that.

12 If we could turn back to the diagram on
13 page 81 under paragraph 180, the blue is
14 something that you added, and that's the dosing
15 regimen for the phase 3 AMD trial disclosed in
16 Dickson for which you agree there's no results
17 data provided, right?

18 A. Not at that time, no.

19 Q. Okay. And then the bottom arrows in
20 green are the phase 2 PRN dosing regimen
21 described in Dickson as well for which there is
22 some data described in Dickson that you just
23 provided in your answer, correct?

24 A. Yes.

25 Q. Okay. One difference between these

1 dosing regimens, aside from the amount of doses
2 that potentially were received, is that in the
3 phase 2 PRN regimen described in Dickson, a
4 fourth loading dose was provided, right?

5 A. Yes.

6 Q. Does Dickson provide any information on
7 what impact the fourth loading dose used in
8 phase 2 PRN dosing regimen was expected to have
9 on visual acuity?

10 A. I'll have to take a look at Dickson. I
11 don't recall if that's addressed.

12 Q. Sure. That's Exhibit 1009.

13 A. Yeah. I have it.

14 It does not address that specifically,
15 no.

16 Q. Okay. And in addition to the fact that
17 Dickson doesn't provide any information on what
18 the expected impact of that fourth loading dose
19 would be on visual acuity, it doesn't actually
20 provide any detail on when the average of 1.6
21 additional doses administered during that PRN
22 period were actually provided, right?

23 A. It does not.

24 Q. Okay. And so they could have been early
25 in that period, or they could have been late in

1 that period, right?

2 MR. SUMMERS: Objection. Form.

3 THE WITNESS: I don't know.

4 BY MR. BRAUSA:

5 Q. Okay. But the PRN period started in the
6 phase 2 PRN dosing regimen at week 12 and went
7 to week 52; is that fair?

8 A. Sorry. After week 12 and went to week
9 52, yes.

10 Q. Okay. So we're talking about a 40-week
11 period of time where the clinicians are
12 determining whether to administer a dose on an
13 as-needed basis, right?

14 A. Yes.

15 Q. Okay. And just to confirm: There's no
16 information provided on when in that 40-week
17 period any doses were administered?

18 MR. SUMMERS: Objection. Form.

19 THE WITNESS: Not in Dickson, no.

20 BY MR. BRAUSA:

21 Q. Okay. And does Dickson provide any
22 information beyond percentages about how many
23 individual patients were actually in that dosing
24 arm?

25 A. I'm not following your question, Counsel.

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1 Q. Okay. You talked about 29 percent of
2 patients experiencing a certain gain, correct?

3 A. Yes.

4 Q. Okay. 29 percent is of how many
5 patients? Do you know?

6 A. I would have to look up the cohort
7 number.

8 Q. Okay. And that's my question. Does
9 Dickson provide the cohort number?

10 A. I believe this refers to a clinical study
11 called the Clear It 2 -- I believe this refers
12 to a clinical study called the Clear It 2 in
13 which there were 157 patients.

14 Q. Okay. And to be clear: You're referring
15 to page 4 in the lower right-hand corner of
16 Exhibit 1009, and that's 157 patients in the
17 entire trial randomized to a five dose groups,
18 right?

19 A. Yes.

20 Q. Okay. Does can Dickson disclose how many
21 of those 157 patients were included in the
22 cohort that received PRN regimen after four
23 loading doses?

24 A. It does not.

25 Q. Okay. And so it's not possible, based on

1 Dickson, to know how many people actually
2 received that dosing regimen in the phase 2
3 study, correct?

4 MR. SUMMERS: Objection. Form.

5 THE WITNESS: If you could clarify
6 your question.

7 BY MR. BRAUSA:

8 Q. Sure. And so when you say 29 percent of
9 patients in that four loading dose, PRN dosing
10 regimen, achieved a certain visual acuity gain,
11 we don't know what that 20 percent refers to in
12 terms of the number of actual patients.

13 MR. SUMMERS: Objection. Form.

14 THE WITNESS: Well, the calculation
15 of 29 percent is based upon numbers that were
16 reviewed by Dickson, but Dickson does not
17 disclose that specific number --

18 BY MR. BRAUSA:

19 Q. Okay.

20 A. -- in the reference.

21 Q. Okay. And then 71 percent of that same
22 cohort receiving the four loading doses and
23 followed by PRN over 40 weeks did not achieve
24 the visual acuity gains that are reported in
25 Dickson, correct?

1 MR. SUMMERS: Objection. Form.

2 THE WITNESS: Yeah, I'm sorry. I'm
3 not -- you're not being clear.

4 BY MR. BRAUSA:

5 Q. Okay. So I think you testified that
6 29 percent of patients in the four loading dose
7 PRN cohort achieved certain visual acuity gains,
8 right?

9 A. Correct.

10 Q. If my math is correct, that means there
11 were 71 percent of patients that did not.

12 A. Who achieve less than 15 letters.

13 Q. Okay. And does Dickson disclose whether
14 they -- what their achievements are, whether
15 they got worse, or maintained it?

16 A. Dickson does not, no.

17 Q. Okay. And so for 71 percent of the
18 patients in this dosing arm of four loading
19 doses followed by PRN over 40 weeks, Dickson
20 doesn't tell you what happened to them, correct?

21 A. No.

22 Q. Okay. Does Dickson identify any
23 correlation between the number of injections a
24 patient received? Again, focusing on the four
25 loading dose PRN regimen we've been discussing

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1 and any visual acuity gains.

2 MR. SUMMERS: Objection. Form.

3 THE WITNESS: Yeah, you're going to
4 have clarify that question for my counsel.

5 BY MR. BRAUSA:

6 Q. Sure. Does Dickson describe the number
7 of injections necessary to achieve certain
8 visual acuity gains beyond the average data
9 we've been discussing?

10 A. Dickson does not.

11 Q. And just to be clear: Dickson does not
12 tell you the average number of injections
13 received by the 29 percent of patients who
14 achieved the visual acuity gain that you
15 referenced previously, correct?

16 MR. SUMMERS: Objection. Form.

17 THE WITNESS: Dickson does not.

18 BY MR. BRAUSA:

19 Q. Okay. And so we don't know if those
20 patients who achieved the visual acuity gain of
21 29 percent that you referred to -- or withdraw
22 that.

23 We don't know if the 29 percent of
24 patients that achieved the visual acuity gains
25 you referred to received more than 1.6 doses or

1 less than 1.6 doses during the PRN period,
2 correct?

3 MR. SUMMERS: Objection. Form.

4 THE WITNESS: That's not in Dickson,
5 no.

6 BY MR. BRAUSA:

7 Q. Okay. Is it in any other references that
8 you've cited?

9 A. I would have to look it up. I don't know
10 if it's in the ref -- if it's in the literature.

11 Q. Okay. And Dickson also doesn't say, for
12 those 29 percent of patients who achieved the
13 visual acuity gain you referenced, when any of
14 the doses they received, for which we don't know
15 the amount, when those were administered during
16 that 40-week PRN period, correct?

17 MR. SUMMERS: Objection. Form.

18 THE WITNESS: Yeah, I'm sorry. Can
19 you restructure that question for me, please?

20 BY MR. BRAUSA:

21 Q. Sure. So I think we established that for
22 29 percent of patients that achieved a visual
23 acuity gain that you referenced, Dickson doesn't
24 say how many doses that they received during the
25 PRN period, does it?

1 A. So for that cohort of patients, the
2 specific numbers of doses provided to each
3 patient in that cohort is not provided in
4 Dickson.

5 Q. Okay. And the specific intervals of
6 dosing for any of those individuals in that
7 cohort are not provided in Dickson either,
8 correct?

9 MR. SUMMERS: Objection. Form.

10 THE WITNESS: Interval for specific
11 patients is not provided in Dickson.

12 BY MR. BRAUSA:

13 Q. Okay. Well, in -- the interval for
14 anyone in that cohort is not provided for the
15 PRN period, is it?

16 A. If you could just rephrase the question
17 for me.

18 Q. Sure. The interval for the doses that
19 were provided during the 40-week PRN period
20 described in Dickson is not provided, right? So
21 it's just described as PRN.

22 A. It's described as PRN in Dickson, yes.

23 Q. Okay. It doesn't say when any patient in
24 that cohort received any dose?

25 A. It does not.

1 Q. And so if that's true, then I think I'm
2 correct that Dickson doesn't disclose at what
3 point in time any patient in that cohort
4 received their last injection before the 52-week
5 point, right?

6 MR. SUMMERS: Objection. Form.

7 THE WITNESS: Again, kind of,
8 restructure the question for me.

9 BY MR. BRAUSA:

10 Q. Sure. Dickson doesn't tell you when any
11 patient received their last injection before the
12 evaluation at 52 weeks, does it?

13 A. It does not.

14 Q. Okay. And so there's no way to determine
15 how close in time to that 52-week point in time
16 any patient received an injection of a
17 aflibercept?

18 MR. SUMMERS: Objection. Form.

19 THE WITNESS: Well, what -- Counsel,
20 what we -- what we know from Dickson is for that
21 cohort, for the patients who received
22 medications, there was an additional 1.6 doses
23 over a period of 40 weeks.

24 BY MR. BRAUSA:

25 Q. Uh-huh.

1 A. And so if you ask do we know specifically
2 when the dose was given for a specific patient,
3 Dickson doesn't disclose -- disclose that.

4 Q. Would you expect that the timing of the
5 doses that an individual patient received during
6 that 40-week PRN period could affect their
7 visual acuity results at week 52?

8 MR. SUMMERS: Objection. Form.

9 THE WITNESS: Let me just review
10 this for a moment. I want to answer your
11 question thoroughly.

12 BY MR. BRAUSA:

13 Q. And just for the record, you're reviewing
14 Dickson Exhibit --

15 A. Yes.

16 Q. -- 1009.

17 A. Yes. So, Counsel, to answer your
18 question, there is some data in Dickson that
19 tells us in general when additional PRN doses
20 were given to the patient cohort, and I would
21 direct you to the last paragraph on page 1576.

22 What it says is during the PRN dosing
23 period, patients initially dosed on a
24 2-milligram monthly schedule received an average
25 of 1.6 more injections, and those initially

1 dosed on a .5-milligram monthly schedule
2 received an average of 2.5 injections.

3 But importantly, is the next sentence.
4 The median time to the first reinjection in all
5 groups was 110 days. So what that means is
6 we're talking about injections after week 12.
7 So the median time to the first injection for
8 all of the patients after the 12th week was
9 110 days. And that means that the -- again, the
10 mean, the bulk, of those patients received their
11 injection within three months of the 12-week
12 injection point.

13 Now, obviously there's a distribution, a
14 distribution curve, the median is the highest
15 number. So the largest number of patients
16 received that injection at that 110 days.

17 So if -- if your point -- if the question
18 that you're getting at, is it possible that the
19 visual acuity gain was due to an injection just
20 before the end of the 52-week period of time,
21 Dickson discloses that it's not. That -- that
22 the mean number -- mean number of days -- that
23 the mean distribution of -- of second injections
24 after the 12-week time was within three months.

25 Q. So just to be clear: It discloses that

1 the median time to the first reinjection was 110
2 days, right?

3 A. Correct.

4 Q. Okay. And that's for all 157 patients,
5 not just for the cohort of four loading doses
6 followed by PRN, right?

7 A. I think this -- this was for the
8 2-milligram and 5-milligram PRN.

9 Q. Right. And just so -- oh, I see. So
10 with respect to that, it's anyone receiving PRN,
11 correct?

12 A. The -- the patients who are in the PRN
13 time point, yes.

14 Q. Okay. And so that includes a
15 .5-milligram cohort as well as the 2.0-milligram
16 cohort that you focused your opinion on, right?

17 A. Correct. And -- and Dickson says that
18 the patients in the .5-milligram cohort actually
19 received a little more average number of
20 injections at 2.5 during that period of time.

21 Q. And do you have any theories as to why
22 that was the case that they received more
23 injections in the .5-milligram cohort?

24 A. Well, I can speculate. I -- I did not
25 participate in the study, but we know that lower

1 doses, while showing almost equivalent efficacy,
2 do not show quite the same equivalent efficacy,
3 and we've seen that the ranibizumab and
4 Anchor/Marina studies, and I think it's -- we
5 can -- we can speculate that that lower dose
6 provides a little bit less benefit than the
7 2-milligram dose.

8 Q. Okay. If -- if we talk about a single
9 injection of aflibercept, would you expect a
10 2-milligram dose to be less effective than a
11 4-milligram dose?

12 A. Not necessarily.

13 Q. Why not?

14 A. It gets to the issue of the
15 pharmacokinetics and pharmacodynamics of the
16 drugs. So I think it's an important question,
17 and I'd like to take a minute maybe to -- to
18 clarify my thoughts on that and -- and discuss
19 why that's the case.

20 As a person of ordinary skill in the art
21 and being a physician, that physician would have
22 gone to a medical school, taken a course in
23 pharmacology. The pharmacology of drugs and
24 their biologic activity in the body is based
25 upon two basic concepts.

1 The first concept is pharmacokinetics.
2 How is the drug absorbed, modified, and excreted
3 by the body. And the second concept is
4 pharmacodynamics. What is the biological effect
5 of that drug on the body? What's it's -- what's
6 the body's response to that medication?

7 So an easy way to think about that is if
8 you have a headache and you take Tylenol,
9 Tylenol blocks the pain receptors. And so if
10 you have a headache, you take Tylenol, and
11 Tylenol is absorbed by the body and then
12 modified and excreted over a period of about
13 four hours. So at the end of four hours, if you
14 still have a headache, the headache pain comes
15 back because the medicine is gone.

16 If you had a severe headache, you would
17 predict that if you took one Tylenol pill
18 instead of two Tylenol pills that it might not
19 impact -- it might not treat your headache
20 effectively. And that may be the case for
21 Tylenol, but it's not the case for anti-VEGF
22 drugs in the eye.

23 So what you have to understand is that
24 these drugs that are injected into the eye have
25 a completely different pharmacokinetic and

1 pharmacodynamic profile. If you look at the
2 pharmacokinetics of anti-VEGF drugs -- and I
3 believe Dickson address -- talks about this as
4 well -- if you look at pharmacokinetics of an
5 anti-VEGF drug in how you inject that medicine
6 into the vitreous, the half life of that
7 medicine, of anti-VEGF agents, is about three
8 days.

9 So what that means is that three days
10 after that medicine is injected, half of it's
11 gone. Three days after that, half of it's gone,
12 and so forth. But we know that the biologic
13 effect of those anti-VEGF agents is sustained.
14 We see therapeutic efficacy for a month, for as
15 long as a month, after that injection. And
16 that's because the impact, the effect, of the
17 medication is different than just blocking
18 receptors like Tylenol does.

19 The blockage of VEGF molecules by the
20 anti-VEGF agents changes the growth factor
21 profile in the eye and has profound impact on
22 the cellular responses to those growth factors.
23 In the absence of those growth factors, a number
24 of different things happen.

25 The "proliferity" of cells stop

1 proliferated; the valves -- the vessels become
2 less leaky; there are transcription pathways
3 that are activated in response to that and in
4 the absence of that. And so the biological
5 response is sustained and is very different than
6 for -- for taking Tylenol.

7 So to get back to your question, the --
8 you asked would you expect a different response
9 if you used a 4-milligram injection of
10 aflibercept versus a 2-milligram injection of
11 aflibercept. What I would tell you is that
12 4-milligram injection of aflibercept is 2
13 milligrams in the eye three days later. And
14 it's 1 milligram in the eye three days later.
15 And it's a half a milligram in the eye three
16 days later.

17 And so -- but the biological effect is
18 sustained over a period of a month, and we know
19 that because the half milligram dose responds --
20 provides a therapeutic benefit, and it's one
21 quarter of the 2-milligram response. There is
22 defined and -- and well-characterized biological
23 response to that -- to those medications even at
24 the lower dose.

25 And so would a person of ordinary skill

1 in the art think that there would be a different
2 response to a 2 -- 4-milligram injection versus
3 a 2-milligram injection over a period of a month
4 after that injection? No, because three days
5 later, it's 2 milligrams in the eye. And yet
6 the biological -- the pharmacodynamic effect
7 lasts for 30 days after that.

8 Q. Why do you think Regeneron tested
9 different amounts of aflibercept that a person
10 of ordinary skill in the art would understand
11 all that?

12 A. Because there's going to be some optimal
13 concentration of the drug that's going to
14 provide efficacy, durability, and also have to
15 consider the ability to make the drug and
16 provide it in a formulation that can be put into
17 the eye.

18 And so the initial studies that were done
19 looking at the efficacy of aflibercept -- and --
20 and -- and this is true for Lucentis as well,
21 initial studies looked at dose escalation
22 studies. What -- what level of drug, what
23 amount of drug create -- demonstrated a
24 therapeutic benefit? And those -- those studies
25 are -- are in the -- were reported.

1 And so understanding where that
2 therapeutic range exists then provides a company
3 with an option to try and optimize it. And I
4 believe that these studies were designed for
5 exactly that purpose.

6 .5 milligrams worked pretty well,
7 2-milligram worked pretty well; 4-milligram
8 worked well, but there's a trade-off. A higher
9 concentration of drug in the eye is potentially
10 creating more risk of inflammation, more issues
11 with respect to formulation, costs issues for --
12 you know, for manufacturing. There -- there are
13 a lot of different aspects to making that
14 determination to -- that the companies need
15 to -- need to decide upon, and these studies
16 were exactly for that purpose.

17 What -- what drug concentration works?
18 What works best? What provides a sustained
19 benefit? That's -- that's what this is all
20 about.

21 Q. And -- and just to be clear, you weren't
22 involved in the design of any of these studies?

23 A. I was not.

24 Q. Okay. You haven't reviewed any
25 literature about the design of the studies

1 beyond what's cited in your reports?

2 A. I have not specifically, no.

3 Q. Okay. And so you don't know, except for
4 what's reported in the literature, why Regeneron
5 was testing 2.0 milligram of aflibercept and 4.0
6 milligrams of aflibercept?

7 A. Well, I know from the literature that,
8 again, the dose escalation studies showed
9 certain results, responses, and those -- and
10 the -- those responses are balanced with safety,
11 and -- and -- and decisions are made to go
12 forward with a dose that meets a number of
13 different criteria for the company.

14 Q. And wouldn't one of the potential reasons
15 for testing amounts of aflibercept higher than
16 2-milligram be that there is a concern that
17 2 milligrams wouldn't be effective?

18 A. I think that PRN dosing, the phase 2 PRN,
19 shows that it is effective and was effective.
20 There was good data to suggest that it was.
21 That doesn't mean the company can't look at
22 other dosing options.

23 I mean, again, I -- I provided this in --
24 from the perspective of a person of ordinary
25 skill in the art at that time, but Regeneron has

1 brought to market a 4-milligram dose, right,
2 recently. So -- so there -- there are -- there
3 are reasons that companies can make decisions
4 regarding that.

5 Q. Let's go to paragraph 182 of your report,
6 Exhibit 1000. Excuse me. And this is paragraph
7 100 -- or paragraph 182 on page 82, using the
8 lower right-hand designation. And let me know
9 when you're there.

10 A. Yes.

11 Q. Okay. And in this paragraph, you state
12 that a POSA would have found it obvious to
13 modify Dickson's phase 3 AMD dosing regimen to
14 include additional initial doses for the same
15 reasons discussed in relation to claim 25,
16 right?

17 A. Yes.

18 Q. And then you go on to say: Modifying
19 Dickson's phase 3 AMD dosing regimen to include
20 four initial doses would bring it further closer
21 to the phase 2 regimen, right?

22 A. Yes.

23 Q. Why would a POSA be trying to modify a
24 phase 3 regimen to get closer to the phase 2
25 regimen?

1 A. It's not about modifying to -- to mirror
2 a regimen. The motivation for a person of
3 ordinary skill in the art to add additional
4 doses relates to the desire to treat a patient
5 with a clinical condition. The -- the goal of
6 injecting patients with -- we're talking
7 about -- this is claim 25, so we're talking
8 about macular -- depending on claim 15, which
9 macular edema, diabetic macular edema.

10 In macular diabetic edema, the swelling
11 of the retina as a result of the diabetic
12 retinopathy is a dynamic process, and it is
13 incumbent upon the treating physician to try and
14 get the retina as dry as possible prior to
15 trying to extend either as a PRN or other
16 process.

17 And so a person of ordinary skill in the
18 art would be motivated based upon the patient's
19 result to add an additional dose or more based
20 upon that patient's response to therapy, and if
21 there is no sufficient, or insufficient, drying
22 of the retina, that would be a motivation to add
23 additional injections.

24 Q. So your answer was with respect to DME
25 treatment, right? Or the treatment of DME?

1 A. Yes. We are talking about in relation to
2 claim 25, correct.

3 Q. Right. This paragraph in a section of
4 your report about claims through 28, right?

5 A. Yes.

6 Q. Claim relates to age-related macular
7 degeneration, not DME, correct?

8 A. Yes.

9 Q. Okay. And so my question is still about
10 this statement that modifying Dickson's phase 3
11 AMD dosing regimen to include four initial doses
12 would bring it further closer to the phase 2
13 regimen.

14 It's still not clear to me why a POSA
15 would modified a phase 3 regimen to bring it
16 closer to a phase 2 regimen that preceded it for
17 AMD. Can you tell me why, Dr. Chaum?

18 A. I -- I'm reviewing my comments.

19 Q. Okay.

20 A. So the concept is about achieving a
21 beneficial result for the patient, and what I
22 say here is that adding -- adding additional
23 doses of the medication would be -- let me
24 restart this.

25 Q. Sure.

1 A. So the goal here is to -- is to mitigate
2 the disease and adding additional doses would
3 serve to mitigate the disease. The concept here
4 is that -- that by modifying the regimen to --
5 to -- to include an additional fourth initial
6 dose would only serve to provide the patient
7 with additional -- an additional dose of
8 medication in the course of that follow-on year,
9 and therefore, it would be a person of ordinary
10 skill in the art would have that expectation
11 that that additional dose of medication would
12 provide additional therapeutic benefit.

13 Q. Okay. And so, again, we're talking --
14 when you're saying additional dose, you're
15 talking about that additional fourth loading
16 dose referenced in the Dickson reference, the
17 phase 2 PRN dosing regimen?

18 A. Yeah. That -- that was correct. Yeah.

19 Q. Okay. Can we turn to paragraph 168 of
20 your report on page 77 using the lower
21 right-hand corner? Do you have that paragraph
22 in front of you, Doctor?

23 A. Do I have paragraph 168?

24 Q. That's correct.

25 A. Yes.

1 Q. And in the first sentence of this, you
2 refer to the 2006 press release and state that
3 it reports that a single 2-milligram dose in AMD
4 patients produced -- and then you provide
5 certain BCBA improvement scores, right?

6 A. Yes.

7 Q. Is that statement accurate in your
8 report?

9 A. Can you provide me with the press
10 release?

11 Q. Sure. Before I do that, you reviewed the
12 press release before you wrote that sentence,
13 right?

14 A. I believe that I did.

15 Q. And it's important that you be careful
16 and accurate when you represent what's reported
17 in the literature?

18 A. Yes.

19 (Exhibit Number 10 was marked.)

20 BY MR. BRAUSA:

21 Q. Okay. This is Exhibit 10, the 2006
22 press release. And this is what you're quoting
23 from in paragraph 168 of your report, right?

24 A. Yes.

25 Q. Okay. Can you direct me to the quoted

1 language on page 1, what you cite in your
2 report?

3 A. I'm sorry, Counsel, what -- what are you
4 asking me?

5 Q. There's a quote in paragraph 168 of your
6 report that refers to a single 2-milligram dose
7 in AMD patients producing certain results,
8 right?

9 A. Yes.

10 Q. And that quote cites to Exhibit 10,
11 page 1, in your report, right?

12 A. It's evidently a typo. It's on page 2.

13 Q. Okay. And where is it on page 2?

14 A. The third bullet.

15 Q. Okay. And does that refer to a single
16 2-milligram dose providing the mean improvement
17 that you recite?

18 A. What it refers to 2-milligram and
19 4-milligram doses.

20 Q. Okay. And you don't refer to the
21 4-milligram dosage in your report, do you?

22 A. I do not.

23 Q. Okay. So now that we've looked at that
24 third bullet that's at page 2, not page 1 of
25 Exhibit 10, do you think the statement in your

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1 report at paragraph 168 is accurate?

2 A. I would say it's incomplete.

3 Q. Okay. How would you edit it to make it
4 more complete?

5 A. A single, 2-milligram, or 4-milligram
6 dose.

7 Q. Okay. And in fact, the 2006 press
8 release does not describe whether it was
9 2-milligram doses, 4-milligram doses, or how
10 many patients within those cohorts, correct?

11 A. Well, it describes the mean.

12 Q. Okay.

13 A. 3 of 6 patients gaining 15 or more
14 letters.

15 Q. Okay. But it doesn't actually say what
16 the gains were for just the patients who
17 received 2 milligrams, right?

18 A. It does not.

19 Q. At the top of this exhibit, it has a,
20 like, header in the margins that says April 6,
21 2023, 11:52 p.m. Do you see that?

22 A. Yes.

23 Q. Your report was served on April , 2023,
24 correct?

25 A. Yes.

1 Q. Do you know whether you had looked at
2 this reference before April 6, 2023?

3 A. I believe that I did.

4 Q. Okay. Do you know who printed this out
5 just before midnight on the 6th of April?

6 A. I do not.

7 Q. Okay. And so based on that third bullet
8 on page 2 of Exhibit 10, the 2006 press
9 release does not say whether the gains were
10 higher for the 4-milligram-dose group compared
11 to the 2-milligram-dose group?

12 A. It reports them as the mean improvement.

13 Q. Okay. And that's across both dosage
14 amounts?

15 A. Yes.

16 Q. So you can't tell whether the gains were
17 primarily due to the people receiving
18 4 milligrams or the people receiving 2
19 milligrams?

20 A. No.

21 Q. If we can go to paragraph 89 of your
22 report, and it spans from page 43 to 44 using
23 the lower right-hand page designations. And in
24 the table on page 44, you provide what you
25 consider to be the plain and ordinary meaning of

1 certain conditions.

2 A. Yes.

3 Q. And one of them is active intraocular
4 inflammation.

5 A. Yes.

6 Q. And that refers to inflammation in the
7 interior of the eye, correct?

8 A. Yes.

9 Q. Do you consider the cornea to be on the
10 interior of the eye?

11 A. No.

12 Q. Would you consider inflammation of the
13 cornea to be intraocular inflammation?

14 A. No.

15 Q. Do you consider the sclera to be on the
16 inside or interior of the eye?

17 A. The inner surface of the sclera is inside
18 the eye, yes.

19 Q. Okay. Is outer surface of the sclera
20 inside the eye?

21 A. No.

22 Q. Okay. So a part of sclera is inside the
23 eye, its inner surface; part the sclera is on
24 outside the eye, the out -- outer surface?

25 A. Yes.

1 Q. Would you consider inflammation of the
2 outer surface to be intraocular inflammation?

3 MR. SUMMERS: Objection. Form.

4 THE WITNESS: Well, inflammation of
5 the surface of the eye can be -- can be
6 associated with intraocular inflammation, yes.

7 BY MR. BRAUSA:

8 Q. Okay. Would you consider inflammation of
9 the outer surface of sclera to itself be
10 intraocular inflammation?

11 MR. SUMMERS: Objection. Form.

12 THE WITNESS: You're asking a
13 nuanced question. The sclera as a structure,
14 you can't -- you can't say that the outer
15 surface is -- has inflammation without including
16 the whole sclera.

17 BY MR. BRAUSA:

18 Q. Okay. And -- and so you can't -- you're
19 not able to distinguish whether it's the outer
20 surface or inter surface that's inflamed?

21 MR. SUMMERS: Objection. Form.

22 THE WITNESS: You wouldn't be able
23 to. The sclera -- if the sclera has
24 inflammation, it's inflamed throughout.

25 BY MR. BRAUSA:

1 Q. Okay. So would you consider inflammation
2 of the sclera to be intraocular inflammation?

3 A. It can be. Again, because the tissue
4 is -- is the entire wall of the eye, and
5 therefore, if it's inflamed, that
6 inflammation -- that inflammation can be inside
7 the eye.

8 Q. Okay. Are there circumstances where that
9 inflammation would not be inside the eye?

10 A. I -- I -- your question is difficult
11 to -- to understand from a -- from a medical
12 perspective.

13 Q. Okay. I'm just trying to understand.
14 You indicated that it can -- that inflammation
15 of the sclera can be considered intraocular
16 inflammation if it's on the inside of the eye,
17 and my -- my question is: Are there
18 circumstances where there's inflammation of the
19 sclera and it's not intraocular inflammation?

20 A. It's -- it's a difficult question to
21 answer. I don't mean to be difficult, but the
22 sclera is a 1-millimeter thick fibrous tissue,
23 of continuous fibrous tissue, and it has --
24 it's -- it has a water component and a fibrous
25 component, and if there is inflammation

1 associated with the sclera, it's not that it
2 stays on the outside.

3 The sclera is inflamed and that -- part
4 of that sclera includes -- is inside the eye.
5 So you can't have scleral inflammation sort of
6 sitting on the surface and not affecting the
7 rest of the sclera. It's homogenous tissue. If
8 it's inflamed, the sclera's inflamed.

9 Q. Okay. So part of it would be on the
10 interior of the eye; part of the inflammation
11 would be exterior to the eye?

12 A. You couldn't -- if -- if -- if the sclera
13 was inflamed, there would be inflammation inside
14 the eye.

15 Q. Okay. You're familiar with the term
16 conjunctivitis, correct?

17 A. I am.

18 Q. And that refers to inflammation of the
19 conjunctiva?

20 A. Infection or and/or inflammation.

21 Q. And so that was my actual next question.
22 What's infectious conjunctivitis?

23 A. So inflammation is -- of tissues is
24 immune response to -- to either infectious or
25 other -- infectious organisms or other aspects

1 of the tissue that -- that excite the immune
2 system.

3 And so conjunctivitis can be associated
4 with infection, like bacterial infection, with
5 viral infection, but can also be associated with
6 -- with inflammatory conditions like dry eye,
7 like lupus, and so a distinction is not
8 independent. Infection is always associated
9 with inflammation, but inflammation isn't always
10 associated with infection.

11 Q. Understood. Is there a term that you use
12 generally to refer to noninfectious
13 conjunctivitis, or is that the term,
14 noninfectious conjunctivitis?

15 A. That -- that would probably be a good way
16 to refer to it.

17 Q. Okay. And so I want to focus on
18 infectious conjunctivitis, which I understand is
19 infection. The inflammation is associated with
20 that infection.

21 What signs and symptoms are you
22 evaluating to indicate that a patient has
23 infected -- infectious conjunctivitis?

24 MR. SUMMERS: Objection. Form.

25 THE WITNESS: So the features of

1 conjunctivitis, whether it's infectious or
2 inflammatory, are going to be similar. But
3 those features are engorgement of the blood
4 vessels, redness, tearing, pain, discharge,
5 those sorts of things.

6 BY MR. BRAUSA:

7 Q. And when we're talking about inflammation
8 that you're evaluating, that's inflammation of
9 the conjunctiva?

10 A. Conjunctiva, yes.

11 Q. Conjunctiva. Excuse me.

12 And then how do you determine that it's a
13 result of infection, that it's infectious
14 conjunctivitis rather than just noninfectious
15 conjunctivitis?

16 MR. SUMMERS: Objection. Form.

17 THE WITNESS: Well, there're --
18 there're different ways to determine it. The --
19 the tissue swab can -- you can send tears or
20 mucus from that eye for a bacteria culture. You
21 can send it for viral culture. You can send it
22 for PCR.

23 Not uncommonly, conjunctivitis is --
24 does not occur in isolation. It's associated
25 with other aspects or other features of eye

1 disease that help a physician determine what's
2 going on. So if there's infections of the
3 lashes and lids, blepharitis, that can be
4 associated with conjunctivitis.

5 If there is dry eye, for example,
6 conjunctivitis can be associated with
7 medications that are noninfectious. But -- but
8 typically if a physician was going to try to
9 distinguish between infectious or noninfectious,
10 they would send some kind of a culture.

11 BY MR. BRAUSA:

12 Q. Okay. Is conjunctivitis an ocular
13 condition?

14 MR. SUMMERS: Objection. Form.

15 THE WITNESS: I'm not understanding
16 your question. It's pretty -- it's pretty
17 obvious a conjunctiva is ocular tissue, so
18 conjunctivitis can be a -- an eye infection, an
19 infectious process. It can also be an
20 inflammatory process that's not infectious.

21 BY MR. BRAUSA:

22 Q. Okay. And -- and so you would consider
23 conjunctivitis to be an ocular condition, I take
24 it?

25 A. Yes.

1 Q. Okay. And do you consider it be to a
2 periocular condition?

3 MR. SUMMERS: Objection. Form.

4 THE WITNESS: So in my own
5 definition, yes.

6 BY MR. BRAUSA:

7 Q. Okay. And when you say in your own
8 definition, what is that?

9 A. Well, periocular is sort of a broad term
10 that can include tissues in and around the eye.
11 So if we -- if we consider the eye, the globe
12 itself, as a structure, then periocular tissues
13 would be the conjunctiva overlying it, tenons,
14 fibrous tissue overlying it, the extra ocular
15 muscles, the fat in the orbit, the bones, et
16 cetera.

17 Q. Okay. Are there any other surrounding
18 tissues that you'd include in your definition of
19 periocular?

20 MR. SUMMERS: Objection. Form.

21 THE WITNESS: Such as?

22 BY MR. BRAUSA:

23 Q. In addition to the ones you named.

24 A. Again, all the aspect -- all the
25 structures of the eye and orbit that are not the

1 globe itself.

2 Q. You're familiar with scleritis, I take
3 it?

4 A. Yes.

5 Q. Is there something called infectious
6 scleritis?

7 A. Yes.

8 Q. And what is that?

9 A. It's an inflammation, infection, of the
10 sclera from an organism.

11 Q. Okay. And similar approach to -- is it a
12 similar approach to figuring out the symptoms
13 indicating that a patient has infectious
14 scleritis?

15 A. I'm not following your question.

16 Q. How do you determine a patient has
17 infectious scleritis?

18 A. There is typically evidence of
19 significant orbital and periocular inflammation,
20 and there's also often evidence that can be seen
21 by looking at the fundus, looking through the
22 lens at the retina and the choroid and the
23 sclera. Scleritis can present with features of
24 disease by looking directly through the eye.

25 Q. Okay. And -- and inflammation is, again,

1 another symptom of infection of the sclera?

2 A. Yes.

3 Q. Okay. And that's -- and is inflammation
4 of any of the surrounding tissue an indicator of
5 infectious scleritis?

6 A. So -- so I'm not quite sure I understand
7 exactly what you're asking.

8 Q. Okay. If you're determining whether
9 someone has inflammation associated with
10 scleritis, are you looking at the sclera or
11 surrounding tissue as well?

12 A. We're looking at primarily the
13 surrounding tissue, but you can see the sclera
14 through the surrounding tissue.

15 Q. Okay. And the surrounding tissue are the
16 types of things you identified previously when
17 we were talking about conjunctivitis, things
18 outside the globe?

19 A. So if we're talking specifically about
20 scleritis, you would be talking about the
21 conjunctiva and tenons and perhaps the muscles.

22 Q. Okay. Anything else?

23 A. Well, again, you would -- you could see
24 the scleritis itself by looking into the eye.

25 Q. Okay. And I take it you're also familiar

1 with keratitis?

2 A. Yes.

3 Q. And there's infectious keratitis,
4 correct?

5 A. That's one form, yes.

6 Q. Okay. What other forms are there?

7 A. There's noninfectious keratitis. There's
8 neurotrophic keratitis. There's dry eye-related
9 keratitis. There are many different forms of --
10 keratitis refers to inflammation and/or
11 infection of the cornea.

12 Q. Okay. And -- okay. With respect to
13 scleritis, do you consider that to be a
14 periocular condition?

15 MR. SUMMERS: Objection. Form.

16 THE WITNESS: I mean, scleritis
17 involves the globe itself, so I would call it an
18 ocular condition.

19 BY MR. BRAUSA:

20 Q. Okay. So it's not a periocular
21 condition?

22 A. It presents with features of periocular
23 inflammation. It presents as a peri- -- as in
24 part a periocular process, but the disease
25 itself is of the globe.

1 Q. What about keratitis? Do you consider
2 that to be a periocular disease?

3 MR. SUMMERS: Objection. Form.

4 THE WITNESS: Well, again, I think
5 my response would similar to the -- keratitis is
6 a disease of the cornea which is part of the
7 globe, but the disease itself can present with
8 manifestations of periocular inflammation and
9 even infection.

10 BY MR. BRAUSA:

11 Q. Are you familiar with the term systemic
12 condition?

13 A. Yes.

14 Q. What's a systemic condition?

15 MR. SUMMERS: Object to form.

16 THE WITNESS: It's -- it can be
17 interpreted as -- as a condition that affects
18 the whole body.

19 BY MR. BRAUSA:

20 Q. Okay. And -- and would a person of
21 ordinary skill in the art distinguish between an
22 ocular condition and a systemic condition?

23 MR. SUMMERS: Objection. Form.

24 THE WITNESS: I'm not understanding
25 your question.

1 BY MR. BRAUSA:

2 Q. Is there a difference, in your view,
3 between a systemic condition and an ocular
4 condition?

5 A. You'll have to give me some context.
6 I -- I don't understand your question.

7 Q. Do you have an understand- -- you just
8 provided a definition of a systemic condition,
9 right?

10 A. Uh-huh.

11 Q. And we've been talking about several
12 ocular conditions. Are the ocular conditions
13 that we've been talking about systemic
14 conditions?

15 MR. SUMMERS: Object to form.

16 THE WITNESS: Ocular conditions can
17 be associated with systemic disease depending on
18 what you're talking about; that's why I'm
19 asking.

20 BY MR. BRAUSA:

21 Q. Okay. Well, let's start with
22 conjunctivitis. Is that a systemic condition?

23 MR. SUMMERS: Objection. Form.

24 THE WITNESS: Conjunctivitis can be
25 associated with systemic disease.

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1 BY MR. BRAUSA:

2 Q. But is conjunctivitis itself a systemic
3 disease?

4 MR. SUMMERS: Objection. Form.

5 THE WITNESS: Is conjunctivitis
6 alone a systemic disease? I would not consider
7 it a systemic disease, no.

8 BY MR. BRAUSA:

9 Q. Okay. And if we focus on scleritis and
10 keratitis alone, would you consider them to be
11 systemic conditions?

12 A. Again, they can be associated with
13 systemic conditions. They can be features
14 associated with systemic conditions, but an
15 isolated scleritis or an isolated keratitis is
16 not necessarily systemic.

17 Q. We're going to get to the pronunciation
18 part of the program. Is endophthalmitis a type
19 of ocular condition?

20 A. Endophthalmitis.

21 Q. Endophthalmitis --

22 A. There will be a quiz at the end.

23 Q. -- a type of ocular infection?

24 A. Yes.

25 Q. Okay. And so I think we've talked about

1 conjunctivitis, keratitis, scleritis,
2 endophthalmitis. Are there any other types of
3 ocular or periocular infections you deal with?

4 MR. SUMMERS: Objection. Form.

5 THE WITNESS: Are you asking me in
6 my practice? Are you asking, you know, for a
7 person of ordinary skill in the art? What --
8 what are you asking?

9 BY MR. BRAUSA:

10 Q. For a person of ordinary skill in the
11 art.

12 A. Every as- -- every disease related to the
13 eye would be in the purview of an
14 ophthalmologist.

15 Q. Okay. And so when we're talking -- if we
16 go back to page -- paragraph 89 of your report,
17 and we're looking at ocular or periocular
18 infection on page 44, that wouldn't be limited
19 to conjunctivitis keratitis, scleritis, and
20 endophthalmitis, correct?

21 A. I'm sorry, go -- if you could ask your
22 question again.

23 Q. I'll try.

24 A. And try and get the pronunciation right
25 this time.

1 Q. Fair enough. You see your plain and
2 ordinary meaning that you provided of active
3 ocular or periocular infection, correct?

4 A. Yes.

5 Q. That's not limited to any particular type
6 of ocular or periocular infection, right?

7 MR. SUMMERS: Objection. Form.

8 THE WITNESS: It's not limited to a
9 specific infection, no.

10 BY MR. BRAUSA:

11 Q. Okay.

12 MR. BRAUSA: Thank you. I have
13 nothing further.

14 MR. SUMMERS: We're done. Will you
15 give me a minute? And I mean a minute.

16 THE VIDEOGRAPHER: The time is

17 . We're off the record. 12:01

18 (Off-the-record discussion was held.)

19 MR. SUMMERS: We're done.

20

21 FURTHER THIS DEPONENT SAITH NOT.

22

23

24

25

1 REPORTER'S CERTIFICATE

2 I certify that the witness in the
3 foregoing deposition, was by me duly sworn to
4 testify in the within-entitled cause; that the
5 said deposition was taken at the time and place
6 therein named; that the testimony of said
7 witness was reported by me, a Shorthand Reporter
8 and Notary Public of the State of Tennessee
9 authorized to administer oaths and affirmations,
10 and said testimony, pages 314 through 419 was
11 thereafter transcribed into typewriting.

12 I further certify that I am not counsel
13 or attorney for either or any of the parties to
14 said deposition, nor in any way interested in
15 the outcome of the cause named in said
16 deposition.

17 IN WITNESS WHEREOF, I have hereunto
18 set my hand the 7th Day of February, 2024.
19
20
21

22 JENNIFER HAYNIE (License No. 403)
23
24
25

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1 Adam R. Brausa, Esq.

2 ABrausa@mofo.com

3 february 7, 2024

4 RE: SAMSUNG BIOEPIS CO. v. REGENERON PHARMACEUTICALS, INC.

5 January 5, 2024-EDWARD CHAUM, M.D., Ph.D.-JOB NO.6381270

6 The above-referenced transcript has been

7 completed by Veritext Legal Solutions and

8 review of the transcript is being handled as follows:

9 ___ Per CA State Code (CCP 2025.520 (a)-(e)) - Contact Veritext
10 to schedule a time to review the original transcript at
11 a Veritext office.

12 ___ Per CA State Code (CCP 2025.520 (a)-(e)) - Locked .PDF
13 Transcript - The witness should review the transcript and
14 make any necessary corrections on the errata pages included
15 below, notating the page and line number of the corrections.
16 The witness should then sign and date the errata and penalty
17 of perjury pages and return the completed pages to all
18 appearing counsel within the period of time determined at
19 the deposition or provided by the Code of Civil Procedure.

20 ___ Waiving the CA Code of Civil Procedure per Stipulation of
21 Counsel - Original transcript to be released for signature
22 as determined at the deposition.

23 ___ Signature Waived - Reading & Signature was waived at the
24 time of the deposition.

25
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1 ___ Federal R&S Requested (FRCP 30(e)(1)(B)) - Locked .PDF
2 Transcript - The witness should review the transcript and
3 make any necessary corrections on the errata pages included
4 below, notating the page and line number of the corrections.
5 The witness should then sign and date the errata and penalty
6 of perjury pages and return the completed pages to all
7 appearing counsel within the period of time determined at
8 the deposition or provided by the Federal Rules.
9 _X_ Federal R&S Not Requested - Reading & Signature was not
10 requested before the completion of the deposition.

1 SAMSUNG BIOEPIS CO. v. REGENERON PHARMACEUTICALS, INC.

2 EDWARD CHAUM, M.D., Ph.D. - JOB NO.6381270

3 E R R A T A S H E E T

4 PAGE_____ LINE_____ CHANGE_____

5 _____

6 REASON_____

7 PAGE_____ LINE_____ CHANGE_____

8 _____

9 REASON_____

10 PAGE_____ LINE_____ CHANGE_____

11 _____

12 REASON_____

13 PAGE_____ LINE_____ CHANGE_____

14 _____

15 REASON_____

16 PAGE_____ LINE_____ CHANGE_____

17 _____

18 REASON_____

19 PAGE_____ LINE_____ CHANGE_____

20 _____

21 REASON_____

22 _____

23 _____

24 WITNESS

Date

25

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Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

(1) Review; Statement of Changes. On request by the deponent or a party before the deposition is completed, the deponent must be allowed 30 days after being notified by the officer that the transcript or recording is available in which:

(A) to review the transcript or recording; and
(B) if there are changes in form or substance, to sign a statement listing the changes and the reasons for making them.

(2) Changes Indicated in the Officer's Certificate. The officer must note in the certificate prescribed by Rule 30(f)(1) whether a review was requested and, if so, must attach any changes the deponent makes during the 30-day period.

DISCLAIMER: THE FOREGOING FEDERAL PROCEDURE RULES ARE PROVIDED FOR INFORMATIONAL PURPOSES ONLY. THE ABOVE RULES ARE CURRENT AS OF APRIL 1, 2019. PLEASE REFER TO THE APPLICABLE FEDERAL RULES OF CIVIL PROCEDURE FOR UP-TO-DATE INFORMATION.

VERITEXT LEGAL SOLUTIONS

COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

Veritext Legal Solutions represents that the foregoing transcript is a true, correct and complete transcript of the colloquies, questions and answers as submitted by the court reporter. Veritext Legal Solutions further represents that the attached exhibits, if any, are true, correct and complete documents as submitted by the court reporter and/or attorneys in relation to this deposition and that the documents were processed in accordance with our litigation support and production standards.

Veritext Legal Solutions is committed to maintaining the confidentiality of client and witness information, in accordance with the regulations promulgated under the Health Insurance Portability and Accountability Act (HIPAA), as amended with respect to protected health information and the Gramm-Leach-Bliley Act, as amended, with respect to Personally Identifiable Information (PII). Physical transcripts and exhibits are managed under strict facility and personnel access controls. Electronic files of documents are stored in encrypted form and are transmitted in an encrypted

fashion to authenticated parties who are permitted to access the material. Our data is hosted in a Tier 4 SSAE 16 certified facility.

Veritext Legal Solutions complies with all federal and State regulations with respect to the provision of court reporting services, and maintains its neutrality and independence regardless of relationship or the financial outcome of any litigation. Veritext requires adherence to the foregoing professional and ethical standards from all of its subcontractors in their independent contractor agreements.

Inquiries about Veritext Legal Solutions' confidentiality and security policies and practices should be directed to Veritext's Client Services Associates indicated on the cover of this document or at www.veritext.com.