

1 UNITED STATES DISTRICT COURT
2 NORTHERN DISTRICT OF WEST VIRGINIA

3 Regeneron Pharmaceuticals, Inc.

4 Plaintiff,

5 VS. CIVIL ACTION NO.

6 1:22-cv-61

7 Mylan Pharmaceuticals, Inc., and Volume 4

8 Biocon Biologics,

9 Defendants.

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11 Proceedings had in the bench trial of the above-styled
12 action on June 15, 2023, before Honorable Thomas S. Kleeh
District Judge, at Clarksburg, West Virginia.

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Transcript produced by computer-aided transcription.

1 Thursday Morning Session,
2 June 15, 2023, 9:30 a.m.

3 - - -

4 THE COURT: We convene for day four of trial. Good
5 morning, everyone.

6 Everyone's curious, the University High Hawks played
7 well yesterday, and rising junior combo guard Noah Kleeh at 12
8 and 18 points in two games yesterday. So summer league is off
9 to a good start. And while sitting at the Marion County
10 Armory, I was reading the Federal Circuit's thoughts on many
11 things as well.

12 Okay. Let me ask this initial question so we can
13 most efficiently use our time today. What witnesses does Mylan
14 plan to call first?

15 MR. McLAUGHLIN: We plan to call Dr. Thomas Albin
16 first.

17 THE COURT: Outstanding. Are there any issues with
18 Dr. Albin that we need to take up before he testifies that
19 anyone's aware of at this point?

20 MR. McLAUGHLIN: None that I'm aware of.

21 THE COURT: Counsel.

22 MS. OBERWETTER: No, Your Honor.

23 THE COURT: Outstanding. Let's do that.

24 Yes, Counsel.

25 MR. HUNT: Your Honor, just a brief administrative

1 matter. Thank you for taking care of the updating us on the
2 Hawks. I was going to check in on that.

3 With regard to Dr. Rabinow, we have an outstanding
4 motion to exclude. Defendants filed an opposition, I suppose
5 early this morning.

6 THE COURT: Yes.

7 MR. HUNT: In the event that the Court is prepared to
8 take up that issue, I think it would be beneficial to the
9 parties and most notably the defendants to assist in witness
10 preparation. So if there's a particular time that the Court
11 would be willing to take that up today, it would be much
12 appreciated.

13 THE COURT: Why don't we do that -- because
14 Dr. Albini has a travel issue. Is that correct? Or travel
15 schedule, I should say, not issues.

16 Hopefully, Doctor, wherever you are, you don't have
17 issues, but I know you have a travel schedule.

18 Let's take that up at morning break or so, and we'll
19 go from there.

20 MR. HUNT: Appreciate it. Thank you, Your Honor.

21 THE COURT: Yes, ma'am.

22 MS. MAZZOCHI: And, Your Honor, the additional
23 administrative matter to bring up has to do with the deposition
24 designations for Karen Chu. So one of the things that we do
25 have -- I'm happy to hand it up to Your Honor -- is we actually

1 went through --

2 THE COURT: I believe I have that.

3 MS. MAZZOCHI: What got filed was the -- that was our
4 letter that we had previously sent where we -- under the
5 pretrial order where we had specified this was Regeneron's
6 objection; this is ours.

7 In response to your instructions yesterday, we did
8 have a meet-and-confer. My understanding is that Regeneron's
9 position is that they believe we had an agreement that,
10 therefore, all of Ms. Chu's testimony was converted from
11 30(b)(6) even if it fell within the notice topics to 30(b)(1).
12 We obviously disagree with that position.

13 So what we -- we do have a copy of the transcript
14 where we basically have gone through and marked these are the
15 different --

16 THE COURT: I have the color-coded -- red, green,
17 yellow. I've not had a chance to review that. So we're going
18 to put a pin in that.

19 MS. MAZZOCHI: I just wanted to know if there was
20 a -- because, again, we were hoping we could play Ms. Chu's
21 deposition testimony today as a 30(b)(6) witness. So I didn't
22 know if that was already something you'd like to take up --

23 THE COURT: We will when we get to it.

24 MR. GREGORY: I'm not -- not seeking to argue this
25 right now, just want to clarify.

1 THE COURT: Not going to, but go ahead.

2 MR. GREGORY: The deposition transcript that I
3 believe you have is actually one from Regeneron. I think it's
4 probably very similar to the one that Mylan's counsel has
5 prepared. We received the email request this morning for those
6 transcripts.

7 We have a machine time limitation on the small
8 printer across the hall. We're running copies. I believe we
9 have provided the Court with two. The next one out of the
10 printer will go to Mylan's counsel. The fourth one will be
11 mine.

12 THE COURT: Understood.

13 MS. MAZZOCHI: Your Honor, how about to the extent
14 let's make sure everybody's got copies so nobody's surprised.
15 I'll give this to counsel.

16 Your Honor, how many copies would you like?

17 THE COURT: Two, please.

18 MS. MAZZOCHI: Thank you, Your Honor.

19 THE COURT: I know we've got some pins on things to
20 deal with. We will take them as they come.

21 Mylan may call its first witness.

22 MR. McLAUGHLIN: Your Honor, I believe we have some
23 binders. Permission to approach to pass out those binders,
24 documents Dr. Albini is going to be relying upon.

25 THE COURT: Granted.

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1 MR. McLAUGHLIN: Good morning, Your Honor. Neil
2 McLaughlin on behalf of Mylan Pharmaceuticals, Inc., and Biocon
3 Biologics, Inc. Biocon/Mylan would like to call Dr. Thomas
4 Albini as its first witness in its invalidity case.

5 THE COURT: Good morning, Doctor, sir. If you want
6 to make your way to the front of the courtroom.

7 **THOMAS A. ALBINI, MD, DEFENDANTS' WITNESS, SWORN**

8 THE COURT: Thank you, Doctor. Once you're seated
9 and comfortable, sir, if you wouldn't mind adjusting that
10 microphone. Don't worry; you can't break it.

11 THE WITNESS: Okay.

12 THE COURT: Does everyone have all their binders,
13 slides, and the rest?

14 If you're settled, Counsel.

15 MR. McLAUGHLIN: Thank you, Your Honor.

16 DIRECT EXAMINATION

17 BY MR. McLAUGHLIN:

18 Q. Good morning, Dr. Albini. Can you please state your
19 full name for the record.

20 A. Thomas Arno Albini.

21 Q. You're here testifying on behalf of Biocon and Mylan,
22 correct?

23 A. That is correct.

24 Q. Did you prepare demonstrative slides to assist the
25 Court with your testimony today?

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1 A. That's correct.

2 Q. And looking at the screen -- this is DDX 6 -- are
3 these the slides that you prepared?

4 A. Yes.

5 Q. So, Dr. Albin, I'd like to first talk about your
6 qualifications and experience that are relevant to this case.

7 What is your area of expertise?

8 A. I am a vitreoretinal surgeon who, among other things,
9 treats patients with angiogenic eye disorders on a routine
10 basis. And I've been doing that now for over 15 years as
11 faculty at the University of Miami Bascom Palmer Eye Institute.

12 Q. Could you describe your academic experience that led
13 to your eventual appointment to Bascom Palmer Eye Institute.

14 A. I finished medical school in 1999 at Johns Hopkins
15 University in Baltimore. I then went to Los Angeles to the
16 University of Southern California Doheny Eye Institute, where I
17 finished a three-year residency in ophthalmology. I also
18 undertook a one-year fellowship in intraocular inflammation and
19 ocular pathology.

20 Subsequent to that, I went to the Cullen Eye
21 Institute at the Baylor College of Medicine in Houston, Texas,
22 where I undertook two years of training as a fellow in
23 vitreoretinal surgery.

24 And immediately subsequent to that, I was hired as an
25 assistant professor at Bascom Palmer, University of Miami.

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1 Approximately six, seven years later, I was promoted to
2 associate professor. And back in 2018 I was promoted to a full
3 clinical professor of ophthalmology at Bascom Palmer.

4 Q. You made a reference to the term "vitreoretinal."

5 Can you describe for the Court what vitreoretinal
6 disorders are?

7 A. Vitreoretinal disorders are a number of diseases
8 within the back part of the eye behind the lens involving
9 surgery and medical -- and/or medical treatment of the retina
10 and the nearby tissues in the back of the eye.

11 So these would be things that people might have heard
12 of, like retinal detachments on the surgical side, epiretinal
13 membranes, and on the medical side, most of the diseases that
14 we'll be talking about, such as macular degeneration and
15 diabetic macular edema.

16 Q. And looking at the next slide, Slide 3 of DDX 6, can
17 you tell the Court a little bit about your experience working
18 as a medical doctor in the field of vitreoretinal disorders.

19 A. Sure. So as I mentioned, I started as an assistant
20 professor back in 2006. I've been a staff ophthalmologist at a
21 fully equipped eye hospital, the Anne Bates Leach Eye Hospital,
22 and at Jackson Memorial Hospital, which is the county health
23 system at University of Miami.

24 Since 2016 I've been codirector of the vitreoretinal
25 surgery fellowship, and then in 2018 I was promoted to full

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1 professor of clinical ophthalmology.

2 As of this morning I have decided to become the
3 medical director of the retinal division within Bascom Palmer
4 Eye Institute.

5 Q. Congratulations.

6 Now, turning to the -- your next slide, Slide 4, can
7 you describe some of the things that you do on a day-to-day
8 basis in your roles at Bascom Palmer?

9 A. We have a number of educational conferences for
10 fellows and surgical and medical retina. I routinely
11 participate in those. I have fellows and residents who are
12 with me in clinic virtually every time I'm in clinic. And part
13 of my responsibilities are not only to manage patients as best
14 I can but also to help educate younger doctors who are becoming
15 vitreoretinal specialists themselves.

16 I also have fellows with me in the operating room,
17 either watching me operate or me watching them operate, and
18 that's also on a routine basis. And I've been doing that for
19 years.

20 Of course, my primary emphasis is on diagnosing and
21 treating vitreoretinal diseases in patients. I have a very
22 busy clinical load. I see somewhere between 4,000 and 5,000
23 patient visits per year, and I operate every week.

24 And as part of those responsibilities, I administer a
25 lot of vitreal anti-VEGF agents such as the ones that we'll be

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1 discussing the rest of this testimony.

2 Q. And turning to the next slide, can you describe some
3 of the other contributions and roles that you have within the
4 vitreoretinal specialist community.

5 A. I've participated in a lot of national and
6 international societies, professional societies, within retina
7 and ophthalmology. I've been given the Senior Achievement
8 Award by the American Academy of Ophthalmology, the Senior
9 Honor Award by the American Society of Retina Specialists. And
10 these awards reflect scientific contributions that I've made to
11 the meetings over the years.

12 I'm a member of The Retina Society and serve on the
13 nominations committee for The Retina Society.

14 I'm a member of The Macula Society, serve on the
15 bylaws committee for the Macula Society. And I'm a founding
16 member of the Vit-Buckle Society, which has now become a large
17 organization focusing on mentorship of young surgeons in their
18 residency and fellowship and in the first part of their
19 careers.

20 I'm codirector now for the last, I think, five years
21 of the annual Angiogenesis meeting that was started by my
22 colleague Dr. Phil Rosenfeld, and I do that along with
23 Dr. Harry Flynn. The three of us are codirectors of one of the
24 largest scientific meetings dealing with angiogenic eye
25 disorders.

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1 I've been editor on the *Journal of Vitreoretinal*
2 *Diseases*, although I stepped down recently due to time
3 constraints. And I've been an editor for a professional
4 magazine called *Retina Today*, I think, for about 12 years.

5 Q. In the context of providing your opinions in this
6 matter, did you provide a definition for a person of ordinary
7 skill in the art?

8 A. Yes, I did. I believe it's on the next slide.

9 Q. Is that definition shown here on Slide 6?

10 A. That's correct.

11 Q. Now, I'm just going to take some time to read this
12 into the record so we have a clear record of what that
13 definition was.

14 THE COURT: Slowly, please, Counsel.

15 MR. McLAUGHLIN: Understood.

16 BY MR. McLAUGHLIN:

17 Q. So from paragraph 91 of your expert report it begins:

18 "After considering the above-mentioned factors, it is
19 my opinion that a person of ordinary skill in the context of
20 both the '601 patent and the '572 patent would have:

21 "1. Knowledge regarding the diagnosis and treatment
22 of angiogenic eye disorders, including the administration of
23 therapies to treat said disorders; and

24 "2. The ability to understand results and findings
25 presented or published by others in the field, including the

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1 publications discussed herein.

2 "Typically, such a person would have an advanced
3 degree, such as an MD or PhD, or equivalent or less education
4 but considerable professional experience in the medical,
5 biotechnological, or pharmaceutical field with practical
6 academic or medical experience in:

7 "1. Developing treatments for angiogenic eye
8 disorders, such as AMD, including through the use of VEGF
9 antagonists; or

10 "2. Treating of same, including through the use of
11 VEGF antagonists."

12 Did I read that correctly?

13 A. That's correct.

14 Q. And in your opinion, do you meet the definition of a
15 POSA with regard to the '601 and '572 patents?

16 A. I believe I do. I hold an advanced degree; I think I
17 can understand a publication result; and I diagnose and treat
18 those disorders.

19 Q. Would you have met that definition in the 2010 time
20 frame?

21 A. Yes, I would have.

22 Q. At this time could you please turn to DTX 8205 in
23 your -- set of binders you've been provided.

24 A. I'm not sure where the binders are. Maybe I should
25 have grabbed that.

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1 THE COURT: Of all people, the witness does not have
2 a binder.

3 One second, Doctor.

4 THE WITNESS: I apologize.

5 You're directing me to Volume 1?

6 BY MR. McLAUGHLIN:

7 Q. DTX 8205.

8 A. I recognize that document. Yes, I see it.

9 Q. Is that a copy of your current CV?

10 A. That's correct.

11 MR. McLAUGHLIN: So, Your Honor, at this point we
12 would like to move to admit DTX 8205, Dr. Albini's CV, into
13 evidence.

14 THE COURT: Any objection?

15 MS. OBERWETTER: No objection, Your Honor.

16 THE COURT: Without objection, so admitted.

17 (DTX 8205 was admitted.)

18 MR. McLAUGHLIN: At this time we also proffer
19 Dr. Albini as an expert in the diagnosis and treatment of
20 vitreoretinal disease.

21 THE COURT: Any voir dire or objection?

22 MS. OBERWETTER: Yes, Your Honor, as follows. We
23 don't have any objection to him being offered as a treater of
24 angiogenic eye disorders. We have some concern there are going
25 to be opinions elicited today on formulation topics. We do not

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1 believe that Dr. Albinì is an expert on formulation issues.
2 And if he intends to speak on his own account about what
3 certain references do or do not disclose about formulations, we
4 do have voir dire from that standpoint, Your Honor.

5 THE COURT: We'll take that up if and when we tread
6 into those grounds.

7 But no objection to the present motion as a treater
8 of these certain eye disorders, correct?

9 MS. OBERWETTER: Correct, Your Honor.

10 THE COURT: Without objection, that motion is
11 granted, and the doctor is deemed so qualified.

12 MR. McLAUGHLIN: Thank you, Your Honor.

13 BY MR. McLAUGHLIN:

14 Q. Turning to Slide 7. Dr. Albinì, before we get to the
15 substance of your opinions, did you conduct your analysis from
16 the perspective of a person of ordinary skill in the art as you
17 described it as of January 2012?

18 A. I did. And I reviewed the subject matter of the
19 dosing patents and of the asserted claims, the prior art
20 prosecution histories, the technology at issues. And I bring
21 to that my 20 years of experience as described.

22 Q. In the context of formulating your opinions, did you
23 review Dr. Csaky's responsive expert report in this case?

24 A. I did.

25 Q. And did Dr. Csaky provide a definition of a person of

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1 ordinary skill in the art that is different from your
2 definition?

3 A. He did.

4 Q. Would your analysis change under Dr. Csaky's
5 definition of a person of ordinary skill in the art?

6 A. No.

7 Q. Let's turn to a little bit of a background about this
8 case, just starting with Slide 9.

9 Have you assessed in this matter the issue of
10 invalidity with respect to U.S. Patent Numbers 10,888,601 and
11 11,253,572?

12 A. I have.

13 Q. Is it okay if I refer to those as the '601 and the
14 '572 patents going forward?

15 A. Yes.

16 Q. Would it also be okay if I refer to those as the
17 dosing patents in some instances today?

18 A. Yes.

19 Q. You'll understand I'm referring to the '601 and '572
20 patents?

21 A. I will.

22 Q. So let's talk about the asserted claims. Do you
23 understand that the claims shown here on Slide 10 are the
24 claims that are being asserted in this matter by Regeneron?

25 A. That's correct.

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1 Q. Those include Claims 11 and 19 of the '601 patent and
2 Claims 6 and 25 of the '572 patent?

3 A. That's right.

4 Q. Are you rendering opinions on the anticipation and
5 obviousness of each of those patents?

6 A. Yes.

7 Q. Do you understand that other experts will be opining
8 on certain elements of one or more of those patent claims?

9 A. Yes.

10 Q. And one of those, you understand, will be
11 Dr. Rabinow --

12 A. That's correct.

13 Q. -- writing opinions with respect to Claim 6?

14 A. That's correct.

15 Q. Did you rely on Dr. Rabinow for opinions regarding
16 Claim 6?

17 A. Yes, I did. I do not see myself as an expert in
18 formulation, just in vitreoretinal disorders and their
19 treatment. So I did rely on him in that regard.

20 Q. If we flip ahead to Slide 11 here, can you briefly
21 provide a description to the Court of the opinions that you're
22 going to be presenting today?

23 A. The basic arguments are going to be that these
24 claims, as you outlined -- the DME, DR claims -- are
25 anticipated by the September 14th, 2009 Regeneron press release

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1 and the 1999 '747 patent; that they are also obvious through
2 those prior art pieces in combination with others; and that the
3 patent Claim 6 of the '572 patent as regards formulation is
4 anticipated and obvious.

5 Q. Dr. Albin, I would like to start by talking about a
6 little bit of scientific background before we delve into your
7 opinions and the ways of treating various angiogenic eye
8 disorders before 2011.

9 Let's start with the anatomy of the eye. Can you --
10 and the Court has heard a lot of this already, but can you
11 briefly describe what you've shown here on Slide 13?

12 A. Sure. This is a cartoon cross section of the eye,
13 showing the front parts of the eye, the cornea -- the clear
14 part that you see when you look into somebody's eyes -- and the
15 lens.

16 And the -- shows deeper into the eye. You have the
17 vitreous gel, which occupies most of the volume of the eye,
18 especially that back component. And then that orange-colored
19 tissue that you see there is sort of the wallpaper lining of
20 the inside of the eye called the retina. This is neurologic
21 tissue that connects to the optic nerve and sends visual
22 impulse information back to the brain for you to be able to
23 see.

24 And if you want to progress the slides, this cartoon
25 starts to move.

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1 When light comes into the eye, it goes -- it's
2 focused by the cornea and the lens onto the fovea. The fovea
3 is a specific part of the macula, the center part of the
4 macula, and the macula is a part of a retina in general.

5 And that's the part where you have your highest
6 definition vision. That is the part that's affected by the
7 diseases at issue here, both diabetic macular edema and
8 exudative, or wet, macular degeneration.

9 In those disease states, either because the blood
10 vessels are leaky, as they are in diabetic macular edema, or
11 because they're leaky because of abnormal growth of vessels
12 that develops in macular degeneration, the retina becomes
13 distorted which, in turn, distorts your vision.

14 And the miraculous discovery over the last two or
15 three decades is that a lot of that disease process is driven
16 by a molecule called vascular endothelial growth factor and
17 that blocking this vascular endothelial growth factor not only
18 causes some of these immature blood vessels to disappear, but
19 it decreases the fluid buildup and consequent distortion of the
20 retina; and, even more miraculously, it improves patient's
21 vision. And this blockage has been responsible for greatly
22 reducing cases of blindness due to macular degeneration and
23 diabetic macular edema over the last few decades.

24 Q. Thank you, Dr. Albin.

25 Now, I'd like to shift to a discussion of state of

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1 the art and the background with regard to what was known prior
2 to 2011, including with respect to some of these VEGF
3 inhibitors that you just made reference to.

4 Do you understand first -- we'll be filling in this
5 timeline as we go along, but do you understand that 2011 to be
6 the year the patents-in-suit were filed?

7 A. That's my understanding.

8 Q. Let's start by talking about the VEGF drugs that were
9 being administered in trials -- or the clinic prior to 2011.

10 Would that have included ranibizumab?

11 A. Ranibizumab and bevacizumab -- a very similar
12 molecule to ranibizumab but different in many ways -- were the
13 two main agents that were in use prior to the 2011 date.

14 Q. And was aflibercept also being tested in clinical
15 trials prior to 2011?

16 A. It was available for clinical trial use only, that's
17 correct.

18 Q. So if we flip to Slide 21, can you describe what's
19 shown here on this slide, Dr. Albin.

20 A. This is a review article that was published in 2009
21 by Dixon and coauthors, and it describes the -- what became
22 known as the aflibercept molecule. It's VEGF Trap-Eye, which
23 was a scientific name, as Dr. Yancopoulos testified the other
24 day, that was used for this molecule prior to the aflibercept
25 name and the Eylea names being given to it. But it is a fusion

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1 protein with key binding receptors of the VEGF receptor 1 and
2 receptor 2 fused with the FC portion of an antibody.

3 Q. And here on the slide you're referring to DTX 0204,
4 pages 1 and 3 from the Dixon reference?

5 A. That's correct. Also here there is another reference
6 from Adis in 2008 which makes reference to the same protein.

7 Q. And Adis, that's DTX 4008 that you're referring to?

8 A. That's correct.

9 Q. What's the year of the Dixon reference?

10 A. 2008.

11 Q. And was VEGF Trap-Eye also known as aflibercept in
12 the prior art?

13 A. That's correct.

14 Q. And is that shown here on Slide 22 in excerpts from
15 DTX 0204 and DTX 4008?

16 A. Especially in the Adis 2008 article. The title of
17 the article itself is "Aflibercept."

18 Q. In the abstract of Adis, the reference is
19 aflibercept, and it says that Regeneron and Bayer are
20 developing the agent for eye disorders?

21 A. That is correct.

22 Q. And turning to the next slide, Slide 23, you've shown
23 the '747 patent on the left hand. Is that one of the patents
24 and references you've relied on in forming your opinions in
25 this case?

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1 A. That is correct.

2 Q. And did the '747 patent recite a molecule called
3 VEGFR1R2-Fc delta C1(a)?

4 A. That is correct. That is the name given to the
5 fusion protein of the VEGF receptor 1 and 2 bound with the Fc
6 receptor that was in clinical use.

7 Q. Is that molecule also known as aflibercept?

8 A. That is correct.

9 Q. Flipping ahead to Slide 24, this is another
10 disclosure from the '747 patent that you provided here.

11 Does the '747 patent disclose a method of treatment
12 for an angiogenic eye disorder?

13 A. It does. In the specification there are outlined
14 patient visits that should occur when the patients are being
15 treated with this molecule, and it says that after the first
16 30 days, the patient should return for periodic examinations on
17 a monthly basis thereafter.

18 It also describes that the patient needs to be
19 continuously monitored through periodic examinations for fluid
20 in the retina. And at the time fluorescein angiography is
21 mentioned as an imaging modality to do that with. And it also
22 mentions that, in a preferred embodiment of what's taught in
23 this patent, the initial treatment is followed by subsequent
24 treatments that are given at dosing intervals ranging from one-
25 to six-month dosing intervals.

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1 Q. And looking at the face of the '747 patent, do you
2 see the date of the '747 patent's priority application?

3 A. I'm not so clear on all of the legal terms; so
4 maybe -- but I see the date there, December 4th, 2007, although
5 my recollection is that this patent was first filed in 1999.

6 Q. Thank you.

7 And flipping to the next slide, Slide 25, is that
8 '747 patent now reflected on this timeline that you've
9 provided?

10 A. Yes.

11 Q. And that '747 patent, that's DTX 2730?

12 A. That's correct.

13 Q. Now, moving on to Slide 26, let's talk about some of
14 the other VEGF inhibitors that were known and being used by
15 ophthalmologists before the '601 and '572 patents were filed.

16 What was the first anti-VEGF antibody approved by the
17 FDA for treating an angiogenic eye disorder?

18 A. The first antibody molecule that was approved was
19 ranibizumab. There was a prior medicine called Macugen, which
20 was an aptamer. It's a slightly different type of technology.
21 It is a binding molecule much like these others all targeting
22 various subtypes of vascular endothelial growth factor.

23 Ranibizumab became FDA approved for use in wet
24 macular degeneration in 2006. And what we have here is a
25 picture of the label of the drug with an excerpt describing

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1 dosing frequencies of intravitreal injection once a month and
2 another approved dosing regimen of one injection every three
3 months for the first four injections and quarterly injections
4 thereafter.

5 The other main drug in use was bevacizumab.
6 Bevacizumab is quite an interesting story. It's another
7 molecule that also targets vascular endothelial growth factor.
8 It was also developed by the Genentech. Both these drugs were
9 developed by Genentech.

10 Ranibizumab was developed specifically for use in the
11 eye while bevacizumab was developed for intravenous use in
12 cancer patients. Bevacizumab was available prior to the
13 availability of ranibizumab. And in 2005 a number of
14 physicians began to inject bevacizumab off-label intravitreally
15 to treat angiogenic eye disorders. There was already good data
16 coming from Phase II studies and other studies showing that
17 there was great efficacy with ranibizumab.

18 And there was a desire to have this efficacy
19 available to patients before the molecule was actually approved
20 by the FDA; so bevacizumab was used. And that quickly in 2005
21 spread throughout the world, where this became the major drug
22 that was used in this sphere. And it remains to this day
23 probably used just as often as the name-brand drugs in the
24 United States.

25 One of the main driving factors for the use of

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1 bevacizumab, even though it's not specifically FDA-approved for
2 this indication, is a huge differential in cost. The
3 ranibizumab was approximately \$2,000 per injection whereas
4 bevacizumab, when you bought a bag of drug for intravenous use
5 and you aliquoted it out to inject it into the eye, the cost of
6 a single ocular injection came out to about \$50. So it was a
7 great drug to have especially for patients of limited means.

8 Q. In your discussion of the ranibizumab label that we
9 just had prior to your discussion of bevacizumab, were you
10 referring to DTX 4056?

11 A. That is correct.

12 Q. Thank you.

13 If we flip ahead, can you briefly tell the Court what
14 you've shown here on Slide 27 with respect to ranibizumab and
15 how it was being used in clinical trials?

16 A. These are three outcomes from trials with ranibizumab
17 that were available in the 2006 to 2008 time frame. And I
18 think these are really important graphs of top-line data from
19 these drugs.

20 The first to the left is the top-line visual acuity
21 results from the ANCHOR trial of monthly ranibizumab for the
22 treatment of wet macular degeneration.

23 The line that you see there going down on the bottom
24 is the control arm. And that was treatment with standard of
25 care at the time, which was a type of laser and photodynamic

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1 intravenous treatment called photodynamic therapy. That was
2 the best treatment that we had when I was a resident. And as
3 seen there, patients continued to lose vision. Although they
4 lost vision less quickly than they might have without this
5 therapy, it just retarded the rate of vision loss, but patients
6 still continued to lose vision.

7 The really earth-shattering result that was seen in
8 ANCHOR study and other studies, the MARINA study which we'll be
9 talking about later, was this quick rise in visual acuity that
10 was then maintained over time as you see in the other two lines
11 that go up to where patients are gaining about ten letters,
12 what we call ETDRS letters of visual acuity. That translates
13 into being able to read two lines further down on the eye
14 chart, roughly, in that area. So that was really a very
15 welcome and amazing improvement in the treatment of macular
16 degeneration.

17 In the center box you see the top-line data from a
18 smaller prospective study called the PrONTO study, which just
19 to have institutional pride, was performed at Bascom Palmer Eye
20 Institute. And this study tested the concept whether we could
21 reduce injections, not necessarily inject patients every month
22 as was done in the original ranibizumab study, but make
23 decisions on a monthly basis whether or not a patient needed an
24 injection by considering certain clinical factors and
25 considering the state of the retina, especially as evidenced by

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1 imaging technologies, newer technologies that were available at
2 the time, especially something called optical coherence
3 tomography, or OCT, examinations, which are now pretty
4 ubiquitous in the retinal world as a way of evaluating the
5 health of the macula.

6 So this study showed, as you can see there, that you
7 could get very profound benefit and visual acuity results,
8 really very nicely mirroring the benefits that you see in
9 ANCHOR with this as-needed treatment strategy. This is the
10 so-called prn treatment strategy which became very popular very
11 quickly in that 2007 and beyond range.

12 And, finally, you have the results of a quarterly
13 dosing study with ranibizumab, the EXCITE study, which showed
14 that monthly dosing, which is the triangle line up on top,
15 outperformed quarterly dosing. So these were initial monthly
16 loading doses and then followed by quarterly dosing. And that
17 although that treatment strategy resulted in a success compared
18 to photodynamic therapy, certainly compared to observation
19 alone and no treatment, it was not as good as monthly dosing.

20 Q. And when you were referring to these charts here,
21 you're referring to excerpts from DTX 4061?

22 A. That's correct.

23 Q. With respect to the PrONTO study, did you also rely
24 in the process of formulating your opinions on DTX 3115, the
25 Fung 2007 reference?

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1 A. I did.

2 Q. Now, turning to the next slide, could you tell the
3 Court a little bit about how bevacizumab was being used in the
4 clinic and how it was being evaluated in clinical trials?

5 A. This is a clinical trial of bevacizumab for exudative
6 macular degeneration, a one-year prospective study, showing
7 that this drug could be used to obtain similar results with
8 that seven- to eight-letter gain by 12 months. And this was
9 also done with initial loading doses and then reinjection of
10 the drug on an as-needed basis going forward.

11 Q. So flipping back to the timeline now, so just to
12 summarize, by 2006 there was an anti-VEGF agent, ranibizumab,
13 that had been approved for monthly dosing and for every-12-week
14 dosing?

15 A. That's correct.

16 Q. And by 2007 the results of the PrONTO study using
17 as-needed maintenance dosing, had that been reported?

18 A. That's correct.

19 Q. And by 2008 had data been reported with respect to
20 the use of bevacizumab in the treatment of AMD and is that
21 reflected here --

22 A. Yes.

23 Q. -- on the timeline?

24 I would like to shift focus a little bit. And can
25 you tell the Court how ranibizumab was being used in the

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1 context of treating DME in that time frame.

2 A. This is a review article by Dr. Lalwani from 2009
3 that reviews the results of a early study with ten patients who
4 received injections of ranibizumab at baseline, month one and
5 month two, so essentially three loading doses, and then
6 received q8-week dosing for the month four and six. And it
7 showed that there was good visual acuity gains from this
8 treatment strategy in this small number of patients with
9 diabetic macular edema.

10 Q. Is that Lalwani reference now referenced on this
11 timeline here at Slide 31?

12 A. That is correct.

13 Q. And that's from DTX 2733?

14 A. That's correct.

15 Q. Now, turning to the next slide and turning back to
16 that Dixon reference which you've referenced earlier, was
17 aflibercept being used in a Phase II AMD trial prior to 2011?

18 A. The Dixon article from 2009 describes both --
19 describes a Phase II study, the CLEAR-IT 2 study, of
20 2 milligrams for 12 weeks of the -- of aflibercept being used
21 followed by a prn treatment regimen after the loading dose
22 phase of the study.

23 And it also describes a Phase III study for wet
24 macular degeneration using the 2-milligram dose administered
25 either every four weeks or every eight weeks and compared to

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1 ranibizumab.

2 Q. And these are selections from DTX 0204?

3 A. That's correct.

4 Q. And flipping to the next slide, Slide 33, can you
5 tell the Court how else aflibercept was being used prior to
6 2011?

7 A. This is a Regeneron press release dated
8 September 14th, 2009. And it describes a Phase III study in
9 retinal vein occlusion. That's another angiogenic eye disorder
10 treated -- VEGF-driven and treated with these same agents. And
11 this describes a protocol with six monthly doses and then prn
12 dosing thereafter.

13 And it also describes a Phase II study in diabetic
14 macular edema with a monthly arm, also an arm where there were
15 three monthly loading doses and then every-eight-week
16 injections and another arm where there were three monthly doses
17 and prn injections going forward.

18 Q. And those selections are from DTX 3198?

19 A. That's correct.

20 Q. Can you tell the Court how aflibercept was being used
21 in the treatment of DME prior to 2011?

22 A. This is a manuscript from Do in 2009. And it
23 describes a small study of a single injection of 4 milligrams
24 of aflibercept in a small number of patients, and it describes
25 a visual acuity benefit from that single injection.

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1 Q. And that visual acuity benefit, again, that was nine
2 letters at one month?

3 A. That's correct, which is an impressive benefit.

4 Q. And are those Dixon disclosures and the Do
5 disclosures referenced here on the timeline at Slide 35?

6 A. Yes.

7 Q. So now we've reviewed what was being done in clinical
8 trials up to now. Let's shift focus and discuss what
9 physicians were doing in actual clinical practice before 2011.

10 So on this next slide, Slide 36, can you explain
11 what's shown here?

12 A. These are excerpts from a roundtable discussion that
13 was published in a professional journal called Retinal
14 Physician in 2007. And I think this is a great way to get a
15 snapshot of what the POSA was thinking at that time.

16 These are three prominent retina specialists in the
17 United States, and they're describing their treatment
18 protocols. The first one there is Dr. Rosenfeld from Miami.
19 He was the lead investigator and designer of the PrONTO study.
20 And he describes his treatment regimen trying to minimize the
21 number of injections but treat the patients until there's no
22 fluid in the retina. And once they're dry, then having the
23 ability to skip those injections.

24 Dr. Reichel from Boston also says that he's a big
25 believer in prn dosing. He gives only one injection on a

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1 routine basis, sees the patient four weeks later, and already
2 makes a decision whether or not to re-treat. So this would be
3 a regimen that would be essentially one loading dose, or just a
4 single primary dose, followed by immediate prn protocol
5 injections.

6 And Dr. Hariprasad from Chicago also gives his
7 opinion that he doesn't necessarily give three full loading
8 doses, but he gives monthly injections until the patient's
9 retina is dry and then presumably stops injecting until there's
10 reaccumulation of fluid.

11 THE COURT: Counsel, if I could interrupt.

12 Doctor, when you reference dry, you're referring to
13 the elimination of any leakage or bleeding from the
14 VEGF-spurred blood vessels and the rest; is that correct?

15 THE WITNESS: Yes. I'm so sorry that I didn't
16 explain that.

17 So we often use that as a colloquial term for seeing
18 that there's been resolution of fluid. And you're right on
19 point there with what that means. That's right.

20 THE COURT: When you say fluid, would there be any
21 other fluids that are offshoots of these various diseases of
22 the eye other than blood?

23 THE WITNESS: So most of the fluid is clear. It
24 doesn't have red blood cells in it. It's a serous fluid that's
25 in there that extrapolates from the vessels. But the red blood

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1 cells are usually contained within the vessels. You can have
2 blood also. So it can be either blood, but the majority of the
3 time it's actually not full blood.

4 THE COURT: But it's fluid that's coming from the
5 blood vessels?

6 THE WITNESS: That's exactly right.

7 THE COURT: Understood. Thank you.

8 Sorry, Counsel. Go right ahead.

9 THE WITNESS: Sorry I didn't explain that better.

10 THE COURT: Oh, no. That's good.

11 Go ahead, Counsel.

12 BY MR. McLAUGHLIN:

13 Q. The excerpts that you've been referring to, those are
14 coming from DTX 2035?

15 A. That's correct.

16 Q. Turning to the next slide, Slide 37, can you describe
17 what's shown here?

18 A. This is a quote from the same roundtable discussion.
19 This is Dr. Brown from Houston, Texas, another prominent retina
20 specialist. And he says that he uses treat and extend from the
21 start. I'd just like to point out to everybody that this is
22 back in 2007 that he's describing this treatment strategy.

23 The treat-and-extend strategy is another strategy
24 that came into vogue slightly after the prn strategy, but the
25 concept here was to not only reduce the number of injections

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1 but to reduce the number of visits that patients needed to come
2 back. And so that if a patient established themselves as
3 someone who was -- who could maintain the retina free of fluid
4 for a longer period of time, then the physicians became
5 comfortable with having those patients come in at longer
6 periods to minimize the burden of visits over time.

7 And so this is just a nice historical document
8 showing that already in 2007 this type of treatment strategy
9 was indeed being employed.

10 Q. Is that something that you employed in your own
11 practice prior to 2011?

12 A. Yes.

13 Q. Was Dr. Brown's description of treat and extend
14 consistent with the general understanding of the
15 treat-and-extend regimen in that time frame?

16 A. Yes.

17 Q. And turning to the next slide, Slide 38, can you
18 describe what you've shown here?

19 A. This is a survey result from a survey that's
20 performed by the American Society of Retina Specialists every
21 year. And it basically serves as a way to communicate amongst
22 the profession what the treatment modalities are, treatment
23 trends are within the community of retina specialists.

24 So this -- for example, this question is asking
25 physicians to identify what their treatment strategy is for

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1 exudative macular degeneration or wet macular degeneration.

2 And in 2010, out of 337 respondents to this survey, 43 percent
3 said they were using a prn strategy and 34 percent were already
4 using a treat-and-extend strategy.

5 Q. Turning to the next -- sorry. Flipping back just to
6 confirm, you're referring to DTX 2040?

7 A. Yes.

8 Q. Flipping to the next slide, Slide 39, can you explain
9 what's shown here?

10 A. This is an article showing a study result for
11 intravitreal bevacizumab -- that's Avastin -- for myopic
12 choroidal neovascularization, a short-term and one-year result.
13 And the interesting thing to me was that this is already making
14 reference to the treat-and-extend approach, just to document
15 that this was already something that was seen as a treatment
16 strategy that was well known within the field in 2009 by the
17 time this was published.

18 Q. And this is from DTX 4113?

19 A. That is correct.

20 Q. So are all these references that you've been
21 discussing over the last several slides represented here on
22 Slide 40 of your presentation?

23 A. Yes.

24 Q. So let's just wrap this up and summarize what we've
25 gone through and what we've now shown on this timeline.

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1 So in terms of drugs that were available, would that
2 have included ranibizumab, bevacizumab, and then aflibercept
3 being in clinical trials prior to 2011?

4 A. Yes.

5 Q. And what types of dosing regimens had been reported
6 with respect to those agents?

7 A. There were fixed regimens such as monthly fixed or a
8 number of loading doses, and then every eight -- then
9 every-eight-week injection on a regular basis; a number of
10 loading doses, and then every-12-week injections given on a
11 fixed basis. There were also individualized regimens such as
12 the PrONTO study that sought to evaluate patients and make
13 decisions about whether or not to reinject on a patient basis.

14 And those included the treat-and-extend protocol that
15 we've discussed, the loading doses and then prn regimens that
16 we've discussed, and continuous injection until the macula is
17 dry as Dr. Hariprasad evidenced in his quote. And this was
18 across the indications of exudative or wet macular
19 degeneration, diabetic macular edema, diabetic retinopathy, and
20 retinal vein occlusion.

21 Q. Dr. Albin, do you intend to provide testimony today
22 regarding the invalidity of the '601 and '572 patent claims?

23 A. Yes, I do.

24 Q. Would that include Claims 11 and 19 of the '601
25 patent and Claim 25 of the '572 patent?

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1 A. That's correct.

2 Q. Is it okay if, going forward, I refer to those as the
3 DME-DR treatment claims?

4 A. Yes.

5 Q. So can you briefly describe for the Court the
6 anticipation opinions that you're going to be giving in this
7 portion of your testimony?

8 A. Every limitation within the claims that we're
9 discussing is either explicitly or inherently available within
10 two single references: the September 14th, 2009, press
11 release from Regeneron and also in the U.S. patent '747 that
12 we've discussed that was filed back in 1999.

13 Q. Let's start -- we're on Slide 46 now. Let's start
14 with a discussion of these claims.

15 So you've reviewed the '601 and '572 patents,
16 correct?

17 A. Yes.

18 Q. Have you reviewed Claim 11 of the '601 patent?

19 A. I have.

20 Q. Is that what's shown here on Slide 46?

21 A. That's correct.

22 Q. And do you understand that Claim 11 of the '601
23 patent depends from independent Claim 10 of the '601 patent?

24 A. Yes.

25 Q. Can you describe in your own words for the Court the

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1 dosing regimens set forth in Claims 10 and 11 of the '601
2 patent?

3 A. Yeah. In these two claims taken together, they
4 describe a dosing strategy using 2 milligrams of aflibercept
5 for treating diabetic macular edema given as five initial
6 monthly loading doses or five initial monthly injections
7 followed with subsequent eight-week injections.

8 Q. And looking at the language of Claim 11, when it says
9 every 28 days, for example, would you understand that the
10 disclosure of something occurring exactly every 28 days as the
11 type of regimen that would fall within the scope of this claim?

12 A. Exactly every 28 days would certainly fall within the
13 scope of approximately every 28 days, that's correct.

14 Q. Turning to the next slide, Slide 48, did you also
15 review Claim 19 of the '601 patent?

16 A. Yes, I did.

17 Q. You also reviewed the claim from which it depends,
18 Claim 18?

19 A. Yes.

20 Q. Can you describe in your own words for the Court the
21 dosing regimen set forth in Claims 18 and 19 of the '601
22 patent?

23 A. This is the same dosing regimen set forth in the 10
24 and 11 claims. And in these claims the disease state is
25 different. This is being used for the larger disease entity

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1 called diabetic retinopathy, including other types of diabetic
2 disorders of the retina in addition to macular edema.

3 And here it describes again the administration of
4 2 milligrams of aflibercept with five initial loading doses
5 followed by q8-week regular dosing.

6 Q. Can you briefly describe the relationship between DME
7 and DR?

8 And by the way, is it okay if I refer to diabetic
9 macular edema as DME and diabetic retinopathy as DR going
10 forward?

11 A. That's fine with me. I hope it's fine with everybody
12 else.

13 THE COURT: I think I've got those acronyms down by
14 now, Doctor. So if it works for you, it works for me.

15 THE WITNESS: Fantastic.

16 So I think that DME is technically a type of diabetic
17 retinopathy. It is a diabetic eye disease of the retina. It
18 is a specific subtype of diabetic retinopathy. It is the most
19 common cause of mild to moderate loss in diabetic patients,
20 very commonly seen. And it is usually described as a
21 complication of diabetic retinopathy or a subtype of diabetic
22 retinopathy.

23 BY MR. McLAUGHLIN:

24 Q. Flipping to Slide 49, have you reviewed Claim 25 of
25 the '572 patent?

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1 A. Yes, I have.

2 Q. And you've reviewed the claim from which it depends,
3 Claim 15?

4 A. Yes, I have.

5 Q. Can you briefly describe the -- how you understand
6 the subject matter of Claims 15 and 25 of the '572 patent?

7 A. These two claims describe an identical treatment
8 strategy for diabetic macular edema, again administering
9 2 milligrams of aflibercept with at least five initial monthly
10 injections and subsequent eight-week injections.

11 Q. In your opinion, are there any substantive
12 differences between Claim 25 of the '572 patent and Claim 11 of
13 the '601 patent?

14 A. No.

15 Q. If we could turn to Slide 50. So turning to the
16 references that you referred to earlier, I believe what you've
17 shown on the left here is the 9-14-2009 press release. Is that
18 the reference that you relied upon?

19 A. That's correct.

20 Q. And shown on the right is the '747 patent. That's
21 patent number 7,303,747, DTX 2730. Is that one of the other
22 references you relied upon in your anticipation --

23 A. That's correct.

24 Q. And turning to the next slide, can you explain what
25 you have highlighted here on Slide 51?

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1 A. This is a text from the Regeneron press release
2 describing a Phase II DME VEGF Trap-Eye, or aflibercept, study
3 using the 2-milligram dose. There were three dosing arms or
4 dosing strategies described in this press release for DME. One
5 was a monthly dosing arm or a three monthly injections followed
6 by prn dosing thereafter. And there was a third strategy
7 described of three monthly injections and then every-eight-week
8 dosing thereafter.

9 Q. When looking at the 2-milligram dose of VEGF Trap-Eye
10 reported here, would a POSA have understood that to refer to an
11 intravitreal dose of aflibercept?

12 A. Yes. VEGF Trap-Eye, as far as I know, was only
13 available for intravitreal use in clinical trials at the time.

14 Q. And just another housekeeping matter. We've used the
15 acronym POSA a couple times. Just so the record is clear --

16 A. A POSA is a person of ordinary skill in the art, of
17 which I believe I am one and was one.

18 Q. Thank you.

19 Turning to the next slide, you mentioned a prn dosing
20 scenario mentioned in this 2009 press release. Can you explain
21 how a POSA would have understood a prn dosing scenario in that
22 time frame?

23 A. So I think that the dosing regimen that's described
24 stipulates that the patient receive three monthly injections at
25 the beginning of treatment. And then thereafter decisions are

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1 made whether or not to inject based on clinical measures and
2 imaging findings for that patient.

3 One can immediately envision that a patient might
4 require three initial loading doses and might require that a
5 fourth injection when they come in for that visit and then have
6 a subsequent visit where there's no injection required,
7 resulting in an eight-week interval.

8 Q. And in typical prn dosing scenarios used in that time
9 frame, monthly visits were the norm?

10 A. That's correct.

11 Q. You mentioned immediately envisioning a dosing
12 scenario. So is that something you've illustrated here on
13 Slide 53 of your presentation?

14 A. Yeah. I think this graphic helps greatly to
15 understand the point here. But what's seen there is the
16 syringes represent injections for the patient, those monthly
17 visits. And the first three are with blue needles, and those
18 represent the monthly loading doses that would be described in
19 that treatment strategy.

20 At Week 12 and Week 16 you see green needles
21 representing doses that are given during the prn portion of the
22 study. At Week 20, presumably, the patient meets criteria by
23 lack of fluid in the retina, does not require that injection,
24 and then comes back at Week 24 and, again, does require an
25 injection.

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1 So in the end what you have is five regular monthly
2 injections with an eight-week gap and then the sixth injection.

3 Q. Turning to Slide 54, can you explain how that
4 scenario relates to Claim 11 of the '601 patent?

5 A. This treatment strategy, this particular iteration of
6 the prn dosing schedule, is identical to the treatment strategy
7 that's laid out in Claims 10 and 11 and 18 and 19. In every
8 real sense the same number of injections are given at the same
9 time periods and are the same treatment.

10 Q. So the three monthly loading doses given at Weeks 0,
11 4, and 8 followed by the two prn treatments at Weeks 12 and 16,
12 those would be injections given every four weeks for the first
13 five injections?

14 A. That's correct.

15 Q. And then the injection given at Week 24, after having
16 skipped an injection at Week 20, that would be an injection
17 given once every eight weeks?

18 A. That's correct. I think the POSA would immediately
19 envision this type of a treatment protocol when a treatment
20 strategy of three monthly loading doses and prn dosing
21 subsequently are entertained.

22 Q. Would that same analysis apply to Claim 19?

23 A. That's correct.

24 Q. Turning to Slide 55, would that same analysis also
25 apply to Claim 25 of the '572 patent?

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1 A. That's correct.

2 Q. Now, the claim language is a little bit different
3 here; so let's just walk through the claim language real quick.

4 The dose given at time zero, that would be the single
5 initial dose of 2 milligrams of aflibercept?

6 A. That's correct.

7 Q. And then the next two loading doses given under that
8 prn scenario followed by the two prn doses at Weeks 12 and 16,
9 those would be the four secondary doses required by Claim 25?

10 A. That's correct.

11 Q. And then the injection given at Week 24, that would
12 be the one or more tertiary doses?

13 A. That's correct.

14 Q. So turning to Slide 56, can you explain to the Court
15 what you have shown here with respect to the '747 patent.

16 A. This is the older patent which we were relying upon
17 as a source for anticipation for the DME-DR claims. And it
18 describes improved pharmacokinetics with the use of the
19 aflibercept or VEGF Trap-Eye molecule for age-related macular
20 degeneration and mentions diabetic retinopathy as well.

21 Q. If we turn to the next slide, Slide 57, you have
22 highlighted here a selection from the '747 patent highlighting
23 that molecule name.

24 Why do you have that molecule name highlighted from
25 the '747 patent?

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1 A. Yeah, just showing that there's a clear line that can
2 describe to the POSA the exact molecule that's being discussed
3 and that there is no ambiguity in the '601 and '572
4 specification that this is aflibercept.

5 Q. Turning to the next slide, Slide 58, what have you
6 highlighted here from the '747 patent?

7 A. The dosing range of aflibercept that's being taught
8 in the '747 patent is a dosing range of 25 to 4,000 micrograms,
9 and I just wanted to make the point that the 2-milligram dose
10 of aflibercept, which we've been mentioning over and over
11 again, falls within that range. That's 2,000 micrograms. So
12 it's within the range of what's described in the '747 patent.

13 Q. Does the '747 patent at this selection here at
14 DTX 2730, page 16, also reference an intravitreal injection of
15 the VEGF inhibitor?

16 A. That's correct.

17 Q. Turning now to Slide 59, looking again at the
18 DTX 2730, '747 patent, does the '747 patent here describe a
19 dosing regimen for the treatment of angiogenic eye disorders?

20 A. Yes. As we've mentioned previously, it describes an
21 initial injection given and then relates it in a preferred
22 embodiment and initial treatment is followed by subsequent
23 treatments given within one- to six-month intervals.

24 Q. Following such a treatment strategy as described in
25 the '747 patent with monthly examinations, would a POSA reading

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1 the '747 patent in 2010 immediately envision a scenario in
2 which a patient received four more monthly injections?

3 A. I believe that's true. In a very analogous fashion
4 to the discussion we just had, one of the iterations that one
5 immediately would envision is five initial doses given four
6 weeks apart and then a subsequent dose given eight weeks apart.

7 Q. And then could a POSA reading the '747 patent in 2010
8 immediately envisage a scenario in which, following a series of
9 monthly loading doses, the patient were assessed at the next
10 monthly visit and a decision was made to not give an injection,
11 for example, at Week 20?

12 A. The specifications for the '747 patent do describe in
13 some detail the need for continuous monitoring of patients,
14 including for retinal fluid, which is exactly what we do. And
15 so I think that, having read that patent, that would be very
16 easily envisioned, this type of a treatment protocol.

17 Q. Following the decision to withhold treatment at
18 Week 20, would a POSA, reading the '747 patent in 2010,
19 immediately envisage a scenario where, on the next visit at
20 Week 24, fluid had recurred and the patient required an
21 injection at that visit?

22 A. Yes.

23 Q. So turning to Claim 61, is that scenario that you
24 described accurately portrayed here on Slide 61?

25 A. That's correct.

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1 Q. Can you describe how that relates to Claim 11 of the
2 '601 patent?

3 A. Yeah. Again, there is a single primary injection
4 that's given at Week 0; and then at Weeks 4, 8, and 12 and 16,
5 a decision is made to reinject. At Week 20 there's no
6 injection required, and at Week 24 there is an injection that's
7 given eight weeks after the prior injection.

8 Q. So those injections at Weeks 0, 8, 12, and 16 would
9 be injections given every four weeks for the first five
10 injections?

11 A. That's right.

12 Q. And then the injection given at Week 24, that would
13 be an injection given once every eight weeks?

14 A. That's correct.

15 Q. Would the analysis be the same for Claim 19 of the
16 '601 patent?

17 A. That's correct.

18 Q. Turning to Slide 62, can you explain the -- or
19 summarize for the Court the opinions you're going to be giving
20 in this section of your testimony?

21 A. Yeah. I believe that, largely based on the same
22 sources in combination with some other sources which we'll go
23 through, that these -- all of these same claims that we've been
24 discussing are rendered obvious given what was known at the
25 date -- in the date.

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1 Q. Turning to Claim 63 -- or Slide 63, did you analyze
2 Claim 12 of the '601 patent in the process of formulating your
3 opinions in this case?

4 A. Yes. Claim 12 is dependent on Claim 10, and it
5 describes that after 20 weeks there's an administration of
6 aflibercept every four weeks, suggesting a change in the dosing
7 frequency at some points of every-four-week dosing at some
8 point after 20 weeks.

9 Q. Would your interpretation be the same for Claim 21 as
10 it relates to Claims 18 and 19 of the '601 patent?

11 A. That's true. Under this claim this particular
12 version of the dosing schedule would be similar to monthly
13 dosing and would be very similar to the monthly dosing regimens
14 which we talked about were the first dosing regimens for
15 ranibizumab that were used back in 2006.

16 Q. In this case did Dr. Csaky provide his interpretation
17 of Claim 12 of the '601 patent?

18 A. Yes, he did. While I think there a number of
19 interpretations that could be made of those two claim
20 combinations, he describes a scenario where the initial five
21 loading doses are given, as you see here, at Weeks 0, 4, 8, 12,
22 and 16. And then there's an eight-week loading dose -- there
23 is an eight-week injection given at Week 24, and at that point
24 the injection frequency is reverted back to a four-week dosing
25 schedule, as described here in this graph.

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1 Q. Did you understand Claim 12 to depend from Claim 10?

2 A. That's correct.

3 Q. Is it your understanding that, because Claim 12
4 depends from Claim 10, that Claim 10 also includes within its
5 scope the dosing scenario of Claim 12?

6 A. That's correct.

7 Q. Turning to Slide 67, was the monthly dosing of
8 aflibercept for the treatment of DME disclosed in the prior
9 art?

10 A. Yes.

11 Q. Where would that disclosure have come from?

12 A. This was in the Regeneron press release that we've
13 been describing from September 14, 2009. Describes a Phase II
14 clinical trial that included an arm with monthly dosing, as
15 we've mentioned before. And the claimed subject matter of the
16 combination of claims that we just discussed, including
17 Claim 12, are virtually identical to monthly loading doses,
18 certainly easily envisioned having a protocol with monthly
19 loading doses that one might miss a month at one point.

20 Q. This is an excerpt from DTX 3198?

21 A. That is correct.

22 Q. Would your analysis be the same with respect to the
23 '747 patent and the dosing regimen described therein?

24 A. That's correct. The dosing regimen described in the
25 '747 patent is somewhat broader, encompassing more treatment

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1 regimen possibilities. But it also describes an initial dose
2 with subsequent treatments given between one and six months
3 apart and so that these treatment strategies would fall within
4 the scope of these teachings as well.

5 Q. And these disclosures are from DTX 2730?

6 A. That is correct.

7 Q. So can you provide to the Court your overall opinions
8 on obviousness of Claims 11 and 19 of the '601 patent?

9 A. I would say that, due to the great similarity between
10 the virtually monthly treatment that's described once Claim 12
11 is incorporated in that Claim 10 and 11 and Claim 20 is
12 incorporated in the Claim 8 and 19 of the '601 patent, that
13 this dosing strategy is virtually indistinguishable from
14 monthly administration of aflibercept, which is well described
15 prior to 2011.

16 Q. Just to clarify the record, I think you said Claim 20
17 of the '601 patent. Would you be referring to -- I'll flip
18 back. Were you referring to Claim 21?

19 A. I was. I'm so sorry. Claim 21.

20 Q. No problem.

21 A. Thanks for catching that.

22 Q. Then can you -- now we're on Slide 70, and can you
23 describe what you've shown here on Slide 70 of your
24 presentation?

25 A. I picked a reference to speak to the reasonable

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1 expectation of success that was available, knowing the clinical
2 data from aflibercept in that period prior to 2011.

3 This is a report of a Phase I study from 2009 by
4 Diana Do that shows the outcomes from a single injection of
5 4 milligrams of aflibercept with, as I think we mentioned
6 already, a very remarkable result of eight- or nine-letter
7 gains from just a single injection.

8 So I think that, given this, the POSA would see a
9 reasonable expectation of success moving forward with dosing
10 regimens that involve more injections.

11 Q. And this is coming from DTX 3102?

12 A. That's correct.

13 Q. Now that the Do reference -- Do 2009, that disclosed
14 just a single vitreal injection of aflibercept?

15 A. That's correct.

16 Q. After obtaining that data, would a POSA have been
17 motivated to seek extended long-term dosing regimens for
18 aflibercept in the treatment of DME?

19 A. Absolutely.

20 Q. And it's your opinion that, based on these results,
21 after a single intravitreal injection of aflibercept, multiple
22 repeated injections of aflibercept would have -- a person of
23 ordinary skill in the art would have had a reasonable
24 expectation of success using such a regimen?

25 A. Absolutely. I think Regeneron had a reasonable

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1 expectation of success and went forward with this clinical
2 project.

3 Q. Turning to the next slide, Slide 71, can you explain
4 the data that's shown here.

5 A. This is from the review article on Lalwani, which
6 we've looked at already, from 2009. And this describes a
7 ten-patient study, the READ 1 study, for diabetic macular edema
8 with injections given at -- three loading injections given at
9 zero, one, and two months and then two-month injection
10 intervals with injections given at month four and month six.
11 And this article also described good visual acuity outcomes
12 amongst these patients.

13 So, again, given this data in ranibizumab, which is a
14 molecule with an identical mechanism or very similar mechanism
15 of action as aflibercept, one would have a reasonable
16 expectation of success for the injection strategies that are
17 being described in the patents at issue.

18 Q. Turning to the next slide, Slide 72, are these the
19 visual acuity gains you had referenced regarding Do 2009? I'm
20 sorry. Lalwani 2009.

21 A. Yes. Patients gained an average of eight letters in
22 the READ 2 study.

23 Q. This is from DTX 2733?

24 A. That's correct.

25 Q. So, overall, what would the disclosures of Do 2009

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1 and Lalwani 2009 tell a POSA about the reasonable expectation
2 of success of using the regimens described in both the press
3 release and the '747 patent?

4 A. I think that, overall, the POSA would have thought
5 that there would be a reasonable expectation of success in
6 using aflibercept in the described dosing strategies, given its
7 efficacy as described in these studies, the safety that was
8 seen in the preliminary study by Do, and again in the efficacy
9 and safety that was seen in the similar compound, the
10 ranibizumab, in the READ 2 study.

11 Q. If we turn to the next couple slides here, so prior
12 to this, you've told the Court about your anticipation --

13 A. That's correct.

14 Q. -- regarding the press release and the '747 patent?

15 A. Yes.

16 Q. Do you rely on these same references to show
17 obviousness of the DME treatment claims of the '601 patent?

18 A. Yes.

19 Q. So turning to the next slide, Slide 75, is this an
20 accurate summary of some of those immediately envisaged
21 scenarios that we described with respect to the press release
22 and the '747 patent that you discussed in your anticipation
23 section?

24 A. That's correct. I think that given the prior
25 teachings, one would immediately envision this type of dosing

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1 strategy as described in the patents.

2 Q. Turning to the next slide, can you tell what was
3 known about VEGF level or what was hypothesized about VEGF
4 levels in DME patients in the 2009 time frame as shown here on
5 Slide 76?

6 A. Sure. The Lalwani review article references a
7 concept that there are higher VEGF concentrations in patients
8 with DME relative to wet macular degeneration, and she talks
9 about strategies that were being clinically investigated at the
10 time to use higher doses of drug in DME relative to macular
11 degeneration. And I think that the POSA would have immediately
12 thought that, if higher doses were not available, it may be
13 more practical to administer more doses of the drug to try to
14 obtain optimal efficacy.

15 Q. Turning to Slide 7, can you explain to the Court what
16 you've shown here?

17 A. I wanted to put together side-by-side DME data, as
18 was described in Lalwani, with injections of aflibercept given
19 over a year.

20 And one sees in this top line data that there is an
21 improvement in visual acuity up to about ten letters at the
22 12-month mark, but it is a slow and steady rise over that time
23 period, whereas the data that I brought back to remind us of is
24 the MARINA data from Rosenfeld in 2006 in wet macular
25 degeneration treated with monthly ranibizumab, showing that

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1 there is an initial rise with ranibizumab and then it plateaus
2 and is maintained, so again evidencing that the diabetic
3 macular edema visual acuity gains are more difficult to obtain
4 and require more injections until you get there than what's
5 seen in wet macular degeneration.

6 Q. What did you conclude with respect to loading doses
7 after reviewing this data?

8 A. I think the POSA would have concluded that more
9 loading doses for DME relative to treatment strategies that are
10 employed in AMD make a lot of sense given that it takes more
11 injections to get a better visual acuity in these patients.

12 Q. Can you summarize briefly your reasonable expectation
13 of success opinions that you're going to be talking about over
14 the next few slides?

15 THE COURT: Doctor, if I could interrupt.

16 We're going to change topics, Counsel?

17 MR. McLAUGHLIN: We will in a few minutes. Or now.
18 It's up to you, either way.

19 THE COURT: Why don't we go ahead and take a break at
20 this point. We'll take ten minutes. We'll take our morning
21 break.

22 Sorry to interrupt, Doctor. Apologies.

23 As you may have heard over the last few days, no one
24 can talk to you during our breaks, and no one's being rude or
25 discourteous when they flee. But you're a man without a

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1 country since you're midstream in your testimony at this point.
2 But you can go ahead and step down if you'd like.

3 THE WITNESS: Great. Thank you.

4 THE COURT: We'll take ten minutes, and then we'll
5 resume, and then we're going to take up the question of
6 Dr. Rabinow's opinions. Then we can resume with the good
7 doctor's testimony. See everyone in ten minutes.

8 (A recess was taken from 11:03 a.m. to
9 11:18 a.m.)

10 THE COURT: Now, Counsel, before we -- what are you
11 doing there?

12 MR. BERL: I thought you wanted to address the
13 Rabinow issue. If you don't want to do that --

14 THE COURT: I'm going to address. I've read all the
15 parties' briefs. I'm going to grant Regeneron's motion. Mylan
16 will be precluded from offering testimony or opinion related to
17 obviousness with respect to the combination of Fraser, Dix,
18 Lucentis, which includes Shams and Gaudreault and Liu, as prior
19 art. The Court is specifically finding, after reviewing the
20 reports and all briefing, that opinion was not disclosed as
21 required under this Court's scheduling order.

22 The separate and independent basis for granting that
23 motion is that, as required under Federal Circuit precedent,
24 that not only the combination but also the explanation as to
25 why the combination of that prior art would support an opinion

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1 or finding of obvious was likewise not disclosed.

2 Let me be clear, though. That is the only relief the
3 Court grants with respect to Regeneron's motion, which is
4 Docket Entry 529. The other opinions previously disclosed
5 remain undisturbed, but that opinion, the Court finds, was not
6 timely disclosed and will not be received here at trial.

7 We will take up the Chu deposition issue at our next
8 break.

9 Anything else we need to take up at this point before
10 we resume the doctor's testimony?

11 MR. BERL: Not from Regeneron, Your Honor.

12 THE COURT: From Mylan?

13 MR. HUNT: No, Your Honor. Thank you.

14 THE COURT: I would note the Court will --
15 recognizing it is a significant issue although a discretionary
16 decision of this Court, there will be a separate order more
17 eloquently stating the Court's reasons for granting Regeneron's
18 motion, again Docket Entry 529.

19 With that said, Counsel, you can resume your direct
20 examination.

21 MR. McLAUGHLIN: Thank you, Your Honor.

22 BY MR. McLAUGHLIN:

23 Q. Welcome back, Dr. Albin. We were at Slide 78 of
24 your presentation here, and we're about to launch into
25 discussing reasonable expectations of success with respect to

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1 this obviousness ground.

2 Can you just give a brief summary of the data and the
3 documents that we're about to walk through over the next few
4 slides?

5 A. Yeah. These are documents dating from 2006 to 2009
6 that I think demonstrate the known efficacy at the time of both
7 ranibizumab and aflibercept in treating DME and AMD, which
8 would have given a POSA reasonable expectation of success.

9 Q. Let's go ahead and take a look at some of these
10 articles. We've seen this one before, Do 2009. It's slide 79,
11 DTX 3102.

12 Can you explain what you've presented here on
13 Slide 79.

14 A. Yeah. Again, this is the Phase I study report
15 authored by Dr. Do that describes a small study with a single
16 injection of 4 milligrams of aflibercept, resulting in a
17 significant visual acuity gains of eight letters.

18 Q. Turning to the next slide, Slide 80, can you describe
19 what kind of data was presented in Dixon that would have given
20 a POSA a reasonable expectation of success?

21 A. In Dixon there is disclosed published results from
22 aflibercept AMD Phase II data showing visual acuity gains
23 from -- in macular degeneration. And I think that, although
24 these are two different diseases, they are both mediated by
25 vascular endothelial growth factor, which is the target of both

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1 of these therapies, and I do think that the success that was
2 seen in macular degeneration was relevant to the reasonable
3 expectation of success in DME regimens as well.

4 Q. Turning to Slide 81, you've had the opportunity to
5 review internal Regeneron documents --

6 A. I have.

7 Q. -- in the process of formulating your opinions?

8 A. I have.

9 Q. And is DTX 8190, shown here on Slide 81, one of those
10 documents?

11 A. That's correct.

12 Q. And on this document did Regeneron state that "We
13 believe that the doses and dosing intervals for VEGF Trap-Eye
14 for Phase III and DME can be selected based on results of the
15 Phase II study in patients with AMD"?

16 A. Yes. And I think that evidence is that the POSA as
17 well would have used results from one disease state to infer
18 reasonable expectations in the other disease state.

19 Q. And this document also states that "We consider this
20 Phase II data as providing an adequate basis for dose selection
21 for the Phase III DME program"?

22 A. That's exactly right.

23 Q. Turning to the next slide, Slide 82, can you describe
24 what's set forth here on this slide in terms of the data from
25 ranibizumab?

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1 A. These are the results for the MARINA prospective
2 randomized trial that was published in the *New England Journal*
3 *of Medicine* with Rosenfeld as the lead author in 2006, and this
4 was really game-changing data within our field, showing great
5 visual acuity improvements with monthly doses of ranibizumab
6 for wet macular degeneration. Again, a different disease but I
7 think relevant across disease states, as evidenced by the
8 Regeneron communication as well.

9 Q. And just to confirm, when you're referring to
10 Regeneron, you're not suggesting that Regeneron -- that your
11 reasonable expectation of success is coming from Regeneron's
12 statements. Those are just confirmatory in nature for a POSA?

13 A. Yeah. My point is simply that it's reasonable to
14 include the ranibizumab data when you're trying to make an
15 opinion about the expectation of success of aflibercept.
16 That's all.

17 Q. If we turn to Slide 83, can you also explain what's
18 shown here and how that's relevant to reasonable expectation?

19 A. Again, this was a Phase I study, the READ 1 study,
20 describing three monthly loading doses of ranibizumab followed
21 by eight-week injection intervals, showing good visual acuity
22 outcomes in diabetic macular edema.

23 Q. If we turn to Slide 84, going back now, is this an
24 accurate summary of the data that you just walked through?

25 A. That's correct. So that there's -- what really,

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1 historically, were impressive visual acuity benefits compared
2 to what was available for patients prior to the advent of these
3 anti-VEGF therapies, that there was good success with either
4 ranibizumab or aflibercept in either AMD or DME already
5 available to the POSA.

6 Q. And did you have the opportunity to review
7 Dr. Csaky's rebuttal opinions in this case?

8 A. Yes.

9 Q. Is that one -- is this, shown here on Slide 85, one
10 of those rebuttal opinions?

11 A. That's correct.

12 Q. And here, do you agree with Dr. Csaky that concerns
13 about overtreatment would have dissuaded a POSA from using five
14 monthly loading doses in the treatment of DME?

15 A. I don't agree. I think that there were studies
16 already available with ranibizumab with another anti-VEGF agent
17 that showed that larger number of doses in diabetics were well
18 tolerated. There was safety data already available from
19 Phase I study with aflibercept showing adequate safety, and I
20 certainly think that it was a concern, but I think that the
21 addition of one or two more loading doses compared to other
22 treatment regimens would not have dissuaded somebody from
23 trying the regimens that are detailed in these patents.

24 Q. And do you agree with Dr. Csaky that use of
25 intravitreal injections and potential side effects, like

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1 elevated intraocular pressure, would have dissuaded a person of
2 ordinary skill in the art from using five monthly loading doses
3 in the treatment of DME?

4 A. I think that Dr. Csaky's comments in this regard were
5 focused on the use of intravitreal steroids, which have a class
6 effect of raising intraocular pressure. And I think they have
7 limited relevance to anticipated complications for anti-VEGF
8 agents, especially by the time that you get to 2010 and '11
9 when there's been such great experience in multiple trials
10 conducted in thousands of patients with these agents without
11 seeing this type of pressure elevation that's seen with
12 intravitreal steroid use.

13 Q. And do you agree with Dr. Csaky's opinions that
14 concerns about systemic side effects would have dissuaded a
15 person of ordinary skill in the art from using five monthly
16 loading doses to treat DME?

17 A. I think that, although there was always concern for
18 systemic side effects, the addition of one or two loading doses
19 would not significantly dissuade the POSA from increasing the
20 number of injections by one or two, especially with the
21 perceptions that we've talked about, the increased efficacy of
22 doing that and the anticipated necessity for more injections
23 that are seen in DME. So overall no, I don't think that this
24 would have dissuaded the POSA from using more injections. And
25 historically that's what happened.

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1 Q. Was it also the case that at that time there were
2 trials, including trials run with aflibercept by Regeneron,
3 that were including monthly dosing regimens that involved
4 monthly dosing out to one year and more?

5 A. That's true.

6 Q. Now, let's talk about some of that data that you
7 talked about regarding the safety and -- the safety of
8 aflibercept and what was known in the prior art.

9 Can you explain what you've shown here on Slide 88.

10 A. This is the article by Do from 2009 showing an early
11 phase study with 4 milligrams of aflibercept. We've seen this
12 before. And it evidences that there were no serious adverse
13 effects in this small study. And they had a reasonable
14 expectation of safety that allowed them to move on to a
15 Phase II study following this.

16 Q. Based on that, would a POSA have a reasonable
17 expectation of success?

18 A. I believe they would go through the same thought
19 process and would reasonably have a good -- a reasonable
20 expectation of success, yes.

21 Q. Turning to the next slide, can you -- this is
22 Slide 89. Can you tell the Court what Dixon disclosed about
23 the safety of aflibercept?

24 A. Again, in this Phase II study of VEGF Trap-Eye and
25 CLEAR-IT, it remarks that the therapy seems to be well

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1 tolerated, with no serious drug-related adverse events.

2 Q. And do you agree with Dr. Csaky that a person of
3 ordinary skill in the art would have felt constrained to just
4 three to four monthly loading doses when designing a DME
5 treatment regimen?

6 A. I don't see anything in the science or in the prior
7 art that would limit the comfort with only three or four but
8 not five loading doses.

9 Q. So is it true, Dr. Albin, that there would have been
10 a range of monthly loading doses that a POSA would have
11 envisioned for use in treating a patient with diabetic macular
12 edema?

13 A. I think that this slide nicely encompasses that
14 range. It demonstrates it. There were available, as we've
15 seen, the CLEAR-IT 2 data in AMD with four monthly loading
16 doses, the DA VINCI study in DME with three monthly loading
17 doses with prn dosing following three monthly loading doses.

18 And in a retinal vein occlusion study that is
19 described in the prior art, even six monthly loading doses
20 followed by prn treatment were all already in the literature
21 and tried. And so I think that anywhere in this range would
22 have been obvious to the POSA in that time period.

23 Q. And, again, you've had the opportunity to review
24 Regeneron internal documents in this case?

25 A. Yes, I have.

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1 Q. Is this one of those documents, DTX 4129?

2 A. Yes, it is. And it shows that Regeneron internally
3 claimed that a target scenario for their novel therapy would be
4 no more than three to six doses, including monthly loading
5 doses for the first three months and described an induction
6 period in the first six months; so saying that they were
7 working -- or demonstrating that they were working within the
8 same dosing range.

9 Q. Thank you.

10 And now we're going to move on to another obviousness
11 ground. This is on Slide 93 going to Slide 94.

12 Before we dive into this ground, I just wanted to
13 make clear. You understand -- or you were led to understand
14 and asked to assume for purposes of this ground only that a
15 priority date of July 12th, 2013, applies to the asserted
16 claims?

17 A. That's my understanding, yes.

18 Q. So turning to Slide 95 and looking at the Do 2012
19 reference here, DTX 3105, can you explain what's shown here on
20 this slide?

21 A. Sure.

22 Do describes a study in treating diabetic macular
23 edema with VEGF Trap-Eye or aflibercept, meaning that
24 highlighted part of the Claim 10.

25 Q. What else did Do 2012 disclose?

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1 A. It disclosed an intravitreal injection of the
2 2-milligram dose.

3 Q. And turning to the next slide, can you explain what's
4 shown in this graphic here, Slide 97 from DTX 3105?

5 A. These are the treatment arms for the study disclosing
6 that in the 2-milligram arms there is an arm with regular --
7 four weekly injections, an arm with three loading doses and
8 then injections given every eight weeks. And there is an arm
9 with prn dosing described where there are three loading doses
10 given by necessity. And then subsequent to that, there are
11 visits at which there may or may not be doses on any particular
12 visit.

13 In that arm that would include the possibility of
14 five loading doses with a q8-week interval subsequent to that,
15 as we've described a couple times already in this testimony.

16 Q. If we were to turn to the next slide, does this slide
17 show the results from that Phase II study?

18 A. Yes. This shows the mean number of injections was
19 7.4, greatly less than the number of injections that were seen
20 in the Q four months. So this describes a protocol where fewer
21 injections were required.

22 Q. And the 7.4 injection number you're referring to,
23 that was from the prn --

24 A. That's correct.

25 Q. -- group?

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1 A. That's correct.

2 Q. This also discloses that in the 2q8 group they
3 required a mean of 7.2 injections over the first year?

4 A. That's correct.

5 Q. Did you have a sense for how that compares to the
6 number of injections that patients received in a prn regimen in
7 the AMD clinical trials?

8 A. Yeah. Dixon teaches that in the AMD VEGF Trap-Eye
9 there was a mean number of 5.6 injections in prn dosing of VEGF
10 Trap-Eye. And for DME it was 7.4, which was in line with the
11 anticipation, as we discussed before, that in DME more
12 intravitreal injections were going to be needed to achieve
13 optimal treatment of patients than there are in AMD.

14 Q. What conclusion would a POSA draw from that data?

15 A. One of the conclusions would be that a greater number
16 of loading doses would certainly be likely to be beneficial in
17 developing a treatment strategy for DME.

18 Q. If we take a look at the data from that Phase II
19 trial displayed here, the visual acuity data, can you explain
20 or walk the Court through what's shown here?

21 A. So one can see the outcomes of the four arms with
22 aflibercept showing an improvement in visual acuity that is
23 maintained then through the life of this 52-week study. And in
24 the laser control arm there is ultimately a decrease of vision
25 starting at about 28 weeks going on.

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1 Q. This is on Slide 101, and this data is from DTX 3105?

2 A. That is correct.

3 Q. If we flip forward to Slide 102, can you tell the
4 Court what you've shown here on Slide 102.

5 A. Highlighted in green is the visual acuity outcomes
6 line from the 2q8 arm. This is 2 milligrams given with three
7 monthly loading doses and then given q8 weeks thereafter. And
8 one can see that, in between the injections given at Week 12
9 and Week 20, at Week 16 there is a drop in visual acuity,
10 suggesting that the addition of a subsequent dose given at that
11 week would improve the visual acuity.

12 I think this data could have been interpreted and
13 would have been interpreted by the POSA, especially in
14 combination with the other points that we've made, that an
15 additional loading dose would be a very effective thing to try
16 in treatment strategies for diabetic macular edema.

17 Q. And is that additional loading dose shown here in
18 green?

19 A. That's correct.

20 And that would essentially be consistent with the
21 therapy of five loading doses followed by q8-week loading,
22 essentially indistinguishable from that treatment strategy.

23 Q. So can you summarize or provide your overall
24 conclusion with respect to the DME -- Claim 11 of the '601
25 patent with respect to Do 2012?

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1 A. I think that the Do article gives a reasonable
2 expectation of success and that it would be obvious to the
3 POSA, having read that article, that a more robust dosing
4 strategy would be needed with more loading doses than have been
5 used with AMD, given the data that showed that it is more
6 difficult to achieve optimal visual acuity benefits with fewer
7 injections in DME relative to AMD. So I think the POSA would
8 have seen that and designed a strategy with more loading doses
9 and could have designed a strategy with a q8-week loading arm
10 thereafter as well.

11 Q. Would that same analysis apply to Claim 19 of the
12 '601 patent as well?

13 A. That's correct.

14 Q. Would that same analysis apply to Claim 25 of the
15 '572 patent?

16 A. That's correct.

17 Q. We're going to switch gears now and leave the DME-DR
18 treatment claims and move over to Claim 6 of the '572 patent.

19 Can you briefly explain to the Court the opinions
20 you're going to be offering in this section of your testimony.

21 A. These opinions are largely based -- as I think we
22 mentioned already early on, on the opinions of Dr. Rabinow,
23 who's a formulation expert, regarding the anticipation and
24 obviousness of the claim regarding isotonic preparation of
25 aflibercept.

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1 Q. Do you understand Slide 108 to summarize Claim 6 and
2 the claims from which it depends?

3 A. That's correct.

4 Q. Do you understand that, with its pretrial order
5 submissions, Regeneron provided a compiled version of Claim 6
6 that incorporated the limitations of the claims from which it
7 depends?

8 A. Yes.

9 Q. Is that what you have shown here on Slide 109?

10 A. That's correct.

11 Q. Is it okay if we use this version of Claim 6 to
12 conduct your analysis in this section of your presentation?

13 A. Yes.

14 Q. Do you also understand that Regeneron has stipulated
15 to the invalidity of certain claims, including Claims 1 through
16 5 of the '572 patent?

17 A. Yes.

18 Q. So is it okay if we mark with highlighting the
19 material -- or the subject matter of Claim 1 and the compiled
20 Claim 6 in yellow highlight as shown here on Slide 111?

21 A. Yes.

22 Q. Are you aware also that the Court issued a claim
23 construction, also called a Markman opinion, that held that the
24 visual acuity elements of the claims do not carry any
25 patentable weight?

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1 A. Yes, I am aware.

2 Q. And you understand that Regeneron also represented to
3 the Court that the visual acuity limitations also did not carry
4 any patentable weight?

5 A. That's correct.

6 Q. So in light of that, is it okay if we highlight in
7 blue that visual acuity element of compiled Claim 6?

8 A. Yes.

9 Q. So, with that, can you tell the Court what remains of
10 Claim 6?

11 A. The text highlighted in green here stipulating that
12 aflibercept is formulated as an isotonic solution.

13 Q. Turning to the next slide, Slide 116. So even though
14 this material has been stipulated, we're still going to walk
15 through very quickly where these dosing regimen elements are
16 found in Dixon.

17 Can you explain to the Court what you have shown here
18 on Slide 116.

19 A. This is the Dixon reference that we looked at
20 numerous times in this presentation. And it does describe a
21 Phase III study for treating an angiogenic eye disorder here.
22 And so we can check off the first check mark there.

23 Q. And that's -- you're looking at the title of
24 DTX 0204?

25 A. The "VEGF Trap-Eye for the treatment of neovascular

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1 age-related macular degeneration" is an angiogenic eye
2 disorder, yes.

3 Q. The Phase III regimen called out there on the bottom
4 of the slide from DTX 0204, that also describes method of
5 treating an angiogenic eye disorder?

6 A. Absolutely.

7 Q. Can you describe what's shown here on Slide 117 from
8 DTX 0204?

9 A. A Phase III study using 2 milligrams of aflibercept,
10 or intravitreal VEGF Trap-Eye, for the treatment of wet macular
11 degeneration.

12 Q. And then does Dixon also disclose a treatment method
13 that involves sequentially administering an initial dose
14 followed by one or more secondary doses of 2 milligrams of
15 aflibercept wherein each of those secondary doses is
16 administered approximately four weeks following the immediately
17 preceding dose?

18 A. That's right. It does that in the highlighted text
19 there.

20 Q. And the highlighted text is the text following three
21 monthly doses?

22 A. That's correct.

23 Q. If we go to the next slide, does Dixon also disclose
24 treatment in which those secondary doses are followed by one or
25 more tertiary doses of 2 milligrams of aflibercept wherein each

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1 of those tertiary doses are administered approximately eight
2 weeks following the immediately preceding dose?

3 A. That's correct.

4 Q. And then, again, you understand the visual acuity
5 limitation to not carry any patentable weight in this claim?

6 A. That's correct.

7 Q. So if we turn to the last element, can you read for
8 the Court what the last element of compiled Claim 6 is.

9 A. Aflibercept is formulated as an isotonic solution.

10 Q. And with respect to that portion of the claim, did
11 you rely on the opinions of Dr. Barrett Rabinow?

12 A. Yes, I did.

13 Q. And are those opinions shown here on Slide 121?

14 A. That's correct.

15 Q. And does he cite to a Dixon article?

16 MS. OBERWETTER: Objection. Your Honor, at this
17 point, because I don't know precisely what Dr. Albini is going
18 to say in response to any particular question, we have an
19 objection to this witness testifying about the reference that
20 is listed here, Dixon, insofar as his testimony would be as to
21 whether it discloses an isotonic solution for two reasons.

22 First of all, his report itself does not contain an
23 opinion that the POSA would have understood Dixon to make such
24 a disclosure.

25 And, second, we believe, from a formulation

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1 standpoint, he is not qualified to render such an opinion.

2 THE COURT: Understood.

3 Counsel, aren't we going to hear this from
4 Dr. Rabinow?

5 MR. McLAUGHLIN: You are going to hear all about
6 isotonicity from Dr. Rabinow. Dr. Albin will be talking about
7 his understanding from the viewpoint of an ophthalmologist of
8 how he would read that aspect of Claim 6 in conjunction with --

9 THE COURT: Has he offered any opinions in his
10 reports on that?

11 MR. McLAUGHLIN: He has. He's talked about Dixon.
12 He's talked about the language from Dixon. And we can call
13 that up.

14 THE COURT: I think I'd like to see what he said in
15 his report, his opinions, because references are one thing,
16 but --

17 MR. McLAUGHLIN: Sure, sure. Permission to approach?

18 THE COURT: Granted.

19 Yes, Ms. Oberwetter?

20 MS. OBERWETTER: I don't know if I'm on or not.

21 I believe we're going to be looking at that
22 paragraph, or the same version, elsewhere. But there is a
23 longer paragraph. And I believe that is the entirety of the
24 opinions on it. And there is nothing in which he says he is
25 opining on whether Dixon disclosed an isotonic solution from

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1 the standpoint of a POSA. And it is a confusingly worded
2 paragraph, but that particular statement is conspicuously not
3 present. As you read it, I will flag that for you, Your Honor.

4 THE COURT: Okay.

5 Counsel?

6 MR. McLAUGHLIN: Well, it's a confusingly worded
7 claim, but what I will direct you to is Dr. Albin's opinions
8 at paragraph 556 of his opening report. That should be on the
9 first tab of the binder that we've handed Your Honor. That's
10 on page 196 of the document. It's Exhibit page 197, DTX 7069.

11 You can see that Dr. Albin, he does cite Dixon about
12 two-thirds of the way down that paragraph. Dixon is an article
13 that's directed to retinal physicians and people in the
14 ophthalmological community, directed to people just like
15 Dr. Albin. This is language that he would have reviewed in
16 reviewing such an article, and it's language that he would
17 understand as a person who administers these types of drugs on
18 a regular basis.

19 MS. OBERWETTER: Your Honor, it's not that the word
20 Dixon isn't in this paragraph; it's that there's no opinion
21 that the POSA would have understood the disclosures in Dixon.
22 That is a conspicuous and notable absence compared to other
23 portions of his report, and it's obvious the reason why,
24 because at the time he wrote the report he was relying on
25 Dr. Rabinow whose testimony you will hear forthcoming. There's

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1 a reason they want Dr. Albinini now to be offering that opinion,
2 and it's not in his report.

3 THE COURT: And what is that reason?

4 MS. OBERWETTER: That Dr. Rabinow's testimony on that
5 point did not hold up, Your Honor.

6 THE COURT: I guess ultimately I will be the judge of
7 that, but -- I understand there will be a challenge to that,
8 Ms. Oberwetter. I'll flag that as a preview.

9 MS. OBERWETTER: Mutual previews, Your Honor.

10 THE COURT: Great. Great. Thank you.

11 Yes, counsel?

12 MR. McLAUGHLIN: I just want to reiterate Dr. Albinini,
13 he's somebody that's administered these formulations on a
14 regular basis for the last 15, 20 years.

15 THE COURT: He concedes in the report -- and, again,
16 I just read paragraph 556 of Dr. Albinini's report -- that
17 formulations are not his bailiwick, for lack of a better term.

18 MR. McLAUGHLIN: They're not his bailiwick, but he's
19 certainly somebody that's qualified to at least talk about the
20 administration of these formulations, how you expect patients
21 to respond to these formulations that are being injected into
22 their eyes. And he's got publications where he talks about --
23 where he compares isotonicity to osmolarity of different
24 formulations.

25 THE COURT: Well, I guess my question then, Counsel,

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1 is what is the relevancy to the questions before this Court?
2 Because paragraph 556, again, of Dr. Albini's report concludes
3 that it's his opinion with respect to the VIEW clinical trial,
4 et cetera -- and Ms. Oberwetter is right. There's no reference
5 to what a POSA would think or expect at that juncture.

6 With all due respect, Doctor, I'm curious as to what
7 his individual opinion is, what its relevance is.

8 MR. McLAUGHLIN: That's -- and a lot of this is just
9 the nature of this bizarrely worded claim to begin with. But
10 leaving that aside, he does rely on Dr. Barrett Rabinow to then
11 talk about does this language communicate to a POSA that this
12 is an isotonic solution.

13 So he's not going to say that those words tell
14 somebody it's isotonic. He relies on Barrett Rabinow for that.
15 But then taking that knowledge from a formulation expert as one
16 would -- as a doctor would who is looking to gain more
17 information from a formulation that he's administering, using
18 that knowledge from Barrett Rabinow, which is what he does in
19 his report as shown here in paragraph 556. He clearly refers
20 to Dr. Rabinow's opinion and his opinions about the isotonicity
21 of this formulation. He then relies on an expert's expert
22 opinion --

23 THE COURT: Which he's entitled to do.

24 MR. McLAUGHLIN: -- and incorporates it into his own
25 opinions about Claim 6 overall.

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1 THE COURT: Anything further, Ms. Oberwetter?

2 MS. OBERWETTER: Only, Your Honor, that he doesn't
3 rely on Dr. Rabinow; he defers to Dr. Rabinow on that question
4 and does not then frame any opinion that he is offering in his
5 report from the standpoint of a POSA on the method of treatment
6 patents. So that opinion is absent, and this is an effort to
7 backfill that.

8 THE COURT: Understood.

9 I'm going to overrule the objection at this point
10 with the coming preview with respect to Dr. Rabinow. And the
11 Court will afford this evidence the weight it believes
12 appropriate. But objection noted.

13 MS. OBERWETTER: My only remaining question is may I
14 voir dire the witness on his formulation expertise?

15 THE COURT: Yes, you may.

16 Counsel, if you wouldn't mind abdicating the podium.
17 Thank you.

18 I would note, Ms. Oberwetter, that the Court has not
19 qualified Dr. Albin as an expert in any fields related to
20 formulation. But with that, a limited voir dire, I think,
21 would be appropriate.

22 MS. OBERWETTER: Yes, Your Honor.

23 VOIR DIRE EXAMINATION

24 BY MS. OBERWETTER:

25 Q. Good morning, Dr. Albin.

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1 A. Good morning.

2 Q. You agree, and I think we've heard you say earlier
3 today, that you are not a formulation expert, correct?

4 A. That is correct.

5 Q. And, in fact, in your report you specifically rely on
6 and defer to Dr. Rabinow in connection with the things that you
7 say about an isotonic solution, correct?

8 A. That is correct.

9 Q. Okay. You are not an expert in the design of
10 therapeutics, correct?

11 A. I'm not an expert in the design, although I read
12 material about such designs on a regular basis when treating
13 patients with pharmacologic agents.

14 Q. Okay. And whatever you may read, you're not an
15 expert in that field, correct?

16 A. That is correct.

17 Q. Okay. And, in fact, you've testified several times
18 in other proceedings on behalf of Mylan, correct?

19 A. That is correct.

20 Q. Okay. Including in IPR proceedings related to the
21 method of treatment patents, some of which are at issue here;
22 some of which are not, correct?

23 A. I have. That is correct.

24 Q. And when you had your deposition -- if I can turn you
25 back in time to a January 20th, 2022, deposition, you were

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1 asked some questions in that proceeding about how the
2 osmolality of a drug could affect its half-life.

3 Do you remember that from 2022?

4 A. Not specifically. I'm sorry. No.

5 Q. Okay.

6 If we could pull up the page from that deposition
7 page.

8 Let me just start with the front, Dr. Albin. This
9 was a deposition you testified in on January 20th, 2022,
10 correct?

11 A. I have no reason to doubt that. Yes. Correct.

12 Q. You do recall testifying in a case at approximately
13 that time?

14 A. Yes.

15 THE COURT: Let me interject just because I saw the
16 word "confidential" on there. Do we need to seal the courtroom
17 for any of this discussion?

18 MS. OBERWETTER: Thank you for asking, Your Honor.
19 No, this is fine for us to have up on the screen.

20 THE COURT: I'm not doubting your statement. But in
21 a trust-but-verify mode, I'll ask Mylan if they have any
22 thoughts to the contrary on that.

23 MR. McLAUGHLIN: With respect to the confidentiality,
24 Your Honor?

25 THE COURT: Yeah. Do we need to seal the courtroom

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1 for a discussion of this testimony? It was an IPR proceeding,
2 I believe.

3 MR. McLAUGHLIN: No.

4 THE COURT: Okay. All right.

5 So, Ms. Oberwetter, my apologies for trusting but
6 verifying. Go right ahead.

7 MS. OBERWETTER: Always appreciated, Your Honor.

8 BY MS. OBERWETTER:

9 Q. If we take a look at page 125 of this transcript.
10 And you recall you were being questioned in that deposition by
11 another attorney for Regeneron, correct?

12 A. That is correct. I do recall that.

13 Q. And you were asked in that proceeding a question
14 about whether the composition of an intravitreally administered
15 drug, including its osmolality and excipients, can affect the
16 half-life of the drug in the vitreous, correct?

17 Do you see that question?

18 A. Let me just take a second to digest that. Hold on
19 one second.

20 Okay. I've read the question.

21 Q. And your answer was you're getting into some very
22 technical issues, correct?

23 A. That is correct.

24 Q. And then if we scroll down to the next several lines,
25 you said, "It happens that, as I sit here before you today, I

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1 think off the top of my head that osmolality would not affect
2 half-life, although it would have many effects. But I could be
3 wrong on that. And, again, I am not an expert in the design of
4 therapeutics."

5 Do you see that?

6 A. That is correct.

7 Q. And then you said, "But as a clinician that uses
8 angiogenic drugs and that has written these declarations, I
9 don't think that sounds reasonable. But I don't really have a
10 strong opinion or a lot of experience in that area."

11 Correct?

12 A. That is what I said.

13 Q. And those are answers that you gave with respect to
14 the osmolality of the drug you were being asked about, correct?

15 A. I don't recall if this was in reference to a specific
16 drug.

17 Q. Okay.

18 MS. OBERWETTER: Thank you, Your Honor. That is the
19 extent of my questions on this topic.

20 THE COURT: Understood. Thank you.

21 The Court's ruling with respect to the objection
22 remains.

23 Counsel, you may resume your direct.

24 MR. McLAUGHLIN: Thank you, Your Honor.

25 DIRECT EXAMINATION (Resumed)

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1 BY MR. McLAUGHLIN:

2 Q. So I will resume my direct, but in the meantime I
3 just want to ask you, Dr. Albin, a few questions about your
4 background. I understand that you don't consider yourself an
5 expert in the design of therapeutics, but would you consider
6 yourself to be knowledgeable about the impact of the injection
7 of an isotonic or nonisotonic solution into the eyes of one of
8 your patients?

9 A. I would consider myself being an expert in the use of
10 these drugs. The question of the importance of the isotonicity
11 and various options for choosing different osmolarity of
12 agents, I'm not an expert in those issues, but I certainly feel
13 myself confident to describe the use of drugs with formulations
14 that have been approved.

15 Q. In the course of your work and your research, have
16 you published -- did you publish an article in 2014 called "Ziv
17 Aflibercept as a Possible Alternative to Aflibercept"?

18 A. Yes, I did.

19 Q. Do you recall publishing that article?

20 A. I do.

21 Q. Do you recall who you published that article with,
22 who your coauthors were?

23 A. I think my coauthors, as I recollect, were Andrew
24 Moshfeghi, and Jonathan Chang.

25 Q. If you can recall -- but we can also put the article

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1 up for you, if you'd like, but can you recall what the subject
2 matter of that article was?

3 A. The subject matter was that there was some early
4 interest, particularly in Brazil as I recall, for using
5 Regeneron's product ziv-aflibercept, which is designed for
6 intravenous use as a cancer therapeutic, to aliquot it in a
7 very analogous fashion as bevacizumab is aliquoted for
8 intravitreal use, to use ziv-aflibercept off-label, again with
9 the goal being of obtaining the -- being able to use the
10 VEGF Trap molecule at a reduced price for patients that could
11 not meet the price point for aflibercept.

12 Q. And is this a copy of your article shown here?

13 A. That's correct.

14 Q. And if we could turn to the second page, I don't know
15 if there's a way to -- is there a way to zoom that in?

16 So in this top paragraph in the upper left of page 68
17 of that article, do you discuss the osmolality of
18 ziv-aflibercept versus aflibercept?

19 A. That is correct.

20 Q. What did you conclude about the osmolality of the two
21 different formulations?

22 A. I haven't actually read this whole thing in a while,
23 but as I recollect, I remember having a concern that the higher
24 osmolarity of ziv-aflibercept relative to aflibercept that's
25 injected in the eye, I think the numbers are there,

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1 815 milliosmoles relative to 260 -- or compared to
2 260 milliosmoles, that this higher osmolarity may cause a
3 clinical problem in that I had been familiar with work that was
4 done by Dr. Marmor in the 1970s -- and, honestly, right now
5 sitting here, I can't remember what the point of this paper
6 was.

7 But I remember that the higher osmolarity of
8 intravitreal injections given by Dr. Marmor in -- I think it
9 was a monkey study, I want to say; it's been many, many years
10 since I've read this paper -- that in that -- with that higher
11 osmolarity, there was a risk, a very high risk, for retinal
12 detachment.

13 And I remember that some of us who were pondering
14 this issue, including me and my coauthors here, were wondering
15 whether ziv-aflibercept was produced with higher osmolarity
16 just to avoid the possibility of intravitreal injection.

17 So that's my recollections on this issue, but I think
18 I was concerned in this particular case about higher osmolarity
19 given my prior familiarity with work done by Dr. Marmor, as was
20 cited in this article.

21 Q. Okay. Now, a few minutes ago you said you couldn't
22 remember what this article was about.

23 You were referring to Dr. Marmor's 1979 article, not
24 the one in front of you here?

25 A. Thank you for the clarification. Absolutely, yes.

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1 The Marmor article that -- I have not read that in -- probably
2 since this article was published.

3 MR. McLAUGHLIN: Okay. With that, with Your Honor's
4 permission, I'm going to resume my direct. See if I can recall
5 where we left off.

6 BY MR. McLAUGHLIN:

7 Q. So Slide 121, we were talking about Dr. Rabinow's
8 opinion. This is his opinion that you relied upon in
9 formulating your opinions with respect to Claim 6?

10 A. That's exactly right.

11 Q. Okay. And this passage that he cites from Dixon,
12 that comes from DTX 0204?

13 A. That's correct.

14 Q. If we could pull that up so we can show the Court
15 this language.

16 This comes -- this is language from Dixon. That's
17 that 2009 article regarding VEGF Trap-Eye; is that correct?

18 A. That's correct.

19 Q. What does Dixon say about VEGF Trap-Eye and its
20 formulation?

21 A. He teaches that it is formulated with different
22 buffers at different concentrations suitable for the
23 comfortable, nonirritating direct injection into the eye.

24 Q. Going back to the slide deck here, turning to the
25 next slide, Slide 122, did you also rely on the Eylea label

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1 when formulating your opinions in this case?

2 A. That's correct.

3 Q. And is this a snapshot of that Eylea label, DTX 3316?

4 A. Yes, it is.

5 Q. And what's this say about Eylea in DTX 3316?

6 A. It says that it is formulated as an iso-osmotic
7 solution.

8 Q. And in your opinion as an ophthalmologist, is the
9 FDA-approved formulation typically the one that was used in the
10 pivotal Phase III trials that were responsible for that FDA
11 approval?

12 MS. OBERWETTER: Objection, Your Honor. That's a
13 fact question, not an opinion question if he's asking about
14 this trial.

15 THE COURT: Repeat that question, Counsel, please.
16 BY MR. McLAUGHLIN:

17 Q. In your opinion as a treating physician, is the
18 FDA-approved formulation typically the one that's used in a
19 drug's pivotal Phase III clinical trials?

20 A. That's my --

21 THE COURT: One second, Doctor. Sorry.

22 Objection overruled.

23 Now you can answer. Thank you.

24 THE WITNESS: That's my opinion and would be the
25 opinion of the POSA.

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1 BY MR. McLAUGHLIN:

2 Q. Did you review Dr. Csaky's rebuttal expert report?

3 A. Yes, I did.

4 Q. And did you review the portion in which he was
5 rebutting -- he was providing his rebuttal opinions with
6 respect to Claim 6 of the '572 patent?

7 A. Yes, I did.

8 Q. Did Dr. Csaky provide any rebuttal opinion indicating
9 that the FDA-approved formulation of aflibercept was not the
10 one used in the Phase III clinical trial?

11 A. No, he did not.

12 Q. Now proceeding forward and now relying upon what you
13 learned from Dr. Barrett Rabinow, the formulation expert that's
14 going to be offered by Mylan, can you provide a summary of your
15 final opinion with respect to Claim 6 of the '572 patent?

16 A. Yeah. I believe that Claim 6 is anticipated by
17 Dixon, given that a suitable, comfortable, nonirritating direct
18 injection of the eye would inherently be isotonic, as taught to
19 me by Dr. Rabinow.

20 Q. And now we're going to shift focus a little bit and
21 talk about obviousness of Claim 6 of the '572 patent.

22 So turning to the Slide 126, can you briefly
23 summarize the opinions you're going to provide in this section
24 of your testimony?

25 A. Given the text that we've discussed and the Dixon

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1 reference, combined with a source used by Dr. Rabinow, Hecht,
2 it is -- it becomes obvious that the comfortable,
3 nonirritating, safe for intravitreal injection solution
4 described by Dixon for aflibercept would be isotonic.

5 Q. We're going to be using the same compiled Claim 6 for
6 your analysis in this portion of your presentation?

7 A. Yes.

8 Q. And that's shown on Slide 127?

9 A. Yes.

10 Q. So in your anticipation opinions you walked through
11 each disclosure from Dixon with respect to these dosing regimen
12 elements of Claim -- compiled Claim 6; so we won't do that
13 again. But you understand -- or you're going to be applying
14 that same reasoning in your obviousness section?

15 A. That's correct.

16 Q. You have the same understanding that the visual
17 acuity limitation of this claim does not have -- does not carry
18 patentable weight?

19 A. That's correct.

20 Q. Now, with respect to the isotonic solution aspect of
21 Claim 6, in your opinion, would a POSA -- again, you relied on
22 the opinion of Dr. Rabinow in this part of your -- formulating
23 your opinions as well?

24 A. That is correct.

25 Q. And you incorporated his opinion regarding the Hecht

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1 reference?

2 A. That is correct.

3 Q. In your opinion, would a POSA have been motivated to
4 administer a formulation of aflibercept that was comfortable
5 and nonirritating?

6 A. That's correct.

7 Q. And do you intend to rely upon Dr. Rabinow's opinion
8 and trial testimony regarding the disclosures of the
9 formulation prior art and reasonable expectation of success at
10 formulating isotonic ophthalmic formulations?

11 A. Yes, I do.

12 Q. And assuming that Dr. Rabinow's later testimony shows
13 the obviousness of formulating an ophthalmic formulation to be
14 isotonic to be obvious, what is your final opinion regarding
15 Claim 6 of the '572 patent?

16 A. That Claim 6 is both anticipated and obvious given
17 the Dixon prior art and the Hecht prior art.

18 Q. Now we're going to shift gears now and talk about the
19 secondary considerations opinions that you provided. So we're
20 now Slide 134.

21 Do you understand that, in rebuttal to your opinions,
22 Dr. Csaky provided five different opinions on secondary
23 considerations?

24 A. That is correct.

25 Q. And are those five different secondary considerations

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1 listed here on Slide 135?

2 A. Yes, they are.

3 Q. That includes long-felt need, failure of others,
4 unexpected results, industry praise, commercial success?

5 A. That's correct.

6 Q. Do you understand, when formulating your final
7 obviousness opinions, that you are to consider -- to take into
8 consideration any evidence of secondary considerations?

9 A. That's my understanding.

10 Q. But you understand that those secondary
11 considerations must have a demonstrated nexus to the claim
12 elements at issue?

13 A. That is correct.

14 Q. Now I'd like to start by reviewing again what was
15 known and disclosed in the prior art before the 2011 --
16 2010-2011 time frame.

17 Could you briefly describe what's shown here in terms
18 of what was known about extended dosing regimens in the art
19 before 2010?

20 A. This is a roundtable from Retinal Physician from 2007
21 that demonstrated that, as early as 2007, there was a variety
22 of extended dosing intervals, including treat and extend, the
23 prn dosing, that were already in use by the leading
24 vitreoretinal surgeons at that time.

25 Q. Can you explain to the Court what's shown here on

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1 Slide 137?

2 A. This -- I believe we've seen this study before as
3 well -- is a study documenting the treat-and-extend approach
4 use with bevacizumab but again showing that the
5 treat-and-extend dosing strategy was -- already had a term and
6 was understood to be a certain type of dosing strategy by the
7 POSA in 2009, as evidenced by its mention here in this article.

8 Q. And is that the same type of treat-and-extend regimen
9 that was disclosed or discussed by Dr. Brown that we saw in a
10 couple slides previous?

11 A. That's correct.

12 Q. Turning to Slide 138, can you describe what's shown
13 on this slide?

14 A. This slide shows a preferences and trends survey from
15 the American Society of Retinal Specialists in 2009,
16 documenting that, in this survey with 433 respondents,
17 91 percent of practicing vitreoretinal surgeons in the United
18 States surveyed at that time were using prn dosing or an
19 extended dosing interval well before 2010.

20 Q. And how many doctors were using a fixed dosing
21 regimen at that point?

22 A. Injection given every four to six weeks regardless of
23 lesion activity was down to 5 percent by 2010.

24 Q. And just to clarify, what we talked about on this
25 previous slide is from DTX 4192; is that correct?

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1 A. That's correct.

2 Q. Now, jumping to Slide 139, can you describe what's
3 shown on this slide?

4 A. This is a 2010 preferences and trends survey asking
5 similar question, describing treatment strategies for exudative
6 macular degeneration, or wet AMD. And you see that 43 percent
7 of respondents in 2010 are using prn dosing and 34 percent are
8 using treat and extend already.

9 Q. This is from DTX 2040, page 24?

10 A. That's correct.

11 Q. And turning to Slide 140, can you describe what's
12 shown here?

13 A. This is the 2011 survey, probably data gathered in
14 the first part of 2011. They're usually reported towards the
15 end of the year at the meeting -- well, middle to end, summer
16 to fall. I don't remember exactly when 2011 meeting took
17 place. But most doctors use prn, 32 percent; and
18 treat-and-extend regimen is being used by 60 percent; and,
19 again, less than 5 percent of physicians are using a
20 follow-and-treat-monthly, active or not.

21 Q. This is from DTX 4194?

22 A. That's correct.

23 Q. And turning to Slide 141, can you tell us a little
24 bit more about the PrONTO study that you discussed in your
25 expert reports?

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1 A. This is a trial result from the two-year data from
2 the PrONTO study, which again was a prospective study using
3 ranibizumab in a prn fashion after loading doses, showing very
4 good visual acuity gains with prn dosing at 24 months, 11.1
5 letters of visual acuity benefit were obtained; 43 percent of
6 patients improved by 15 letters or more -- which were, I think,
7 very impressive results at the time -- showing that this could
8 be achieved with an extended dosing regimen.

9 Q. Is that also summarized here on Slide 142, DTX 3131?

10 A. That's right. But the highlighted text here makes
11 the point that, with fewer than half the number of injections
12 in the PrONTO study as compared to the MARINA and ANCHOR
13 studies, very similar visual acuity gains were obtained.

14 Q. If we turn to the next slide, this is also a
15 selection from DTX 3131; is that correct?

16 A. That's correct.

17 Q. Can you tell us what's shown on Slide 143.

18 A. This shows a text from the paper detailing that the
19 PrONTO study was designed to minimize the number of treatments
20 but not the number of visits and discussing already other
21 treatment strategies that may yield similar or even better
22 visual acuity outcomes that require fewer visits, and it
23 discusses the treat-and-extend treatment strategy that we've
24 discussed a number of times and that this was in -- published
25 in 2009 already.

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1 Q. And can you just briefly summarize then for the Court
2 why the PrONTO results were important?

3 A. I think in regards to this testimony, they were
4 important because they detailed that in 2009 the need for an
5 extended dosing regimen was already met. And in terms of the
6 weight of those secondary considerations, the variable dosing
7 regimen had already been achieved and in use and certainly
8 would have been readily envisioned by the POSA.

9 Q. And is this study leading the physicians away from
10 using fixed regimens like monthly dosing?

11 A. I think very quickly after these data were available,
12 there was a shift. Whether that's causation or just
13 coincidence, I guess is debatable. But certainly it seemed
14 that at around the same time period, physicians started to use
15 prn dosing regimens as evidenced by the *Retinal Physician*
16 roundtable that we've discussed a few times already.

17 Q. If we turn to the next slide, this is Slide 145, the
18 Engelbert reference, DTX 3215, can you explain what you've
19 shown here?

20 A. Yea. This paper published in 2010 just evidences
21 that PrONTO-style dosing has become popular within the retinal
22 community. That's the extended prn dosing that we've been
23 talking about. And it also details treat-and-extend dosing
24 with fewer patient visits in addition to fewer monthly
25 injections. So that concept was already there and practiced in

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1 2010.

2 Q. And to clarify, DTX 3215 also specifies that, as a
3 result of the PrONTO study, PrONTO-style dosing has become
4 popular in the retina community?

5 A. That is correct.

6 Q. Is that consistent with your recollection as well?

7 A. Yes.

8 Q. Then, again, you've had the opportunity to review
9 internal Regeneron documents in the process of formulating your
10 opinions; is that correct?

11 A. That's correct.

12 Q. Are one of those documents shown here, Slide 146?

13 A. That's correct.

14 Q. Is this a 2007 email from George Yancopoulos?

15 A. Yes.

16 Q. Is one of the statements that he makes in this email
17 "published prn approaches, which are being widely adopted as
18 current standard of care"?

19 A. That's correct.

20 Q. Now, did you review Dr. Csaky's secondary
21 considerations opinions in the process of formulating your
22 reply opinions in this case?

23 A. Yes, I have.

24 Q. Is one of those opinions shown here regarding
25 long-felt need from Dr. Csaky?

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1 A. That's correct.

2 Q. So in your opinion, as of the 2010 time frame, was
3 there a long-felt need for an extended dosing regimen for the
4 treatment of an angiogenic eye disorder?

5 A. I don't think so. I think, given everything that
6 we've looked at right now, you can see that, as early as
7 2007/2008, that extended dosing regimens were very commonly
8 employed and this need had already been met.

9 Q. Turning to Slide 148, do you understand that
10 Dr. Csaky also offered opinions regarding purported failure of
11 others?

12 A. Yes, I do.

13 Q. Do you agree that there was a failure of others to
14 achieve extended dosing regimens before 2011?

15 A. I do not. I think that we've detailed a number of
16 studies that have showed success with very good visual acuity
17 outcomes with extended dosing regimens. And certainly given
18 the data that we've gone through in a number of studies with
19 ranibizumab and aflibercept in DME and in AMD, I think there
20 was a reasonable expectation of success that a POSA would have
21 had for an extended dosing interval.

22 Q. And is this an accurate summary here on Slide 149 of
23 some of the disclosures of extended dosing regimens that were
24 known and being practiced prior to 2011?

25 A. That's correct.

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1 Q. That includes those -- some of the different
2 scenarios that were offered in the 2007 *Retinal Physician*
3 article?

4 A. That is correct.

5 Q. And that includes the treatment of DME using
6 ranibizumab and Lalwani 2009?

7 A. Yes.

8 Q. Does it also include the treatment of AMD using
9 various regimens in Dixon 2009?

10 A. Yes.

11 Q. Does that include the treatment, including the
12 disclosure of treat and extend, in Spielberg 2009?

13 A. Yes, it does.

14 Q. Treat and extend was one of the same regimens that
15 was disclosed in the 2007 *Retinal Physician* article?

16 A. Yes. That was disclosed by Dr. Brown in particular,
17 yes.

18 Q. And was this also confirmed by PAT Surveys in the
19 2010-2011 time frame?

20 A. It was confirmed that these were very popular
21 treatment strategies in those years, yes.

22 Q. Now I'd like to shift gears and talk a little bit
23 about unexpected results.

24 THE COURT: Counsel, before we do that, if we're
25 gear-shifting again, is this a good spot for a lunch break?

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1 MR. McLAUGHLIN: It is.

2 THE COURT: Perfect.

3 Doctor, we're going to take a break. As I advised, I
4 think, Dr. Trout yesterday or some others, they are permitted
5 to feed you, but they're not permitted to talk to you. And
6 they are hereby ordered to feed you but, otherwise, not talk to
7 you.

8 But we'll take a lunch break.

9 No one can talk to you because you're midstream on
10 your testimony, but you're free to step down, sir.

11 THE WITNESS: Fair enough. Thank you.

12 THE COURT: Thank you.

13 Counsel, let's take a break until 1:00 from our
14 perspective, and then we'll resume with Dr. Albinini's testimony.
15 Thank you all very much.

16 (A recess was taken from 12:24 p.m. to
17 1:08 p.m.)

18 THE COURT: Counsel, are you ready to resume?

19 MR. McLAUGHLIN: We are, Your Honor.

20 THE COURT: You may proceed.

21 BY MR. McLAUGHLIN:

22 Q. Welcome back, Dr. Albinini.

23 A. Thank you.

24 Q. So can I go to Slide 147, please.

25 Just want to make sure that we wrap things up here.

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1 Now, going back to Dr. Csaky's rebuttal opinion with respect to
2 secondary considerations, do you agree that there was a
3 long-felt need for an extended dosing regimen for the treatment
4 of angiogenic eye disorders by the 2011 time frame given all
5 the material that we reviewed in the slides prior to this?

6 A. I think it's been fairly well documented that that
7 need had been answered by 2011.

8 Q. Thank you.

9 And going forward to the next slide, Slide 148.

10 And do you agree with Dr. Karl Csaky, Regeneron's
11 expert, that there was a failure of others to achieve extended
12 dosing regimens with ranibizumab by 2010-2011?

13 A. I think that there were a number of successes, as
14 we've discussed throughout this testimony.

15 Q. And then I think we were turning to unexpected
16 results when we broke for lunch. So let's go back to Slide 150
17 here in front of you.

18 This is showing DTX 0204, the Dixon reference. Can
19 you describe what's shown here in this section of Dixon.

20 A. In this section of Dixon he's describing the
21 CLEAR-IT 2 Phase II study, which utilized a four monthly
22 loading doses followed by prn dosing and achieved good visual
23 acuity outcomes.

24 Q. If we turn to the next slide, are these some of these
25 outcomes that you're referring to?

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1 A. That's correct. In that arm with q4 loading doses
2 and prn treatment thereafter, patients achieved mean
3 improvement of nine ETDRS letters, which is a very good visual
4 acuity result, with 30 percent gaining three lines or more of
5 vision by 52 weeks. So I think these were excellent results.

6 Q. And is this -- can you describe what's set forth here
7 on Slide 152 of your presentation.

8 A. Yeah. This details the clinical trial results that
9 would have been available to the POSA prior to the filing
10 patents at issue showing very good visual acuity results with a
11 number of different regimens across diseases and across agents,
12 again, I think really making it difficult to make an argument
13 that good results were unexpected.

14 Q. What else did Dixon show about the frequency of the
15 injections that were required for reaching those visual acuity
16 outcomes that they saw?

17 A. That patients were receiving 2-milligram injections
18 with, on average, 1.6 injections over the loading phase time.
19 So over the 40-week prn loading protocol, patients only needed
20 1.6 injections on average, again showing that, even with
21 extended treatment, good visual outcomes were obtainable.

22 And the median time to first reinjection in all
23 groups was 110 days, again, further speaking to the extended
24 dosing interval that could be used to achieve good visual
25 acuity results.

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1 Q. And, again, this is coming from DTX 0204?

2 A. That's correct.

3 Q. Turning to the next slide, Slide 154. So have you
4 reviewed the unexpected results opinions of Dr. Csaky?

5 A. Yes, I have.

6 Q. Do you agree with Dr. Csaky?

7 A. No, I do not. I think that the trials that we have
8 discussed already paint a picture of a lot of industry
9 successes, and I don't see the argument for overwhelming
10 industry failure.

11 Q. And then actually I want to back up and ask you about
12 one additional document. So if we look at Dixon. I believe
13 you have it at DTX 0204 in your binder. If you could turn to
14 that, please.

15 A. I found it.

16 Q. And if you turn to page 4 of that reference and look
17 at that section on Phase II that you've been discussing.

18 A. I don't know if you can help me. My pages -- oh, I
19 see it. Never mind.

20 Q. It's at .00 -- yeah, there you go.

21 A. I got it. Yep.

22 Go where? I'm sorry.

23 Q. The discussion in Section 2.6.2 about the Phase II
24 clinical trial.

25 A. Yes.

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1 Q. Do you see there's a reference to Reference 45 there?

2 A. Reference 45, I see that.

3 Q. So if you turn to the back and take a look at what
4 Reference 45 is. Can you do that?

5 A. Yes. I see that.

6 Q. And that Reference 45, is that a presentation
7 entitled "VEGF Trap-Eye in Wet AMD, CLEAR-IT 2: Summary of
8 One-Year Key Results. Paper presented at Retinal Society
9 Annual Scientific, September 28, 2008, Scottsdale, Arizona"?

10 A. I see that reference.

11 Q. Is that another one of the references that you
12 reviewed in connection with formulating your opinions in this
13 case?

14 A. I have seen the slides from that presentation, yes.

15 Q. Okay.

16 Can we put those slides up, please. That's DTX 3173.

17 Is this the presentation that you've reviewed and
18 relied upon?

19 A. Yes.

20 Q. Okay.

21 And if we go ahead to Slide 6, please, of the slide
22 presentation of DTX 3173.

23 Is this a depiction of the study arms from that
24 study?

25 A. Yes, it is.

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1 Q. And if we jump to Slide 9, what were some of the
2 conclusions that were reported with respect to some of the
3 results from the Phase II CLEAR-IT study?

4 A. You see them here, that there was a significant
5 improvement in visual acuity, a significant reduction in
6 central retinal thickness. That means decreased swelling. The
7 groups dosed at baseline and at Week 12 showed improved visual
8 acuity and retinal thickness, although this effect was not as
9 robust as that seen in monthly dosing in the early phase. All
10 the maintenance phase here was prn.

11 Maintained effect on visual acuity with a single dose
12 to eight weeks and was generally well tolerated with no
13 drug-related serious adverse events -- with no serious adverse
14 events.

15 Q. If we jump to Slide 16 of this presentation,
16 DTX 3173, can you explain what we're looking at here?

17 A. These are the visual acuity results from the arm that
18 is a .5 milligrams of the low dose with monthly loading doses
19 followed by prn dosing after Week 12 shown in the blue. And
20 the 2-milligram dose, a higher dose, shown in the green
21 squares, with visual acuity. This arm was also four loading
22 doses initially and then maintained with prn injections after
23 Week 12.

24 Q. Thank you. And if we could go back to the main slide
25 deck, DDX 6.

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1 And if we could turn now to the issue of industry
2 praise, that secondary consideration. We're at Slide 155, now
3 156. Did you review the opinions of Dr. Karl Csaky with
4 respect to reported industry praise?

5 A. I did.

6 Q. Did you agree with Dr. Csaky's opinions?

7 A. I agree that there was great praise from the
8 industry, but I don't see the connection of that praise to the
9 dosing regimens which we are discussing in the claims today or
10 to the isotonicity issue.

11 I think that there was great praise for this molecule
12 and there was great efficacy of the molecule; but, to me as a
13 POSA, because these dosing strategies were actually not widely
14 adopted and retina specialists continued to use prn and
15 treat-and-extend dosing instead of fixed eight-week dosing as
16 described in the claims, I really don't see the connection to
17 claim that the industry praise was due to the practices
18 outlined in the claims in question.

19 MS. OBERWETTER: Your Honor, I have an objection and
20 motion to strike in part the prior response.

21 Dr. Albin's report does not contain a disclosure
22 with respect to the isotonic solution limitation as it relates
23 to secondary indicia or industry praise in particular.

24 THE COURT: Understood.

25 Counsel?

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1 MR. McLAUGHLIN: I think what Dr. Albini was doing
2 was just responding to Dr. Csaky's opinions, which he noted did
3 not address isotonicity or the aspects of Claim 6 in any way.

4 THE COURT: I'll overrule the objection at this point
5 considering it's a motion to strike.

6 Counsel, obviously, you'll be free to address that in
7 the posttrial briefing. And if it was not properly disclosed,
8 the Court would disregard it, but we'll address that posttrial
9 at this juncture. Noted, however.

10 You may proceed, Counsel.

11 BY MR. McLAUGHLIN:

12 Q. Let me ask it this way: In reviewing Dr. Csaky's
13 opinions, did you see any industry praise in those opinions
14 regarding anything having to do with an isotonic solution?

15 A. I did not.

16 Q. Did you see in Dr. Csaky's opinions any evidence for
17 any industry praise for the use of five monthly loading doses
18 followed by every-eight-week dosing in the treatment of DME?

19 A. I did not.

20 Q. If we could turn now to the issue of commercial
21 success. Dr. Albini, were you asked to provide opinions
22 regarding commercial success in this case?

23 A. I was.

24 Q. Do you understand that Dr. Csaky also provided
25 opinions regarding commercial success?

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1 A. Yes.

2 Q. Did you review those opinions?

3 A. Yes.

4 Q. Is one of those opinions set forth here on Slide 158?

5 A. Yes.

6 Q. In reviewing his opinions, did you see where
7 Dr. Csaky attributed any of the commercial success of Eylea to
8 the DME-DR treatment regimens of five monthly loading doses
9 followed by fixed every-eight-week dosing?

10 A. I do not see that specifically mentioned.

11 Q. And did you read the day two trial testimony
12 transcript from Dr. Csaky?

13 A. Yes.

14 Q. Okay.

15 If we could pull that up.

16 This is from -- we're going to PDF page 109. There
17 we go.

18 Did you see Dr. Csaky testify as follows when he was
19 asked, "When you say you've used Eylea to treat patients with
20 DME and DR according to the method of Claim 25, have you also
21 done that for secondary doses step?"

22 And his response was, "Yes. In certain cases where
23 there's severe DME, you need five injections, multiple
24 injections. And, again, having, as I said before, that
25 confidence of five injections gets us to a good place both

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1 anatomically and visually is a nice approach to take in some
2 patients."

3 In your opinion, is a regimen that's used in some
4 circumstances of severe DME in some patients something that
5 sounds like being responsible for the commercial success of
6 Eylea?

7 A. No.

8 Q. If we could go back to the slide deck, please, DDX 6.
9 Thank you, Dr. Albin.

10 You also have provided opinions regarding the
11 pharmacologic attributes of the aflibercept protein; is that
12 correct?

13 A. I have.

14 Q. Can you explain for the Court what you've provided
15 here on Slide 159 in this callout from DTX 2745.

16 A. This is an early paper from 2002 describing VEGF
17 Trap-Eye, at that point in preclinical testing, describing that
18 it has a higher affinity and improved pharmacokinetics relative
19 to antibody therapeutics that were being developed at the time.
20 Again, showing that there was reason to believe that this
21 molecule would be a better agent based on its pharmacokinetics
22 early on prior to any consideration of dosing regimen.

23 Q. And when was this disclosure published?

24 A. 2002.

25 Q. If we turn to the next slide, what else was published

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1 regarding the pharmacologic attributes of aflibercept?

2 A. This is from the Dixon reference that we've
3 referenced many times in 2009, where it also remarks on the
4 high affinity of the molecule and the benefits of the Trap
5 complex increasing its durability and its long duration of
6 effect in the eye, again pointing the potential success of the
7 molecule to its pharmacologic properties rather than to any
8 specific dosing regimen.

9 Q. What you're looking at here is DTX 0204?

10 A. That's correct.

11 Q. Let's go on to the next slide, Slide 161. Can you
12 explain to the Court what you've shown here with respect to
13 this April 28, 2008, press release, DTX 2731.

14 A. Yeah. This article describes again that, due to its
15 high affinity for all isoforms of VEGF-A as well as its long
16 residence time in the eye, Dr. Quan Nguyen, one of the
17 investigators in the early Regeneron trials, is claiming that
18 that scientific -- or those pharmacologic properties of the
19 molecule are predictive of clinical success.

20 Q. If we turn to the next slide, Slide 162, is this a
21 summary of those pharmacologic attributes of aflibercept that
22 you've just reviewed?

23 A. That is correct.

24 Q. And, in summary, starting with the assumption that
25 Eylea has been a commercial success, in your opinion, is that

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1 success attributable to the properties of the molecule itself
2 or to the features of the isotonicity or the five monthly
3 loading dose DME aspects of the asserted claims?

4 A. I see not much praise or remark about isotonicity of
5 the molecule. I think that, with regards to the dosing
6 frequency, one of the most telling pieces of information to me
7 was the email from Dr. Yancopoulos that we had a few slides
8 back where he overtly declared that the success of the molecule
9 will be based not on its dosing strategy but that it will be
10 better than the antibody molecules available regardless of
11 dosing strategy. And I think that's the way the success of the
12 molecule was perceived in the community as well.

13 Q. So in your opinion, the commercial success of Eylea
14 is not attributable to the five monthly loading dose dosing
15 regimen followed by every-eight-week dosing in the treatment of
16 DME patients?

17 A. Yes.

18 Q. So do you agree, then, with Dr. Karl Csaky's final
19 opinion with respect to commercial success?

20 A. No.

21 Q. The next -- you were asked to provide opinions as to
22 how certain patents assigned to Regeneron might influence
23 whether someone could practice the subject matter claimed by
24 the '601 and '572 patents?

25 A. That's correct.

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1 Q. Are some of those blocking patents shown here?

2 A. Yes. Due to the patented molecule, it would have
3 been difficult for people other than Regeneron to have
4 performed studies to demonstrate various dosing strategies and
5 their success.

6 Q. So the '746 patent claims a method of treating
7 retinal neovascularization; is that correct?

8 A. That's correct.

9 Q. And in your opinion, would that have prevented
10 somebody from being able to practice the claimed methods of the
11 '601 and '572 patents?

12 A. Yes.

13 Q. If we take a look at the '747 patent, that's -- the
14 claim there is drawn to a therapeutic method for treating or
15 ameliorating an eye disorder?

16 A. Yes. That would also preclude it.

17 Q. And so, in your opinion, that would preclude the
18 ability to conduct the dosing regimens of the '601 and '572
19 patents?

20 A. Exactly right.

21 Q. And for the purposes of this analysis, have you been
22 asked to assume that the sequence IDs set forth in these claims
23 are the sequences of aflibercept?

24 A. Yes.

25 Q. If we turn to the next slide, one of these is the

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1 '799 patent, 7,306,799, DTX 4116. Is Claim 1 there drawn to a
2 therapeutic method for treating an eye disorder?

3 A. Yes.

4 Q. And in your opinion, would that have blocked somebody
5 from conducting or operating the claimed dosing regimens
6 claimed in the '601 and '572 patents?

7 A. Yes.

8 Q. And for the '758 patent, it's drawn to a method of
9 inhibiting vascular endothelial growth factor activity in a
10 mammal. Do you see that?

11 A. Yes.

12 Q. Would that claim have prevented somebody from
13 operating the claimed regimens of the '601 and '572 patents?

14 A. Yes.

15 Q. I want to revisit one more aspect of your testimony
16 earlier today.

17 So if we could pull up DTX 07 -- sorry -- DTX 7069,
18 paragraph 556.

19 I just wanted to ask one final question on this. Did
20 you -- you stated earlier that you did review Dr. Csaky's
21 opinions in this regard?

22 A. Yes.

23 Q. Did Dr. Csaky offer any rebuttal regarding whether or
24 not the language from Dixon suitable for the comfortable and
25 nonirritating direct injection into the eye inherently

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1 disclosed isotonicity?

2 A. I do not recall any rebuttal on that specific remark.

3 Q. Thank you.

4 MR. McLAUGHLIN: Nothing further from Mylan, Your
5 Honor, with --

6 THE COURT: Thank you, Counsel.

7 MR. McLAUGHLIN: -- obviously, reservation for
8 redirect.

9 THE COURT: Certainly.

10 Cross?

11 MS. OBERWETTER: Yes, Your Honor. Can I have just a
12 minute or two to get set up at the podium?

13 THE COURT: You may.

14 Whenever you're ready, Counsel, you may proceed.

15 MS. OBERWETTER: Thank you, Your Honor.

16 CROSS-EXAMINATION

17 BY MS. OBERWETTER:

18 Q. Good afternoon, Dr. Albini.

19 A. Good afternoon.

20 Q. Dr. Albini, you've been working with Mylan's
21 litigation counsel since 2017, correct?

22 A. That sounds correct, yes.

23 Q. Okay. So for the past five or six years?

24 A. Yes.

25 Q. That was years before this case even got filed,

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1 correct?

2 A. I'm not aware of when exactly this case was filed.

3 Q. All right. One of Mylan's attorneys, Mr. McLaughlin,
4 and some of these colleagues would fly down starting back in
5 2017 to meet with you down in Miami, correct?

6 A. That's correct.

7 Q. And you would meet in a conference room at the
8 hospital where you worked in Miami, right?

9 A. That's correct.

10 Q. And you would sit in a room and look at Regeneron's
11 patents, correct?

12 A. Among other things, yes. That's correct.

13 Q. And you were retained at that time to help Mylan
14 generate ideas on how to invalidate the patents, correct?

15 A. I was hired for my opinions about -- mostly at that
16 time we were discussing what the POSA or what the standard
17 retina specialist at the time would have envisioned as
18 reasonable dosing regimens to use. So I was not really engaged
19 in a way to -- I think you said the words "to create strategy"
20 or "to develop strategies."

21 I was more engaged in a way to guide them through the
22 prior art and the scientific literature that was available as
23 well as other types of literature that we've seen in my
24 testimony such as the PAT Surveys and some of the articles from
25 trade journals and other types of literature that may have been

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1 more obscure to attorneys new to this area.

2 Q. Dr. Albin, you've had your deposition taken in this
3 case, correct?

4 A. Yes.

5 Q. That was a few months ago, earlier in the spring?

6 A. That's correct.

7 Q. And we did that deposition down in Miami, right?

8 A. That's correct.

9 Q. You were under oath?

10 A. I was.

11 Q. Okay.

12 And if we could please cue up the video clip.

13 Did I ask you these questions we're about to play and
14 did you give these answers?

15 (Video playing.)

16 "Q And those are conversations that -- I
17 guess starting in roughly the 2017 time period,
18 what was your level of activity in working on
19 this matter over the years through the present?

20 "A I think that early on every couple of
21 months, Neil and a colleague or two would fly out
22 to Miami, and we would sit in a conference room
23 much like this one but usually on-site at the
24 hospital, and go through these patents. And
25 they -- they would ask me my opinions about the

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1 treatment strategies and what was currently known
2 about various treatment strategies at the time
3 and what the prevailing practice patterns were
4 among retina specialists at the time with regard
5 to the treatment of angiogenic eye disorders with
6 anti-VEGF medications.

7 "Q Were you retained at that time to help
8 generate ideas on how to invalidate the patents?

9 "A Yes.

10 "MR. McLAUGHLIN: I just want to
11 counsel you going forward, you know, to the
12 extent that this goes to any privileged
13 discussions or conversations, that I'll
14 instruct you not to answer."

15 (Video ends.)

16 BY MS. OBERWETTER:

17 Q. Dr. Albin, you know that that role is not the same
18 as being an independent expert, correct?

19 A. I think that my input into guidance of what -- as I
20 described in that clip, guidance through what the literature
21 was available and what the prevailing practice patterns at the
22 time, I think that is my role as an independent expert.

23 I can see your concern about my answering yes to the
24 question about developing strategies. I certainly can't tell
25 you exactly what was going through my head as I said yes, but I

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1 think that my answer was that I was involved in developing
2 strategies insofar as my independent opinions of the state of
3 the art and what retina specialists were doing at the time is a
4 very important component of any strategy that one would use.

5 But I'm not an attorney. I did not develop any of
6 these arguments. I have no experience in patent law. I would
7 be a very poor source to obtain information about how to
8 invalidate a patent. I have no idea. My role --

9 Q. Sir, I think you've answered the question.

10 THE COURT: Counsel, he wasn't finished.

11 Go ahead.

12 THE WITNESS: No, I just wanted to reiterate again
13 that my role was just to provide my experience and my opinion
14 of what the state of the art was at the time in question.

15 BY MS. OBERWETTER:

16 Q. I'd like to pull up a slide from your opening deck,
17 which is Demonstrative 6.152, or Slide 152. This is a slide
18 summarizing, I think you said, the clinical trials from the
19 relevant time period?

20 A. That's correct.

21 Q. And there are some AMD trials that are up at the top
22 of this slide. There's three of those there, right?

23 A. That's correct.

24 Q. And only one of those, the CLEAR-IT 2 trial, relates
25 to Eylea, correct?

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1 A. That's correct.

2 Q. Okay. And then below that you've got a couple of DME
3 clinical trials that are listed there, right?

4 A. That's correct.

5 Q. And the visual acuity scores that you can get vary by
6 trial; is that right?

7 A. That's correct.

8 Q. And the selection of trials on this page, you decided
9 which trials to include on this page, correct?

10 A. That's correct.

11 Q. Everything -- and CLEAR-IT 2, I think we determined,
12 was the Eylea Phase II trial in AMD?

13 A. That's true.

14 Q. You would agree that Lucentis, referred to on this
15 page as ranibizumab, was further along in development than
16 Eylea was at this point, right?

17 A. That's correct.

18 Q. You would also agree that there was much more data
19 for Lucentis in AMD than in DME at this point, correct?

20 A. That's correct.

21 Q. And if we take a look at the two DME trials that are
22 listed on this page, the first one is called READ 1. Do you
23 see that one?

24 A. I see it.

25 Q. How many patients were in that trial, sir?

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1 A. I think it was a low number of patients. I hope I'm
2 not misspeaking. But to the best of my recollection, it was a
3 very small study.

4 Q. It was ten, correct?

5 A. That sounds right, yes.

6 Q. Ten patients in the READ 1 study?

7 A. Yes.

8 Q. The DME Phase I study on that page, how many patients
9 were in that study?

10 A. I believe it was a similar number, about ten
11 patients.

12 Q. Was it five?

13 A. It could have been.

14 Q. You don't know?

15 A. I don't remember the exact number right now, but it
16 was a very small Phase I study.

17 Q. These were both Phase I studies?

18 A. That is correct.

19 Q. You would agree that knowledge of how a particular
20 drug performs expands as the number of patients increases in
21 trials over time, correct?

22 A. That's correct.

23 Q. You would agree that, once you start treating more
24 people, you are obtaining more information, and that can either
25 confirm or contradict what you've seen in the preceding phase

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1 of your testing, right?

2 A. That is correct.

3 Q. You'd also agree that even a low rate of serious side
4 effects can mean you would be considered not to have a safe
5 trial, right?

6 A. In certain circumstances, yes.

7 Q. Okay. There are situations where there's even a low
8 rate of really bad side effects, and that can make a trial
9 deemed unsafe, correct?

10 A. That's correct.

11 Q. There are drugs that enter into Phase III that fail
12 their Phase III clinical trial end points. Isn't that true?

13 A. That is true.

14 Q. And so a drug can get all the way to Phase III and
15 still not make it to the market, correct?

16 A. Yes. And even further, a drug can pass Phase III and
17 make it into the market and still fail in the real world.

18 Q. Okay. We'll come back to that.

19 There was recently an anti-VEGF drug with the maybe
20 not catchy name of KSI-301 that failed its Phase III trial,
21 correct?

22 A. That's correct.

23 Q. And you worked on a clinical trial for a different
24 anti-VEGF drug called abicipar or abicipar?

25 A. That's correct.

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1 Q. And even during the Phase III trials for abicipar
2 significant intraocular inflammation issues emerged, correct?

3 A. That's correct.

4 Q. That drug did not make it to the market?

5 A. That's correct.

6 Q. I think you touched on one that passes its Phase III
7 trials and then still runs into problems. Beovu is an example
8 of an anti-VEGF agent in that category, correct?

9 A. That's correct.

10 Q. Beovu came onto the market in early 2020. Do I have
11 that right?

12 A. That sounds right.

13 Q. You only used it twice?

14 A. That's my recollection, yes.

15 Q. All right. And that's because, after launch,
16 everyone learned that there is a 1-in-200 risk of severe vision
17 loss for patients that have Beovu, right?

18 A. That is correct.

19 Q. And those safety issues for Beovu only became known
20 to doctors after Beovu was approved?

21 A. That is correct.

22 Q. And after it passed its Phase III trials?

23 A. That is correct.

24 Q. All right. And, in fact, the experience with Beovu
25 made doctors appreciate how lucky -- and I think you've used

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1 the word "lucky" -- doctors have been on the safety side with
2 the first main anti-VEGF drugs like Eylea and Lucentis and
3 bevacizumab, correct?

4 A. That is correct.

5 Q. And it's certainly possible that more went into that
6 than luck, right?

7 A. Yes.

8 Q. This area of medicine is so difficult that you might
9 not even know if an approved biosimilar will perform the same
10 as the label drug, correct?

11 A. I would say that's not particular to this area of
12 medicine. There are many areas of medicine that are just as
13 difficult or challenging, but I think that, yes, it's -- it is
14 true that the anticipated success doesn't always materialize.

15 Q. When deciding on how to design the arms of a clinical
16 trial using an agent like an anti-VEGF, you would agree there's
17 a lot of moving pieces to that, correct?

18 A. Yes.

19 Q. All right. You need to consider the route of
20 administration?

21 A. Yes.

22 Q. You need to consider how often a drug needs to be
23 administered?

24 A. Yes.

25 Q. You need to consider at which visits to the doctor

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1 the drug might be administered?

2 A. Correct.

3 Q. You need to consider the concentrations of the drug
4 being administered?

5 A. Correct.

6 Q. You need to think about whether and how many loading
7 doses to use?

8 A. That is correct.

9 Q. You need to consider whether to have a fixed loading
10 dose component to the regimen?

11 A. That is correct.

12 Q. And you need to consider whether there's a fixed
13 extended dosing component to the regimen?

14 A. That is correct.

15 Q. You'd have to consider whether to have intervening
16 visits between periods set for fixed dosing intervals, right?

17 A. That is a decision that -- yes, that is a decision
18 that needs to be made when designing protocol for sure.

19 Q. You would agree that in the 2010 time period there
20 was uncertainty as to what the best dosing approaches were for
21 anti-VEGF agents, wouldn't you?

22 A. I think that, as was documented in this -- in my
23 testimony so far, there were a number of protocols that had
24 succeeded with a number of dosing strategies that involved
25 three to six loading doses followed by prn or fixed interval

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1 dosing regimens, either at 4 weeks or with other 8- or even
2 12-week dosing regimens.

3 So I think there were a number of protocols to choose
4 from, but it also wasn't an infinite field of reasonable things
5 to try.

6 Q. You would agree there was uncertainty as to what the
7 best dosing approaches were for anti-VEGF agents?

8 A. Yes.

9 Q. You know that throughout the development period for
10 Eylea, both before 2011 and afterward, Regeneron had access to
11 data about the performance of Eylea that the public didn't,
12 correct?

13 A. I'm aware that such data existed, but I don't know
14 much about it.

15 Q. Okay. They, of course, had access to such data
16 because it was their development program, right?

17 A. That makes sense.

18 Q. I'd like to talk a little bit about some of the
19 terminology that we've been using in this case. Let's talk
20 first about the phrase pro re nata, or prn. Prn means as
21 needed, correct?

22 A. That's correct.

23 Q. All right. And prn means you only treat as needed
24 determined by the findings of an OCT scan and other components
25 like clinical examination and visual acuity measurements,

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1 correct?

2 A. I think that's the way the POSA would have defined
3 it.

4 Q. And so when you use prn dosing, the decision to
5 redose the patient depends on the outcome of an assessment at
6 the time you see the patient, right?

7 A. That is correct.

8 Q. And you don't know until you check the patient
9 according to those things that I just mentioned?

10 A. That is correct.

11 Q. All right. And if instead you want to have an
12 ex-ante decision, an ex-ante regimen where you don't have to go
13 to the doctor between injections to get assessed, that would be
14 an extended interval fixed dosing regimen, not a prn regimen,
15 correct?

16 A. I think there's some ambiguity in the way that the
17 term "extended interval" would be used. It was not, as I
18 recall, a commonly used phrase among retina specialists at the
19 time, extended interval.

20 So I think -- I can't think of cases in my head right
21 now to give me guidance about how the POSA would have used the
22 term "extended interval," whether that would necessarily mean
23 extended injections or extended visits.

24 I certainly think it's reasonable to use it in either
25 way. I just don't want to leave the impression that there was

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1 a preferred way to use that term in the years that I'm aware
2 of.

3 Q. Okay. You had your deposition taken in this case, I
4 think we established, correct?

5 A. Yeah, that's correct.

6 Q. Okay. And if we take a look at page 241 from your
7 deposition, I asked the following question: "If you want to
8 have a regimen that doesn't have a required monthly visit to
9 the doctor every month, that would be an extended-interval
10 fixed dosing regimen, not a prn, correct"?

11 And your answer was, "Correct."

12 Did I read that correctly?

13 A. I don't think there's -- as I said, I don't think
14 there's any problem in using the term that way, and I stand by
15 what I said here in the deposition. I just don't want to leave
16 the impression that that was a commonly used definition of the
17 term by retina specialists back in 2010.

18 Q. You understood it when I asked you that question at
19 your deposition?

20 A. I understood what you meant, yes.

21 Q. All right. You would also agree that prn and treat
22 and extend are two different treatment strategies, correct?

23 A. Yes.

24 Q. All right. I'm going to change topics a little bit.
25 You talked during your testimony about a document. I

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1 believe it was DTX 2039 was the version used.

2 If we can pull that up.

3 That's a -- you recall generally being asked about
4 this document during your direct examination?

5 A. Yes, I do.

6 Q. And the cover says "VEGF Trap-Eye in Wet AMD CLEAR-IT
7 2."

8 This was about a Phase II AMD trial called
9 CLEAR-IT 2, correct?

10 A. That is correct.

11 Q. And before I ask you additional questions about this,
12 do you have personal knowledge as to whether this was the
13 version that was publicly presented?

14 A. I have no reason to think it wasn't.

15 Q. Do you have -- my question was a little bit
16 different. Do you have personal knowledge as to whether this
17 was the version that was publicly presented?

18 A. I don't have any independent knowledge except that
19 it's labeled this way, and I have no reason to believe that
20 these weren't the slides presented.

21 But -- you know, I was -- don't have independent
22 documentation that these are the exact slides that were
23 presented or that all these slides were remarked on by the
24 investigator, but this is given as a document of that
25 presentation and available online.

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1 Q. I'm sorry. You did not go find this online?

2 A. Honestly, I don't recall -- it was so many years ago
3 that we brought this out -- who found it. But I've seen it,
4 and I believe I've googled for it with PDF and CLEAR-IT 2, but
5 I don't know. So many years ago.

6 Q. You were not at a September 2008 Scottsdale, Arizona,
7 presentation, correct?

8 A. I was not.

9 Q. You would agree that the CLEAR-IT 2 trial did not
10 have an arm that tested an eight-week fixed dosing interval
11 regimen, correct?

12 A. That is correct.

13 Q. And it also did not have an arm that had three
14 loading doses, correct?

15 A. Can we go to the slide that shows the different arm
16 treatment strategies? I just want to make sure -- I can't
17 remember now if it was three or four.

18 There was an arm with monthly loading doses, but with
19 so many of these studies I don't want to give you the wrong
20 answer. It was either three or four that they had, one of
21 those two.

22 Q. It's possible it was four, right?

23 A. Certainly possible, yes.

24 Q. Okay. We can take that slide -- we can take that
25 presentation down.

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1 I'd like to talk a little bit about a study that your
2 counsel asked you about, which was a PrONTO trial. You're
3 familiar with the PrONTO trial?

4 A. I am.

5 Q. And I know you mentioned you had institutional pride
6 about the PrONTO trial. That trial was before you got there,
7 right?

8 A. I was there in 2006; so I think the results were --
9 those papers were published -- what years? I don't have it.
10 You may have it in front of you -- 2008, 2009. So it was still
11 certainly being talked about at the time when I was there.

12 Q. If we pull up the Lalwani 2009 article that is
13 DTX 3113, this is an article that you were asked about on
14 direct; is that right?

15 A. That's correct.

16 Q. And Dr. Lalwani is a well-regarded retina specialist?

17 A. That is correct.

18 Q. The PrONTO trial looked at three loading doses
19 followed by prn treatment for wet AMD using ranibizumab.

20 Do I have that correct?

21 A. That's my understanding.

22 Q. And the PrONTO trial was generally viewed as having
23 some positive results, I think you testified?

24 A. That's correct.

25 Q. In your opinion, the PrONTO trial initiated a major

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1 change in the way that ophthalmologists were administering
2 anti-VEGF agents.

3 Would you agree with that?

4 A. It was roughly at the same time. As I sort of
5 semi-jokingly said during my direct testimony, I don't know
6 whether it's cause and effect, how much credit you can give to
7 this one trial. There is no doubt that prn dosing became very
8 popular at around the same time. Maybe it would have done it
9 without this trial; I don't know.

10 But I certainly remember a lot of people talking
11 about this trial as evidence for prn dosing back at that time.
12 So I think it very likely this trial was, at least to some
13 small degree, responsible for the wide adoption of prn dosing
14 back in the 2007-2008 time frame.

15 Q. The adoption of prn dosing itself was a major change
16 in the way that ophthalmologists were providing these drugs,
17 correct?

18 A. Yes.

19 Q. All right. In your opinion, the PrONTO regimen
20 opened the door to more ophthalmologists making use of
21 individualized prn treatment regimens for anti-VEGF agents,
22 correct?

23 A. Yes.

24 Q. And in this publication by Dr. Lalwani, if we go down
25 to the bottom of page 1, she says in part, "While the Phase III

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1 trials used monthly injections, it is unclear at this time if
2 monthly dosing is the best dosing interval. Observations made
3 after the earlier Phase I-II studies with intravitreal
4 ranibizumab suggested a role for OCT in determining the
5 appropriate dosing interval for each patient."

6 Do you see that?

7 A. I do.

8 Q. And her reference to OCT, that's prn dosing because
9 that's how you determine whether to re-treat, correct?

10 A. I think OCTs could be obtained with monthly dosing as
11 well. So I have to be honest. Right now, I'm not exactly
12 certain that I can pull up in my head what data she's referring
13 to here. So I don't want to mislead and say that I know that
14 that was prn dosing. That might have been monthly dosing and
15 that these observations that she's talking about were made from
16 diagnostic imaging that was obtained on patients that were
17 dosed monthly. I don't know that.

18 Q. Okay. Well, Dr. Lalwani, in any event, is pointing
19 to a lack of clarity as to whether monthly dosing is the best,
20 correct?

21 A. That's correct.

22 Q. All right. There's another trial that was not
23 discussed I don't think during your direct examination, which
24 was the PIER trial.

25 You know the name PIER trial?

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1 A. I'm familiar with that trial, yes.

2 Q. And the PIER trial was an effort to do a 12-week
3 extended dosing interval for Lucentis, correct?

4 A. That is correct.

5 Q. And that was after three loading doses?

6 A. That's my recollection.

7 Q. And when they tried that in the PIER trial, you agree
8 that the results were not as good as the PrONTO prn results,
9 correct?

10 A. They were not as good, but they were still good.

11 Q. They were not as good.

12 A. I answered your question.

13 Q. Those results were viewed as somewhat discouraging
14 with respect to attempting a 12-week dosing interval for
15 ranibizumab, correct?

16 A. It depends by whom. I mean, they made it into the
17 label for the drug. So they weren't discouraging enough not to
18 have made it into the label.

19 Certainly the FDA thought that that was an
20 appropriate dosing interval for some instances. I think you
21 and I may have talked about this before at my deposition, but
22 as I recall from the time, there were clinical trials that were
23 using the PIER arm as their standard of care arm, and that was
24 approved by the FDA.

25 So certainly it wasn't clear to everybody that that

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1 was an inappropriate dosing regimen. I think it wouldn't have
2 made it into the label if there weren't some people who thought
3 it was absolutely appropriate.

4 Q. Dr. Albin, we did talk about that at your
5 deposition. If we can pull up page 176 of your deposition and
6 look at lines 16 to 19.

7 I asked you:

8 "Q And the results of the PIER trial were
9 viewed as somewhat discouraging with respect to
10 attempting a 12-week dosing interval, correct?

11 "A With ranibizumab, yes."

12 And that's the answer you gave at your deposition,
13 correct?

14 A. I think that's not in contradiction with what I just
15 said.

16 Q. We can take that down.

17 If we take -- so the PIER results were published in
18 an article by Dr. Regillo in 2008; is that right?

19 A. To the best of my recollection, yes, and I have no
20 reason to doubt that what you're saying is true.

21 Q. If we pull up DTX 4099, do you recognize this as the
22 Regillo publication about the PIER study and its one-year
23 results?

24 A. Yes, I do.

25 Q. If we take a look in particular at DTX 4099.0009 and

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1 go down toward the bottom conclusion paragraph at the bottom
2 right, Dr. Regillo wrote, "In conclusion, ranibizumab
3 administered monthly for three months and then quarterly
4 provided VA benefit to patients with neovascular AMD and was
5 well tolerated. However, observations from the MARINA and
6 ANCHOR trials suggest that the PIER regimen of dosing every
7 three months after three monthly doses provides less benefit in
8 VA on average than continued monthly dosing. Monthly dosing
9 may be necessary in some patients to achieve maximal treatment
10 benefit from ranibizumab."

11 Do you see that?

12 A. I do.

13 Q. Dr. Regillo did not propose in this article continued
14 efforts at extended fixed interval dosing, correct?

15 A. I would have to read the entire article to see what
16 else he may or may not have proposed. I think the words speak
17 for themselves that there was a benefit and there was
18 demonstrated safety of this treatment regimen.

19 The outcomes were not as good as monthly dosing, and
20 monthly dosing may be necessary. Again, I would highlight the
21 word "may." He did not conclude that it definitively was. And
22 he really doesn't make much comments on other types of dosing
23 regimens that may be appropriate.

24 Q. He certainly doesn't suggest any there, correct?

25 A. In these couple of sentences that I'm seeing here,

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1 no.

2 Q. You would agree that -- we can take that down.

3 You would agree that what most people were doing in
4 the 2010 to 2011 time period were individualized assessments to
5 determine dosing, correct?

6 A. I believe that's true, yes.

7 Q. All right. I want to talk about another document
8 that came up during your direct examination. You talked some
9 about a quote from a Dr. Dave Brown who practices in Houston,
10 if we take a look at Slide 37 from the opening.

11 I'm sorry. It was Slide 37 from the direct
12 examination. Thank you.

13 And this is the quotation I'm referring to just so
14 you have it in mind. Do you see that?

15 A. I do see that.

16 Q. Okay. And if we take a look, actually, at the
17 underlying exhibits, DTX 2035, and go to page 0002 where that
18 language is found, Dr. Brown made his comments about this
19 regimen in the context of ranibizumab, right?

20 A. Ranibizumab and bevacizumab probably.

21 Q. Not Eylea?

22 A. That is correct.

23 Q. All right. And he limits his comment about who he
24 would go to treat-and-extend with to the population of patients
25 with good initial visual acuity or where it's the primary eye,

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1 correct? That's what he says there?

2 A. That's correct.

3 Q. And he excludes individuals, if you look down at that
4 last sentence, you have extrafoveal lesions, right?

5 A. Can you repeat the question? I'm sorry.

6 Q. He says, "I administer three doses in all cases
7 except extrafoveal lesions," correct?

8 A. That's what he says, yes.

9 Q. That's an exclusion on what he is doing?

10 A. I mean, he doesn't say what he's doing in the cases
11 of extrafoveal lesions, but, yes, he's making a differentiation
12 in terms of his treatment strategy depending on the location of
13 the lesion.

14 Q. Okay. He's also not talking here about an eight-week
15 fixed extended dosing interval going forward, right?

16 A. I don't see any evidence. In fact, I think a
17 disinterested reading of this would say that he is recommending
18 a prn or treat-and-extend type of protocol. The assumption is
19 that he -- after three loading doses or potentially in some
20 cases after fewer loading doses, depending on these exclusions
21 that he's putting in there, that he's making an assessment as
22 he goes along about how the patient is doing. And also he
23 comments here that he's extending the interval to ten weeks in
24 certain situations, documenting that he's employing some
25 extension in the technique.

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1 I don't think that he's rigorously following any
2 particular set-down treatment regimen that's written down
3 somewhere, advised someplace. I think he's using his best
4 clinical judgment in incorporating all the data, clinical data,
5 that was available to the POSA at the time to make
6 individualized decisions for individual patients about dosing
7 frequency and the visit intervals.

8 Q. There's another part of this document I'd like to
9 take a look at if we go forward to page 4.0004. And there's a
10 comment partway down by Dr. Reichel right after "it is
11 reassuring to know."

12 Do you see that part of the document?

13 A. I do.

14 Q. Am I saying --

15 A. Reichel.

16 Q. I hope I'm saying Dr. Reichel's name correctly. What
17 Dr. Reichel says in response to a comment about -- in the prior
18 paragraph where it is unlikely that treating more than often --
19 more often than is absolutely necessary is deleterious,
20 Dr. Reichel says, "It may not be harmful, but we may be
21 increasing the risk of endophthalmitis and the economic burden
22 by treating more often than is absolutely necessary."

23 Do you see that, Dr. Albin?

24 A. I do.

25 Q. And Dr. Reichel is noting that you don't want to

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1 treat more often than necessary, correct?

2 A. Yes, he is making that point.

3 Q. Okay. You would agree --

4 We can take that document down.

5 You would agree that the -- strike that. Let me
6 start over.

7 In preparing your report, you did not identify any
8 literature suggesting prior to 2011 that ranibizumab ought to
9 be administered at an every-eight-week fixed interval, correct?

10 A. I think I found evidence that it was in some cases
11 administered at an every-eight-week interval in that, for
12 example, the dosing strategies that were employed by the
13 prominent vitreoretinal specialists in that 2007 *Retinal*
14 *Physician* roundtable shows a great deal of variability in both
15 intervals between visits and intervals between injections, and
16 I'm sure that there were, among those patients, certain
17 patients that were being injected at every-eight-week interval.

18 So I'm sure that that did exist for some particular
19 patients, but I think the overall concept is that the treatment
20 regimen was being individualized to the patient and there are
21 going to be some patients that are q8-week injection patients.

22 Q. I'm just going to try my question again.

23 You did not identify, in preparing your report, any
24 literature suggesting that prior to 2011 ranibizumab ought to
25 be administered at an every-week fixed interval?

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1 A. What I did not find is any literature that
2 specifically said that ranibizumab ought, must, should always
3 be injected at a q8-week interval. I did not find that
4 documentation. That is true.

5 What I did find was that, from the evidence of the
6 way in which physicians were employing injection frequency and
7 injection intervals, there is no doubt, I think, to the POSA
8 that there were patients who were identified as patients who
9 needed q8-week dosing, and those patients were indeed receiving
10 injections q8-week. But it was not given as an ultimatum that
11 all patients need to be q8-week. It was just patient-specific.

12 Q. Dr. Albin, I want to take a look at another document
13 that was addressed during your direct testimony if we look at
14 Slide 38.

15 You received some questions about a couple of what
16 are called, colloquially, PAT Survey documents; is that right?

17 A. That is correct.

18 Q. And on this page in particular, I just want to direct
19 your attention to the top line. And this corresponds to
20 DTX 2040, correct?

21 A. That is correct.

22 Q. All right. And if you look at the top line on the
23 right-hand side, it says "Anti-VEGF therapy q1 month."

24 Do you see that?

25 A. I do.

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1 Q. And that's reflecting that 17.5 percent were using
2 monthly dosing of -- monthly dosing of anti-VEGF agents,
3 correct?

4 A. That's correct.

5 Q. And that is what was the first regimen recommended on
6 the Lucentis label, right?

7 A. That is the first regimen recommended on the Lucentis
8 label. Yes, it is.

9 Q. We can take that document down.

10 I'd like to look at Slide 26 from your direct
11 examination, which references DTX 4056, I believe. And on the
12 left-hand side you see the -- an excerpt from the ranibizumab
13 prescribing label, correct?

14 A. That is correct.

15 Q. I think during your direct testimony you focused on
16 the one injection every three months after the first four
17 injections, is there in the second bullet.

18 Do you see that second bullet?

19 A. I mentioned both, I think, but yes. I see the
20 bullet, yes.

21 Q. And to clarify, this is just the early Lucentis label
22 that had wet AMD, right?

23 A. I think so. That's my recollection from reading it,
24 but I'm struggling through the block label what's on there, but
25 certainly -- it could be that, yes.

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1 Q. Okay. The first regimen that was recommended on the
2 Lucentis label for wet AMD was monthly, right?

3 A. I believe so, yes.

4 Q. And the second, the one that's here in the second
5 bullet, starts "although less effective," right?

6 A. That's correct.

7 Q. And that's what Genentech was required to say in its
8 label when recommending less than monthly, correct?

9 A. I don't know for sure that they were required to say
10 that or that they just chose to say it, but that's what's
11 stated there, yes.

12 Q. We can take that document down.

13 I have a couple of questions for you about the
14 isotonic solution opinions that you offered in connection with
15 Claim 6.

16 In relying on Dr. Rabinow in your testimony today,
17 did you review his deposition transcript?

18 A. Yes.

19 Q. And my other question is you have not disclosed an
20 opinion as to what specific range outside of isotonicity you
21 would or wouldn't use to treat the eye?

22 A. I have no such opinion.

23 Q. Okay. I'd like to turn to talking briefly about
24 diabetic macular edema, and I'd like to talk about some of the
25 considerations for treating patients with diabetes.

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1 You would agree that diabetics have a different set
2 of comorbidities than wet AMD patients, right?

3 A. That is true.

4 Q. Diabetics have a higher rate of peripheral vascular
5 disease than AMD patients?

6 A. That is true.

7 Q. Peripheral vascular disease can increase the risk of
8 a stroke in a patient, correct?

9 A. That is true.

10 Q. You would also agree that during the -- what I'll
11 call the pre-January 2011 time period there was, I think as we
12 talked about earlier, an interest in avoiding treating patients
13 more than was absolutely necessary, right?

14 A. That is true.

15 Q. And we've heard some about it in this case, but shots
16 in the eye are not pleasant for anyone, right?

17 A. That is true.

18 Q. Okay. You're also not aware of any publications
19 prior to 2011 that talked about using five loading doses for
20 the treatment of DME, correct?

21 A. As we've discussed, there were a number of treatment
22 regimens that would have resulted in five early doses, and
23 given how the -- how it took more injections to achieve visual
24 acuity results in DME than it did in AMD, I think that it was
25 very likely that a lot of patients were being treated according

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1 to prn and did wind up getting five monthly injections or more
2 going forward.

3 So I do think that five monthly doses up front were
4 given to a lot of patients, yes.

5 Q. That actually was not my question.

6 My question is you're not aware of any publications
7 prior to 2011 that talked about using five loading doses for
8 the treatment of DME?

9 A. Not directly in those terms.

10 Q. Okay. You're not aware of any that talked about six
11 loading doses for DME either?

12 A. I don't think so.

13 Q. Okay. And you're not aware of any from before July
14 of 2013 either?

15 A. Not that I can tell you with confidence sitting here
16 right now, no. I hope I'm not forgetting anything.

17 Q. You also didn't identify anything during your direct
18 examination publications that talks about five loading doses
19 specifically for diabetic retinopathy, correct?

20 A. That is correct.

21 Q. And you didn't identify any publications that talked
22 about six loading doses for diabetic retinopathy?

23 A. I don't recall anything that specifically stated six
24 loading doses. But again, the caveat is that many dosing
25 strategies resulted in patients getting six injections off the

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1 top. So even though they weren't specifically labeled as six
2 loading doses, there were many patients that were being treated
3 in exactly that way.

4 Q. You have not quantified that in your report?

5 A. Quantified it?

6 Q. Right.

7 A. I think I've made the case that it's a permutation,
8 I'd say even a common permutation, of some of the prn dosing
9 regimens. I've made that case. I haven't quantified what
10 percentage of patients got five initial doses, no.

11 Q. I'd like to take a look at the Diana Do 2012 article
12 that has been discussed some in the case, including on your
13 direct. If we can pull up DTX 3105.

14 This article -- and you agree Diana Do is a
15 well-regarded retina specialist, right?

16 A. Yes.

17 Q. This article discussing the Phase II DA VINCI trial
18 for DME, right?

19 A. That's correct.

20 Q. That's the Phase II Eylea trial for DME?

21 A. That's correct.

22 Q. And this article is what you might call the official
23 write-up of the DA VINCI trial?

24 A. That's correct.

25 Q. At page 7 of the document, if we skip ahead into the

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1 document, about midway down the left-hand column, there's a
2 discussion of safety issues regarding anti-VEGF agents in DME
3 patients. About partway down she writes, "Most of the systemic
4 adverse events observed were attributed to the underlying
5 medical conditions and cardiovascular comorbidities of these
6 diabetic patients."

7 Do you see that?

8 A. I do see that.

9 Q. And likewise she says, "Studies have shown that
10 individuals with diabetes seem to have an approximately two- to
11 fourfold greater risk for both heart disease and stroke,"
12 right?

13 A. That is true.

14 Q. And that is consistent with the understanding at the
15 time that diabetic patients have special comorbidities that can
16 expose them to adverse events, right?

17 A. That sounds fair.

18 Q. She also notes, if we go down a little bit further,
19 that the DA VINCI study was not powered sufficiently to assess
20 the relationship between VEGF inhibition and systemic adverse
21 events or mortality, right?

22 A. That is correct.

23 Q. That is her communicating to the reader of this
24 article a limitation on what can be concluded from this
25 article, correct?

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1 A. That is correct.

2 Q. If you take a look a little bit -- let me ask you a
3 different question.

4 In this write-up Dr. Do -- you've read this article,
5 right?

6 A. Yes.

7 Q. Dr. Do didn't propose five loading doses in this
8 article?

9 A. No.

10 Q. And, actually, if we go down a little bit further on
11 page 7, in the paragraph starting "because," she writes,
12 "Because there is considerable individual variation in the
13 progression of DME, patients could benefit from an
14 individualized as-needed treatment regimen," correct?

15 A. I see that.

16 Q. That's what she wrote in this article?

17 A. That's correct.

18 Q. And if you go down a little bit further in that same
19 paragraph, she wrote, "The results of this study support
20 additional Phase III clinical studies with every-two-month
21 dosing of VEGF Trap-Eye after an initial loading dose."

22 Do you see that?

23 A. I see that.

24 Q. That's what Dr. Do, the lead investigator on the
25 study, wrote as a take-away from the study, correct?

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1 A. I believe so, yes.

2 Q. We can take that document down.

3 You agree that DME is a slower-progressing disease
4 than wet AMD?

5 A. I think that's true.

6 Q. And that is something that has been known for a
7 while, correct?

8 A. That's correct.

9 Q. Lucentis was approved for DME in August of 2012.
10 Does that sound about right?

11 A. That sounds about right.

12 Q. The dose amount in the FDA-approved label for DME
13 was .3 milligrams, right?

14 A. That's correct.

15 Q. And that's lower than the dose amount that was
16 approved for AMD, which is .5 milligrams, correct?

17 A. That's correct.

18 Q. You understood that the reason for the lower dose in
19 the Lucentis label was that the FDA was concerned about
20 possible systemic side effects from a higher dose of
21 ranibizumab, right?

22 A. That in conjunction with the fact that there was no
23 significant benefit to the higher dose, yes.

24 Q. All right. I'd like to change topics a little bit
25 and start talking about the Lalwani 2009B article -- or the

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1 Lalwani review article from 2009, if we pull up DTX 2733.

2 And this is an article you addressed on your direct
3 testimony, right?

4 A. That is correct.

5 Q. You would agree that in her 2009 review article that
6 we're looking at here, Dr. Lalwani does not propose an ultimate
7 solution for how to treat DME, does she?

8 A. I'm just thinking about that question. I think
9 physicians very rarely propose ultimate solutions on treatment.
10 She does not -- she's reporting data that's available and
11 discussing some interpretation of that data that may help
12 educate her therapeutic decisions towards her patients. There
13 is no ultimate treatment regimen proposed or advised.

14 Q. If you take a look -- if we go forward a little bit
15 to .0002 of this document, there is a paragraph partway down
16 where she writes, in connection with the trial she's been
17 discussing, "Both these higher-dose trials demonstrate a
18 clinical and statistical superiority to sham treatments in
19 terms of visual acuity and decrease in CRT. Additional trials
20 will be necessary to determine the most effective dosing and
21 treatment interval strategies," right?

22 A. I see that the article says that, yes.

23 Q. That's what she disclosed after going through her
24 review of some of the current DME trials, right?

25 A. I think she's specifically here talking about two

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1 trials. I'm not exactly aware of which two trials she's
2 talking about.

3 Q. All right. If we take a look at the conclusion of
4 this article.

5 A. Okay.

6 Q. She writes in part, going down toward the bottom
7 there, "Unlike neovascular AMD, which has in most cases
8 responded to direct VEGF blockade, it appears likely that the
9 treatment of DME will be more of an art form with tailoring of
10 treatments for individual patients," correct?

11 A. That's what she said, yes.

12 Q. She's proposing an individualized treatment approach?

13 A. I'm just trying to understand what the context of
14 this sentence -- do you mind repeating the question again?

15 Q. I'll get it as close to the same as I can.

16 Here in this article at her conclusion for treating
17 DME, unlike she says AMD, it "will be more of an art form with
18 tailoring of treatments for individual patients," and that is
19 the approach she is proposing.

20 A. I think what she's trying to draw a distinction
21 between is that in AMD -- and I hope I'm not taking this out of
22 context, but my reading of this here is that what she means by
23 direct VEGF blockade is that an intravitreal anti-VEGF
24 injection is going to be the most beneficial and probably be
25 used consistently among the entire population of exudative AMD

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1 patients, whereas in DME patients the treating physician may
2 have to take into account other factors -- I'm not exactly sure
3 what, but one could envision maybe the overall health of the
4 patient and the risk for systemic side effects -- in choosing
5 among the different treatment strategies across different
6 pharmaceutical products that might be most appropriate for that
7 patient.

8 I think that's what she's trying to say because I'm
9 not sure direct VEGF blockade, how that's in contradistinction
10 to tailoring treatment for individual patients. I don't think
11 she's just talking about prn dosing because that's also direct
12 VEGF blockade, right? So I think she's talking about choosing
13 among various different types of treatment strategies that are
14 listed in the second half of this review article.

15 Q. Dr. Albin, this article is what's sometimes referred
16 to as a review article?

17 A. That's correct.

18 Q. And she does not -- you've studied this in connection
19 with your testimony today?

20 A. I've read it a few times, yes.

21 Q. She does not identify any trials in which the
22 investigators were experimenting with different loading doses,
23 correct?

24 A. She describes a few trials, including CLEAR-IT that
25 we've talked about and RESOLVE trial and so on, that have

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1 loading doses. So, no, I don't think your statement is
2 correct. She describes quite a few trials that have -- that
3 are experimenting with loading doses.

4 Q. She does not identify any trials that are
5 experimenting with different numbers of loading doses against
6 each other, correct?

7 A. I'm just trying to think. The READ and the RESOLVE.
8 I don't think within each -- any trial there are arms pitted
9 against each other with different loading dose strategies the
10 way they were in CLEAR-IT. I think that's true, yes.

11 Q. I'd like to touch briefly on a different -- I'd like
12 to go to one other article. One of the trials that Dr. Lalwani
13 talks about is the RESOLVE trial. Do you recall that?

14 A. I do.

15 Q. And let's pull up DTX 4209. And this is a
16 publication summarizing the 12-month RESOLVE Phase II study; is
17 that right?

18 A. That's correct.

19 Q. And RESOLVE trial was experimenting with different
20 dose amounts of ranibizumab and DME, right?

21 A. It had a dose-doubling component to the methodology
22 where, if patients met certain clinical criteria, the dose, for
23 a particular injection, could be doubled, yes.

24 Q. The RESOLVE trial did not have five loading doses,
25 right?

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1 A. I believe it had regular loading doses. I don't want
2 to say off the top of my head what the number is. I would
3 guess it's three, maybe four. Maybe you can tell me. But I
4 think that it did have then prn dosing. So, again, there were
5 some patients that would have -- would have indeed received
6 five regular doses at the beginning of the trial. That's, at
7 least, my recollection of the way this study was designed.

8 Q. It did not involve anything called five loading
9 doses. You know that?

10 A. I don't believe that the terminology that you're
11 proposing was used, but I do want to offer to the Court that
12 there were some patients who did in this trial, to the best of
13 my knowledge, receive five regular doses at the beginning of
14 the trial, yes.

15 Q. I'd like to go to the conclusion paragraph. This is
16 by -- the lead author here is Pascale Massin. Is that right?

17 A. I'm not sure how to pronounce his name. I'm with you
18 on this one. Massin? I don't know.

19 Q. That's fine.

20 A. He's French.

21 Q. That's fine, Dr. Albin. So we'll share that same
22 perhaps botched pronunciation.

23 A. Okay.

24 Q. So if we go down to the bottom of -- I'm actually
25 looking to go down to the bottom of .0006, or the paragraph

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1 that starts "given the nature of diabetes." It's actually --
2 yes, thank you.

3 And if we pull that out, what Dr. -- we'll call
4 Massin says is "Given the nature of diabetes and variability in
5 patients with DME with regard to disease progression and vision
6 loss, there is a need for an individualized treatment regimen."

7 Do you see that?

8 A. I do see that.

9 Q. And what Dr. Massin concluded in his resolve
10 write-up?

11 A. I do see that, yes.

12 Q. We can take that down.

13 As of late 2010, there were not any approved
14 anti-VEGF treatments for DME at all, were there?

15 THE COURT: What year was that, Counsel, again? I'm
16 sorry.

17 MS. OBERWETTER: I'm sorry. Do you want me to
18 repeat?

19 THE COURT: Yes, please. Sorry.

20 MS. OBERWETTER: Oh, of course.

21 BY MS. OBERWETTER:

22 Q. As of late 2010 there weren't any approved anti-VEGF
23 treatments to diabetic macular edema at all, correct?

24 A. I don't think that ranibizumab was approved by 2010.
25 I recall that Macugen, I think, did get a label for DME at some

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1 point, but I can't recall right now off the top of my head what
2 year. But anyway, it probably doesn't matter.

3 But I just want to put that in there because Macugen
4 may have been approved. I'm not 100 percent certain about
5 that. But to the best of my recollection, ranibizumab was not.

6 Q. Okay. As of late 2010, Regeneron had not reported
7 the results of its Phase II DA VINCI trial, its one-year
8 Phase II DA VINCI trial, correct?

9 A. I don't think so.

10 Q. Okay. Do you know of a doctor named Ursula
11 Schmidt-Erfurth?

12 A. Yes.

13 Q. She is well known to the retina community?

14 A. Yes.

15 Q. If we take a look at DTX 8151-A -- and we have
16 appended the A to it because it was given to us as part of a
17 broader 8151 collection -- this is a review early about the
18 state of DME treatments.

19 Do you see that?

20 A. I do.

21 Q. It's the same type of article as the Lalwani 2009
22 review article we were just looking at a few minutes ago,
23 right?

24 A. I don't remember if I've ever read this article in
25 its entirety, but I'm assuming. It certainly looks like it on

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1 the surface of things, yes.

2 Q. The date of this article, if we look at the bottom of
3 the first page in the right-hand corner or the left-hand --
4 that's fine -- is -- actually, if we go down to the publication
5 date in the bottom right, it's December 2010.

6 Do you see that?

7 A. I do.

8 Q. If we take a look at page 4 of this article, there's
9 a discussion of the DA VINCI Phase II trial on this page.

10 Do you see that?

11 A. I do now, yes.

12 Q. Okay. And what Dr. Schmidt-Erfurth -- first of all,
13 she identifies the ongoing DA VINCI trial up there at the top,
14 right?

15 A. I see.

16 Q. And then she says, "The study will follow these
17 patients for 52 weeks, and it will be interesting to see if the
18 results suggest that the dosing frequency with anti-VEGF
19 compounds can be reduced from monthly injections based on these
20 results," correct?

21 A. I see that.

22 Q. All right. She doesn't offer a prediction there
23 based on the work in her review article, correct?

24 A. She doesn't here. She's saying that she's interested
25 to see what the outcome is, but I think you cannot infer either

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1 a positive or a negative anticipation of success from what
2 she's saying. Sounds like a very neutral statement.

3 Q. The neutral statement doesn't offer a prediction?

4 A. Of course not, no.

5 Q. If we go to the conclusion of her article that spans
6 pages 5 and 6, she notes, first of all, that laser was still
7 the standard of care, correct? If you look at "Thus the
8 current standard of care is still appropriate."

9 A. I think one has to be careful when interpreting this
10 comment about the standard of care. I think that, first of
11 all, this physician doesn't practice in the United States; so
12 she's practicing in a community that has very different
13 regulatory bounds on it. And they're of some importance when
14 discussing the treatment of DME in that time period prior to
15 2010 because in that time period bevacizumab used off-label was
16 increasingly used and, I'm sure by 2010, was fairly routinely
17 used in the treatment of DME.

18 So in European countries -- she practices in
19 Austria -- I think there is -- there was actually a slower
20 acceptance of bevacizumab and there was more heightened
21 regulation of having to use the governmentally approved
22 substance.

23 So in her treatment environment, she may not have had
24 an anti-VEGF available for her to use for AMD, but that is not
25 the case for sure in the United States after the advent of

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1 bevacizumab in 2005.

2 Q. What she wrote midway through that paragraph was
3 "This article presents an overview of the current state of
4 knowledge regarding treatment mechanisms and modalities under
5 investigation for DME," correct?

6 A. I see that she wrote that.

7 MS. OBERWETTER: Move to admit into evidence
8 DTX 8151-A.

9 THE COURT: Any objection?

10 MR. McLAUGHLIN: No objection, Your Honor.

11 THE COURT: Without objection, so admitted.

12 (DTX 8151-A was admitted.)

13 BY MS. OBERWETTER:

14 Q. Dr. Albin, you've cited this Dr. Schmidt-Erfurth
15 article a couple of times in some of your IPR declarations; is
16 that right?

17 A. I'll be honest. I don't recall the specific areas
18 where I've cited it, but I'm not surprised to hear that.

19 Q. And just to refresh your recollection, if we pull up
20 DTX 8151-B, which again we have marked individually out of a
21 broader DTX 8151 compilation, this is your declaration from one
22 of the IPR proceedings where you have offered written
23 testimony?

24 A. Yes.

25 Q. And if we go down to paragraph 62 on page 34.

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1 And you can see down toward the bottom of that
2 excerpt that you have cited Dr. Schmidt-Erfurth's December 2010
3 review article previously, correct?

4 A. Yeah. Let me just -- I'm sorry. There's a lot of
5 parentheses here. I'm just trying to figure out what I was
6 trying to say.

7 Yeah, I have to admit I'm not 100 percent certain
8 that that text in brackets there, "The ranibizumab PRONTO study
9 suggested that flexible OCT-guided treatment would sustain
10 visual acuity with fewer injections, a concept which has since
11 become a popular model in clinical practice, particularly in
12 Europe."

13 I'm assuming that's from that article, but I'm not
14 100 percent certain. But if you're asking me whether I had
15 cited this article, if that's a correct reference, yeah, I did.
16 I see that.

17 Q. Okay. You did not include Dr. Schmidt-Erfurth's
18 December 2010 review article about DME on your materials
19 considered list for this case, correct?

20 A. I don't recall. I don't think so, but I'm not
21 certain.

22 Q. Okay. We can take that document down.

23 Dr. Albin, I want to go back to Slide 152 from your
24 direct examination. And Slide 152 we looked at a little bit
25 earlier for its listing of some of the clinical trials that

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1 existed in the pre-2011 time period.

2 Do you see that?

3 A. That's correct.

4 Q. You cite a READ 1 trial, correct?

5 A. That's correct.

6 Q. There was also a READ 2 trial, wasn't there?

7 A. That's correct.

8 Q. You chose not to include READ 2 on this chart?

9 A. That's correct.

10 Q. And that was your decision?

11 A. That's correct.

12 Q. You actually cited READ 2 in your opening report in
13 this case; is that right?

14 A. I believe so.

15 Q. Let's take a look at your -- an excerpt of your
16 opening report. If we go to PTX 487.

17 And you recognize this as a copy of your opening
18 report from this case?

19 A. Yes.

20 Q. And if we go to paragraph 327 of your report.

21 THE COURT: Before we do that, Counsel, again
22 recognizing there's confidential information in this report,
23 any concerns from defense?

24 Negative head shakes. Okay.

25 MR. McLAUGHLIN: No concerns from us, Your Honor.

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1 THE COURT: Understood.

2 Go right ahead, Counsel.

3 MS. OBERWETTER: Thank you, Your Honor.

4 BY MS. OBERWETTER:

5 Q. If we take a look at paragraph 327 of this report,
6 you've got a reference to Dr. Lalwani's article and then a
7 reference to the READ 1 article, and then at the last sentence
8 says, "The author further notes the READ 2 program that
9 followed READ 1 employed monthly dosing through 12 months."

10 Do you see that?

11 A. Yes.

12 Q. Okay. Now, you didn't put READ 2 on your list of
13 clinical trials, right?

14 A. It's not on that list that we talked about, that's
15 correct.

16 Q. All right. READ 2 did not actually employ monthly
17 dosing, did it?

18 A. You know, I have to apologize. There's so many
19 different trials and so many different but yet very similar
20 dosing regimens in these trials. Obviously, when I wrote this,
21 I thought it did. If I'm in error, I apologize.

22 But it looks -- as I read my text here today, it
23 looks that I was under impression that it employed a monthly
24 dosing regimen through 12 months.

25 So the way you're asking the question, I'm guessing

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1 that I was wrong about that. I apologize if that's true.

2 There's a lot of different studies here. So not that I didn't
3 take this seriously, but these reports are very, very long, as
4 you know, and there are many, many citations here.

5 But please tell me if I did get that wrong.

6 Q. Let's take this document down.

7 Let's take a look at a document that we've marked as
8 PTX 3304 that we can pass around.

9 MS. OBERWETTER: Approach the witness, Your Honor.

10 THE COURT: You may.

11 BY MS. OBERWETTER:

12 Q. Dr. Albin, what I handed you -- I've been asked to
13 correct the record -- is actually PTX 3340, just so the number
14 is correct.

15 A. I see that.

16 Q. Does this -- the title of the article is "One-Year
17 Results Showing Ongoing Benefit of Ranibizumab for DME."

18 Does this article refresh your recollection that
19 there was a different clinical trial regimen in READ 2?

20 A. As I'm skimming it here, yes. I see that this
21 article describes "Beginning at six months re-treatment was
22 performed on a prn basis." I'm assuming that's in all the
23 arms. I'm not sure.

24 But, anyway, I see that it's certainly not 12 monthly
25 injections, which is what I inferred from my opening report

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1 that you showed me.

2 Q. Okay. I gather you're not familiar with the READ 2
3 trial even though you cited it in your opening report?

4 A. I believe that I may be confused about the exact
5 dosing regimen. I wouldn't say that I'm not familiar with the
6 trial, but I would say that I can't recollect the exact dosing
7 regimen.

8 Q. Is this a trial that you chose not to include on your
9 list of trials or one that you didn't think about?

10 A. I think I thought about it, as evidenced by the fact
11 that it was cited, although possibly incorrectly. So I
12 wouldn't say that I didn't think about it.

13 I think that it may have not been evidence -- either
14 because of the timing of when the results were announced or
15 because of the data that was there, it may have not been the
16 best trial to choose to make the point that I was trying to
17 make.

18 So I don't think that the work that's been submitted
19 is an exhaustive compendium of all the clinical trials with
20 anti-VEGFs that were available at that time. I certainly don't
21 think that this was left out with any sort of covert intention
22 or for some reason.

23 I think there's only -- so, I mean, this took already
24 six hours today. I don't know how many more trials we could
25 have gone through. There's a limit to what all can be covered.

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1 But so my intention wasn't to have been exhaustive about
2 everything that was there.

3 Q. The date of this article is February 1, 2010,
4 correct?

5 A. Of this particular publication. I don't know when
6 the formal publications came out. I'm not exactly sure what
7 the context of this -- this is clearly an internet -- oh, looks
8 like this is an article from *Ophthalmology Times*, and I assume
9 that's dated February 1st.

10 Q. There were -- if you look at the number of patients
11 who are described in READ 2, it's 126, correct?

12 A. That's correct.

13 Q. That's more than ten?

14 A. I would not disagree with that.

15 Q. More than ten in the READ 1 trial?

16 A. That's true.

17 Q. In the READ 2 trial you would agree that there was a
18 six-month phase where various arms were tested, if you look
19 down at that fifth paragraph of this document.

20 A. Sorry. The fifth paragraph of the document. The
21 paragraph that starts "initially patients"?

22 Q. Yes.

23 A. Okay. I see what's described there.

24 Q. First of all, one of those arms had a group that
25 received an injection of .5 milligrams at baseline in month one

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1 and in month three and in month five.

2 Do you see that?

3 A. I see that. So that sounds like three loading doses
4 and then q8-week interval.

5 Q. Could that be two loading doses if you do two and
6 then go further?

7 A. I think the supposition usually in clinical trials is
8 that the patients are treated at month zero. So there's a
9 first initial treatment, and then -- unless this is a very
10 unusual trial and they didn't treat on the first visit, but
11 typically they're treated at zero.

12 Q. So, Dr. Albin, I don't want to get too hung up here,
13 but there's one at baseline and one at month one and then they
14 skip one, correct?

15 A. You're right. You're right. I apologize. Yes. So
16 two monthly loading doses followed by two q8-week loading
17 doses. Yes, that's true.

18 Q. All right. And then starting in the next paragraph,
19 it notes that "Beginning at six months, re-treatment was
20 performed on a prn basis."

21 Do you see that in the next paragraph?

22 A. I do see that.

23 Q. And then it says, "Starting at six months, patients
24 in the ranibizumab arm could be re-treated no more than once
25 every two months and laser re-treatment no more than once every

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1 three months."

2 Do you see that?

3 A. I see that.

4 Q. And that was a every-two-month prn schedule, correct?

5 A. That's what it sounds like from this description,
6 yes.

7 Q. All right. Now, at the top of this same page that
8 we've been on, there's a quote from Dr. Do that says, "The
9 results from the READ 2 trial Phase II study demonstrate this
10 anti-VEGF agent has biological activity in treating DME," and
11 then it goes on to say that "More frequent injections may be
12 needed to achieve enhanced visual acuity benefits."

13 Do you see that, sir?

14 A. I do. I see it.

15 Q. And that's a point that Dr. Do made in this article
16 about the READ 2 one-year results in ranibizumab.

17 A. Is that a question or a statement?

18 Q. That's a question.

19 A. Yes, I believe so.

20 Q. And then if you go to page 2 of this document, it
21 notes that by the end of 12 months the ranibizumab group had
22 gained a mean of, I think, 6.69 letters.

23 Do you see that?

24 A. Not really.

25 Q. It's down under "Outcomes Comparison."

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1 A. "Outcomes Comparison." I see that.

2 Q. And then if you go down a little further where Dr. Do
3 concludes the article, she notes that "Genentech's Phase III
4 trials for DME were testing monthly ranibizumab," correct?

5 A. She does say that, that's correct.

6 Q. And you know that those were the RISE and RIDE trials
7 that were ongoing as of this point in time?

8 A. That's what she says there, yes.

9 Q. That's not just what she says. You know the RISE and
10 RIDE trials were ongoing at that time?

11 A. That's correct.

12 Q. You did not mention the RISE and RIDE trials in your
13 direct examination either, right?

14 A. That's correct.

15 Q. We can take that down.

16 Now, the READ 2 trial actually continued into a third
17 year, correct?

18 A. I'd have to refresh my memory.

19 Q. You're not familiar with what happened in year three
20 of the READ 2 trial?

21 A. I don't know that I can give you all the details of
22 it. I don't -- I would have to refresh my memory. I don't
23 think I've looked at the three-year results of the READ 2 trial
24 in quite some time.

25 Q. Let's take a look at another exhibit that I will pass

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1 around, which will be PTX 3342.

2 MS. OBERWETTER: And before I proceed with this one,
3 I'd move to admit PTX 3340.

4 THE COURT: Any objection to 3340?

5 MR. McLAUGHLIN: We do object, Your Honor. So we've
6 been scrambling over here a little bit to find out when it was
7 produced to us. Doesn't appear on their original pretrial
8 exchanges of their exhibits. This is the first time we're
9 aware of this being offered to us. So we do object to it being
10 moved into evidence.

11 THE COURT: Previously disclosed, Counsel?

12 MS. OBERWETTER: This is impeachment material, Your
13 Honor.

14 THE COURT: Overruled.

15 BY MS. OBERWETTER:

16 Q. Dr. Albin, do you have PTX 3342 in front of you?

17 A. Yes.

18 Q. Okay.

19 THE COURT: Yes, Counsel.

20 MR. McLAUGHLIN: Your Honor, it's my understanding
21 that the parties agreed that impeachment materials would not be
22 moved into evidence.

23 THE COURT: We're going to have a discussion about
24 the parties' agreement. The rules of civil procedure permit
25 the use of impeachment material solely for that purpose. It

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1 wasn't previously disclosed. At this point the objection is
2 overruled.

3 BY MS. OBERWETTER:

4 Q. Dr. Albin, you have PTX 3342 in front of you,
5 correct?

6 A. I do.

7 Q. And this relates to the three-year outcomes for the
8 READ 2 trial; is that right?

9 A. That's correct.

10 Q. And the first author on this paper is Diana Do?

11 A. That's correct.

12 Q. And the dates listed on this paper, if you go over to
13 the middle right of the first page, are -- there's a
14 publication of 2013 but also published online October 8th,
15 2012.

16 Do you see that?

17 A. I'm sorry. Published online 2012. I'm not -- oh,
18 over here. I see it. Yes, I see it.

19 Q. And if we take a look at page 142 of this article
20 under the header "Need for Ranibizumab Injections in Year 3."

21 A. I see that.

22 Q. Do you see that page? And it says, "During year
23 three, 14 to 28 patients, 50 percent, in the ranibizumab group
24 met the re-treatment criteria at more than six visits and thus
25 needed injections more frequently than every two months."

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1 Do you see that?

2 A. I see that.

3 Q. Okay. And that is what Dr. Do is reporting happened
4 in year three of the READ 2 trial?

5 A. That appears to be what she's reporting, yes.

6 Q. And if we take a look at the bottom of page 143 and
7 continuing on to the top of page 144.

8 If we can pull that up.

9 And if we look down a little bit, please feel free to
10 read that paragraph. But it says, "Despite a good visual
11 outcome, substantial residual macular edema was noted in
12 several patients, suggesting that receiving intraocular
13 injections of ranibizumab only as frequently as every two
14 months was not sufficient for many of them."

15 Do you see that?

16 A. I see that.

17 Q. And that is the conclusion that she reported in
18 writing up year three of the READ 2 study, right?

19 A. I see that that's what she reported, yes, or
20 concluded, yeah.

21 Q. And this is not a component of the READ 2 trial that
22 you included either in your report or in your statements on
23 direct examination, correct?

24 A. That's correct.

25 MS. OBERWETTER: Move to admit PTX 3342.

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1 THE COURT: Any objection to 3342?

2 MR. McLAUGHLIN: Your Honor, at this time, yes, we do
3 object for the same reasons as the previous one. And just to
4 get some clarity, we're not objecting to the use of this on
5 impeachment; our sole objection is its movement into evidence
6 with respect to this one and the prior document.

7 THE COURT: Understood. For same reasons, overruled.

8 So the record's clear, 3340 and 3342 will be deemed
9 admitted, recognizing it is being used as impeachment and will
10 be afforded the weight it should be moving forward.

11 MR. McLAUGHLIN: Is it all right to address that in
12 the posttrial briefing?

13 THE COURT: I'm sure if Madam Court Reporter has it
14 down, of course, Counsel.

15 (PTX 3342 and 3340 were admitted.)

16 MR. McLAUGHLIN: Thank you, Your Honor.

17 MS. OBERWETTER: We can take that document down.

18 BY MS. OBERWETTER:

19 Q. There's a different document that was addressed in
20 your direct examination, Dr. Albin, which was DDX 6.92, so
21 Slide 92.

22 Dr. Albin, you have this slide back up in front of
23 you?

24 A. I do.

25 Q. And it's referencing DTX 4129, correct?

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1 A. That's correct.

2 Q. And I'd like to -- first of all, this is an internal
3 Regeneron document that you cited, right?

4 A. That is correct.

5 Q. And you cited it with reference to that "no more than
6 three to six doses" language down in the bottom right hand of
7 the page?

8 A. Right. That that would be a target product profile
9 for aflibercept in DME.

10 Q. You've not found a publication that includes the
11 language "no more than three to six doses," right?

12 A. I have not.

13 Q. Okay. It also lists -- it says monthly -- it says,
14 "No more than three to six doses including monthly loading for
15 first three months."

16 Do you see that?

17 A. Yes.

18 Q. And you are not -- first of all, that's the only
19 number of loading doses that appears on this page, is three?

20 A. That's the only number of doses termed as loading
21 doses, but the range of up to six doses given in the first six
22 months is described there.

23 Q. So. You -- I apologize.

24 A. That would be a dose every month for six months.

25 Q. You have not cited or relied on any testimony

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1 explaining the reference to induction, correct?

2 A. Explaining the reference for induction?

3 Q. Let me -- go ahead, Doctor.

4 A. Well, I think what I am citing here is that within
5 Regeneron, they were discussing the need for three to six doses
6 within the first six months in initiating treatment, which is
7 the way that I read that -- the term "induction" there.

8 Q. My question is a little bit different.

9 You haven't relied on any fact witness testimony to
10 explain what the reference to induction is there, correct?

11 A. I have not.

12 Q. All right. There's also nothing in that section of
13 the document about fixed extended interval dosing, correct?

14 A. I do not see anything about fixed interval --
15 extended interval dosing.

16 Q. When was this document written relative to when the
17 DA VINCI trial commenced?

18 A. That, I don't know.

19 MS. OBERWETTER: We can take that document down.

20 I'm going to change topics a little bit.

21 THE COURT: Counsel, if we're going to do that, good
22 time to take a break?

23 MS. OBERWETTER: This works fine for a break, Your
24 Honor.

25 THE COURT: Okay. We'll break. I don't want to

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1 interrupt the flow, but let's do that.

2 Doctor, you continue to remain midstream; so no one
3 can converse with you. No one is being rude or discourteous.
4 It's just the rules we abide by. You get to step down, take a
5 personal comfort break, whatever you need, sir.

6 THE WITNESS: Fair enough. Thank you.

7 THE COURT: We'll take a break and be back in ten
8 minutes. Thank you all.

9 (A recess was taken from 2:57 p.m. to
10 3:11 p.m.)

11 THE COURT: Counsel, are you ready to proceed?

12 MS. OBERWETTER: I'm ready to proceed, Your Honor.

13 THE COURT: Doctor, are you ready?

14 THE WITNESS: I sure am.

15 THE COURT: Great. Go right ahead.

16 BY MS. OBERWETTER:

17 Q. Dr. Albin, I'm going to return briefly to some of
18 the opinions you've offered on Claim 6 and the isotonic
19 solution limitation we were talking about earlier.

20 A. Okay.

21 Q. You would agree there could be formulations,
22 comfortable and nonirritating, that are outside of the range of
23 isotonic, right?

24 A. Not through what I've learned from Dr. Rabinow. So,
25 no, I'm not sure that what you're saying is true.

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1 Q. You don't know anything about that absent
2 Dr. Rabinow, correct?

3 A. I am definitely relying on him because I have not
4 offered myself as an expert in formulation. So I am using his
5 teaching in addition to my reading of Dixon to make a
6 conclusion about that issue.

7 Q. You would agree that, as of 2011, it was not known
8 publicly what formulation Eylea was?

9 A. I would anticipate that that's true. I don't know
10 for a fact what exactly about the formulation of Eylea was
11 known in 2011. So I can't be 100 percent certain, but I would
12 guess that the exact -- that the exact formulation was not
13 known.

14 Q. You would agree that it was not public in 2011 what
15 formulation was used in the Phase III trial described in Dixon,
16 correct?

17 A. When you say what formulation, I believe that it
18 was -- it's -- that the POSA and myself as a POSA would have
19 interpreted that the formulation used in the clinical trials
20 was the same as the formulation that was used in the
21 commercially available product.

22 Q. The commercially available product was known later,
23 right? Not in 2011?

24 A. Was known later?

25 Q. Right. It came onto the market after the Phase III

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1 trials, correct?

2 A. Yes, but it was known well before it came out to the
3 market.

4 Q. You would agree that it was not public in 2011 what
5 formulation was used in the Phase III trial described in Dixon
6 prior to Eylea coming onto the market?

7 A. As I've said, I think that the POSA would have known
8 that the formulation that's used in the clinical trials is the
9 same as the formulation that's brought to market.

10 Q. You know that once the product is brought to market,
11 not before, correct?

12 A. No, I think you'd know that the product that will be
13 brought to market is the product that's studied in the trials.
14 I think there's an assumption that it's the same product;
15 otherwise, we wouldn't use the clinical trials to help guide us
16 with the use of new product.

17 Q. You have not identified a publication that spells out
18 the formulation of Eylea publicly prior to it coming onto the
19 market?

20 A. I have not.

21 Q. Okay. I'm going to change topics.

22 I'd like to -- you offered some opinions on your
23 direct testimony about the '747 patent and anticipation.

24 Do you recall that generally?

25 A. I do.

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1 Q. So let's pull up DTX 2730 and go to Example 17, which
2 is at Column 20.

3 Dr. Albin, you agree that Example 17 does not itself
4 talk about diabetic macular edema, correct?

5 A. I believe that this patent directs itself at
6 angiogenic eye disorders.

7 Q. So my question was different. There's a title on
8 Example 17 that says "Treatment of Age-Related Macular
9 Degeneration," correct?

10 A. Yes.

11 Q. Example 17 does not talk about DME?

12 A. That is correct.

13 Q. Example 17 does not contain a reference to a loading
14 phase of dosing a patient, correct?

15 A. It does not use that term "loading phase," that is
16 correct.

17 Q. And, in fact, Example 17 discusses repeated visits
18 back to the doctor during the first month, right?

19 A. It does.

20 Q. You have to go outside of the embodiment of
21 Example 17 in this patent to find DME anywhere, right?

22 A. I believe that's true.

23 Q. And in forming your opinions in this case, you did
24 not attempt to calculate the total number of regimens that are
25 contained in Example 17, correct?

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1 A. I did not quantify that, no.

2 Q. Or in the patent as a whole, correct?

3 A. That's correct.

4 Q. And I think you testified at your deposition you
5 weren't interested in doing that because you don't like to do
6 infinite things; is that right?

7 A. I don't recall if that's exactly what I said, but I
8 think I would be very bad at doing something that's infinite.

9 But there's a very large number of possible regimens
10 that are covered by this if one doesn't have a limit on the
11 time extension that you're looking at.

12 But within a 6-month period or a 12-month period,
13 there's a more limited number of regimens. But even within
14 that period, I have to admit I have not calculated the exact
15 number of permutations possible.

16 Q. Looking at Example 17 during your deposition, you
17 referred to it as "infinite"; is that correct?

18 A. Honestly, I don't remember that text in the
19 deposition, but I can't see why you would be misleading me.
20 I'm sure that I did.

21 Q. I'd like to talk a little bit about the September
22 2009 press release that was the subject of your direct
23 testimony, if we can pull up PTX 2617.

24 And this is the September 2009 Regeneron press
25 release that you testified about.

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1 A. That's correct.

2 Q. There is a section on page 2, if we scroll forward to
3 that, that talks about the Phase II development program in DME.

4 Do you see that right above "about wet AMD"?

5 A. I see that.

6 Q. Now, that discussion talks about three monthly
7 loading doses on its face, correct?

8 A. Yes.

9 Q. And after the loading doses, any additional doses are
10 based on prn assessment, correct?

11 A. That's correct.

12 Q. Those are not going to be fixed interval doses,
13 right?

14 A. The most frequently they can occur is every month.
15 So in that sense, they're fixed interval in that they certainly
16 can't happen at every two weeks or every three weeks or
17 something like that. So they are partially fixed. But they
18 are not fixed in that patients are not going to be necessarily
19 getting an injection every single month, although they might.

20 Q. In your anticipation analysis that you performed in
21 this case, you're also assuming that these are monthly prn
22 visits, correct?

23 A. That's correct.

24 Q. Okay. And let's take a look at Slide 52 from your
25 direct examination. This is a slide that you used to talk

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1 about anticipation in connection with the September 2009 press
2 release; is that right?

3 A. Yes.

4 Q. Giving someone three loading doses and then a prn
5 regimen does not necessarily result in that person receiving a
6 dose at Week 12, correct?

7 A. The Week 12 dose is one possibility from that dosing
8 regimen, but it is not necessarily going to occur.

9 Q. And if you give someone three loading doses and then
10 you give them a prn dose at Week 12, that also does not
11 necessarily result in that person receiving a dose at Week 16,
12 correct?

13 A. It would -- correct. It would depend on the
14 assessment of the patient at that visit.

15 Q. You would agree that the terminology of "loading
16 doses" implies an early adherence to monthly treatment
17 regardless of patient outcome for a certain number of doses,
18 correct?

19 A. That sounds fair.

20 Q. Okay. And prn doses after loading doses would be
21 quite different because it would include regular visits but
22 doses only when needed, right?

23 A. That's correct.

24 Q. We can take that slide down.

25 I want to return briefly to we talked about the

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1 RESOLVE trial a little bit in connection with dosing studies
2 for ranibizumab.

3 Do you recall that?

4 A. I do.

5 Q. You have not undertaken an analysis of the RESOLVE
6 trial to understand if anyone in that trial got five initial
7 doses, whether you call them loading doses or not, right?
8 That's not an analysis you performed?

9 A. You mean historically whether that actually occurred
10 to go back and look at the trial data and find how many
11 patients may have obtained that? I have not had access to the
12 data to be able to do that.

13 Q. Okay. You haven't found out how many, if any,
14 correct?

15 A. I haven't found out how many, that's true.

16 Q. Okay. I want to change topics a little bit. And
17 let's look at Slide 91, which was part of your direct
18 testimony.

19 There's a reference in the bottom line to the
20 Copernicus trial. Do you see that?

21 A. I see that.

22 Q. You mentioned there the Copernicus trial you refer to
23 always having six monthly loading doses on that page. Do you
24 see that?

25 A. I do see that.

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1 Q. Let's take a look at DTX 3198, which should be
2 another press release.

3 And we're back at a September 2009 press release, and
4 if we go again to page 2 of the press release, there's a
5 reference in that top paragraph to the COPERNICUS trial.

6 Do you see that?

7 A. I do.

8 Q. There's no terminology there that refers to six
9 loading doses, correct?

10 A. I don't see the term "loading doses," but again, it
11 seems to describe six monthly intravitreal injections of VEGF
12 Trap-Eye.

13 Q. Dr. Albin, it refers to six monthly injections when
14 there is a primary end point of six months, correct?

15 A. That is correct.

16 Q. We can take that document down.

17 I'm going to change topics a little bit. I have a
18 few questions for you about VEGF agents generally. You would
19 agree that early on in the development of aflibercept,
20 researchers recognized the promise of targeting angiogenesis as
21 a therapeutic strategy for treating diseases characterized by
22 increased vascularity?

23 A. Specifically neovascularization, but yes.

24 Q. You agree that angiogenic eye disorders are generally
25 characterized by increased vascularity?

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1 A. Specifically new vessels and also by decreased
2 patency of less of the vessels where there's fluid that leaked
3 into the retina. By both those characteristics, yes.

4 Q. Prior to the January 2011 date that we've been
5 talking about, there was literature that, in your view, that
6 VEGF Trap may be useful in the treatment of retinopathies given
7 the contribution of pathological angiogenesis, correct?

8 A. That is correct.

9 Q. You also believed that the medical community believed
10 before January 2011 that VEGF Trap-Eye could translate to good
11 clinical efficacy outcomes, correct?

12 A. I think that was evidenced by a number of the
13 publications that were reviewed towards the end of my direct
14 testimony.

15 Q. Okay. And that's good clinical efficacy outcomes for
16 angiogenic eye disorders, correct?

17 A. That is correct.

18 Q. And you believe that subsequent work by Regeneron
19 reinforced VEGF Trap's potential as a possible angiogenic
20 therapy for vascular eye diseases, correct?

21 A. That is correct.

22 Q. You understand that some of the claims in the patents
23 use the word "approximately"; is that right?

24 A. I've seen that, yes.

25 Q. And the terms "approximately every four weeks" and

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1 "approximately monthly" can be understood as meaning the same
2 thing in the context of anti-VEGF dosing regimens, correct?

3 MR. McLAUGHLIN: Objection, scope. It's beyond the
4 scope of his testimony, Your Honor.

5 MS. OBERWETTER: Your Honor, it's in his report,
6 which is context for the patent claims which he is purporting
7 to talk about in this case.

8 THE COURT: Is it in his report, Counsel?

9 MR. McLAUGHLIN: If it is, I would like to see it.
10 I'm not sure exactly what Ms. Oberwetter is referring to.

11 MS. OBERWETTER: Why don't we pull up paragraphs 144
12 to 145.

13 BY MS. OBERWETTER:

14 Q. Dr. Albin, in your report you wrote that, in your
15 opinion, you viewed --

16 THE COURT: Hold on, Ms. Oberwetter, before he gets
17 any questions.

18 Counsel, does that fall within this line of
19 questioning?

20 THE WITNESS: I see that.

21 THE COURT: One second, Doctor. Thank you.

22 MR. McLAUGHLIN: I see the paragraphs that counsel's
23 referring to, but this is not something where he provided an
24 opinion on what the word "approximately" means. What he's
25 talking about here is the difference between every four weeks

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1 and monthly with respects to Claim 11, I believe -- yeah,
2 Claim 11 of the '601 patent.

3 But he has not offered an opinion, nor did I ask one
4 on his direct, what his views of "approximately" are in this
5 claim.

6 THE COURT: Okay.

7 MS. OBERWETTER: Two responses Your Honor. One is we
8 heard three hours of testimony this morning about the claims,
9 which he is interpreting and applying, and I think this is
10 relevant to his understanding of them.

11 Point two, I would rather do this all as a whole
12 rather than figure out do we have to recall Dr. Albin in our
13 case? I'd rather do this today. It makes sense to do it.
14 This is part of his opinions that were disclosed and that he
15 has said are his views.

16 THE COURT: Understood. Overruled.

17 Ask your question again, Counsel.

18 BY MS. OBERWETTER:

19 Q. Dr. Albin, you understand the terms "approximately
20 every four weeks" and "approximately monthly" as meaning the
21 same thing in the context of anti-VEGF dosing regimens,
22 correct?

23 A. I think that what I was trying to say here -- and it
24 is somewhat confusing with this language and the way this claim
25 is written, but I do think that four weeks and monthly have an

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1 equivalence to them. They are nearly the same thing. There
2 may be differences in the way that "approximately" modifies the
3 four-week period versus the monthly period.

4 So as to say as the time around the four-week period
5 that's approximated, the range of time that would fall within
6 that "approximately every four weeks" may be different than the
7 range of time that falls in the term "approximately monthly" so
8 that, when you say approximately monthly -- and this is just my
9 interpretation of common usage of the English language -- I do
10 agree that this claim is difficult to understand completely.

11 I would think that "approximately monthly" could mean
12 monthly plus/minus one month, and approximately every four
13 weeks could mean every four weeks plus/minus one week so that
14 that interval might be difference if you really get down to it.
15 Obviously, the terms are very, very similar.

16 Q. Dr. Albin, in your report you understood the phrases
17 "approximately every four weeks" and "approximately monthly"
18 sufficiently to equate them as meaning the same thing, right?

19 A. I did write that they mean the same thing. I may
20 have not been focused as you've asked me -- or as least as I've
21 perceived you've asked me to do here to look at the meaning of
22 the word "approximately" within that.

23 And I do appreciate that "approximately" may be
24 applied in slightly different ways to a four-week time interval
25 versus a monthly interval, but I do think that monthly and four

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1 weeks are very, very similar and the same thing.

2 Q. We can take that slide down.

3 Dr. Albin, you would agree that as of 2011, the POSA
4 would have known how to intravitreally administer an anti-VEGF
5 agent, correct?

6 A. That is correct.

7 Q. And the POSA would have known how to do that
8 approximately every four weeks?

9 A. Well, on the face of it, the obvious answer to the
10 question is, if a POSA knows how to do it once, they know how
11 to do it at any time interval.

12 The part that I'm hesitant about is I don't know that
13 it would have been obvious necessarily what "approximately"
14 means in and of itself. Certainly I think that, for example,
15 if you were conducting a clinical trial and the trial said
16 we're going to inject this drug approximately every four weeks,
17 the trialist or the principal investigator would want to know
18 what exactly does "approximately" mean? How big is that
19 window? Can we be off by two days? by three days?

20 So I don't know that -- certainly the POSA would know
21 how to do the injection. The question is whether the POSA
22 would need more clarification as to that time interval.

23 Q. Dr. Albin, I'm going to see again if you remember
24 your deposition in this case.

25 A. Sure.

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1 Q. If we could please pull up page 230 from your
2 deposition. And if we can put that side by side with 231.

3 I asked you, if you go down to line 18: "Okay. And
4 maybe I'll get a similar answer here. But would the" --

5 Actually, I'm sorry. Can we pull that down and go up
6 a little further? Apologies.

7 I asked at line 8:

8 "Q Would the POSA know how to do that
9 approximately every four weeks?

10 "A He would know how to. He may not
11 choose to, but he would know how to do that,
12 yes."

13 And then I asked again at line 18:

14 "Q Maybe I'll get a similar answer here,
15 but would the POSA know how to perform
16 intravitreal injections approximately once every
17 eight weeks?

18 "A I think if he can do it once, he can do
19 it at any time interval."

20 Do you see that?

21 THE COURT: One second, Doctor.

22 Yes, Counsel?

23 MR. McLAUGHLIN: I'd like to object based on this
24 being improper impeachment testimony. These are not the same
25 questions that he was just asked, and he's not providing any

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1 inconsistent testimony here.

2 THE COURT: I don't think that's been suggested yet.

3 Understood. Overruled.

4 BY MS. OBERWETTER:

5 Q. Dr. Albin, these are the answers to my questions
6 about "approximately" that you gave at your deposition,
7 correct?

8 A. I think that, if you look at the context there, I was
9 careful to say I'm still talking about the physical steps of
10 doing it as opposed to understanding how the span of the time
11 interval between the injections.

12 So if you're asking me would the POSA know how to
13 administer the drug? Yes, they would know how to administer
14 the drug. Would they know necessarily what "approximately
15 every week" means? I don't think that they could know that
16 without further clarification.

17 Q. That is not --

18 A. And I think that is consistent with the testimony
19 that's on here.

20 Q. That is not clarification you sought when I asked you
21 these questions at your deposition.

22 A. It's right there. I mean, I don't know. Do you not
23 see it? I said, "And I'm still talking about the physical
24 steps of doing it."

25 Q. Dr. Albin, would you agree that as of -- I'm going

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1 to change topics slightly.

2 Dr. Albin, we haven't spoken much yet about Avastin.

3 That's bevacizumab, correct?

4 A. That's correct.

5 Q. And that was originally approved as a cancer
6 treatment, correct?

7 A. That's correct.

8 Q. And we talked about how it's now used off-label to
9 treat angiogenic eye disorders?

10 A. That's correct.

11 Q. I think you've testified on whatever the exact number
12 is, it's inexpensive, and whether it's \$50 or somewhere south
13 of \$200, it's in that range?

14 A. That's correct.

15 Q. In your view, any difference in efficacy -- this is
16 your view -- any difference in efficacy between Avastin and
17 Eylea is small, correct?

18 A. That's correct.

19 Q. You think Avastin is a good drug?

20 A. That's correct.

21 Q. And in your practice you've used a lot of Avastin,
22 correct?

23 A. That's correct.

24 Q. Including through the present?

25 A. That's correct.

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1 Q. Dr. Albin, you agree that important advancements in
2 treating retina need to come from industry, right?

3 A. I know that I've said that on many occasions, and I
4 think that given the complexity now of bringing a drug to
5 market, I stand by that statement; they need to come from
6 industry.

7 What I think might not be 100 percent true is to say
8 that they can only come from industry. Avastin is a great
9 example of a drug that was developed as a therapeutic agent for
10 angiogenic eye disorders in spite of industry.

11 So I think there are few such examples in medicine,
12 but I do think that Avastin is a good example where that rule
13 that I -- or that teaching that I've given on the importance of
14 industry and the further development of therapeutics, I think
15 that that's an exception that proves the rule, but there are
16 likely to be other exceptions too of important therapeutic
17 advances that occur either without the support of industry or
18 in spite of industry.

19 Q. Okay. And you have said there's an important role
20 for industry because large organizations have more resources to
21 bring to bear to get products to market, correct?

22 A. That is true.

23 Q. And those are things that cannot necessarily be done
24 by physicians alone, correct?

25 A. Well, I wouldn't say cannot. So, again, I'll use the

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1 example of bevacizumab. There, Dr. Rosenfeld pretty much
2 single-handedly brought that drug to its use. I'm sure other
3 individuals were involved. But it was largely done by an
4 academic institution and by a particular provider.

5 And so I don't know that it always has to be
6 industry. I think in the vast majority of major progresses
7 that are going to be made, I think it's safe to say most of
8 them will have industry as a component of a product's success.

9 Q. Dr. Albin, you agree that a drug's formulation can
10 be important to whether it is a good drug or not, correct?

11 A. I do agree.

12 Q. And, in fact, the formulation of a drug can be the
13 key to the clinical success and efficacy of a treatment,
14 correct?

15 A. I don't think the formulation can be a key to the
16 efficacy of a treatment. I think that formulation can
17 certainly get us into trouble with toxicity, presumably. But I
18 think that formulation alone, aside from things like, you know,
19 intravenous fluids, very simple things, if you're getting into
20 more complicated molecular therapeutics, formulation alone can
21 definitely not bring great efficacy.

22 Q. I'd like to take a look at page 129 of your June 22,
23 2022, deposition. And if we can put that side by side with
24 130.

25 And you were asked -- this is questions put to you in

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1 another deposition by another attorney, but you see at line 10
2 on 129 you were asked:

3 "Q Okay. And what I'm trying to
4 understand is is it fair to say that, while the
5 attributes of the molecule may be necessary, that
6 they're not alone sufficient for the molecule to
7 work on a given dosing regimen?

8 "A Certainly there are other attributes
9 other than the molecule that are very important
10 in the clinical success and efficacy of a
11 treatment. The formulation, for example, is
12 key."

13 Is that testimony you provided?

14 A. Yes, it is.

15 THE COURT: Yes, Counsel?

16 MR. McLAUGHLIN: Just want to object to this as being
17 beyond the scope. This is a deposition that was taken in a
18 different matter on a different patent and not this litigation.

19 THE COURT: Understood.

20 Counsel.

21 MS. OBERWETTER: Yes. It's proper impeachment
22 evidence taken from another -- it wouldn't matter what case it
23 was taken from.

24 THE COURT: What point are we impeaching the doctor
25 on with this?

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1 MS. OBERWETTER: Where he said he would not call
2 formulation key.

3 THE COURT: Understood. Overruled.

4 MS. OBERWETTER: We can take that down.

5 BY MS. OBERWETTER:

6 Q. Dr. Albin, you would not prescribe a drug if it had
7 an unsafe formulation, correct?

8 A. It depends on the context. I think that everything
9 is a risk-benefit ratio. So if there was something that was,
10 quote/unquote, unsafe about a drug but it was -- that the
11 patient was certain to either go blind or lose their life
12 without the drug, I think that you would administer that drug
13 regardless of safety concerns.

14 So I think there's always a risk-benefit ratio. It's
15 not -- I don't mean to make it sound as if it's always so stark
16 between life and death, but there can be gradations within
17 there.

18 Sometimes drugs with imperfect safety have such a big
19 potential efficacy improvement that it makes sense to use them
20 even with the safety concerns.

21 Certainly no drug is without safety concerns. We'd
22 use no drugs ever if we never used any drugs with some safety
23 issue.

24 Q. And you would agree that all attributes of a drug can
25 be important to its commercial success, including things like

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1 its stability, its binding capacity, and its clearance,
2 correct?

3 A. I believe all of the properties of a drug can be
4 important attributes for that drug's safety and efficacy, yes.

5 MS. OBERWETTER: Nothing further, Your Honor. Pass
6 the witness.

7 THE COURT: Understood. Thank you, Counsel.
8 Redirect?

9 MR. McLAUGHLIN: Yes, I do. Thank you, Your Honor.

10 REDIRECT EXAMINATION

11 BY MR. McLAUGHLIN:

12 Q. So I'd like to revisit with you, Dr. Albin, some of
13 the questions that you heard from counsel today.

14 So when providing your opinions on reasonable
15 expectation of success, you were considering the visual acuity
16 outcomes, correct?

17 A. That's correct.

18 Q. And you understand that a reasonable expectation of
19 success analysis, like what you've conducted in formulating
20 your opinions in this case, requires a different standard than
21 what is required for FDA approval; is that right?

22 A. That is correct.

23 Q. Do you also agree that drugs can fail for a number of
24 reasons that are not related to the visual acuity outcomes,
25 like the visual acuity that we've been discussing here today?

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1 A. That's correct.

2 Q. You were asked at one point about uncertainty as to
3 the best dosing approaches for anti-VEGF agents.

4 Can I ask you, in your experience, in your practice,
5 how were you treating patients in the clinic prior to 2010?

6 A. I think that much like what was described in that
7 2007 *Retinal Physician* report, I was using a prn and then
8 progressing -- I don't remember exactly when I might have
9 shifted -- to a treat-and-extend protocol.

10 And I don't think that I made that transition -- you
11 know, that I decided one day I'm going to shift from one to the
12 other. It was done on a patient-by-patient basis depending on
13 issues. Certainly patients that had difficulty with
14 transportation and coming in would be patients that I would
15 shift to a treat-and-extend- protocol earlier than patients who
16 had no problem coming in for their visits.

17 So I think there was a gradual transition where I
18 shifted from prn dosing. I think I also used fewer loading
19 doses as time went on in that time period from 2007 to 2010.

20 Q. But you don't dispute that there were regimens like
21 treat and extend, as you indicated and showed in your
22 presentation today, in use as early as 2007; is that right?

23 A. Absolutely. And documented in the literature, as was
24 in my testimony.

25 Q. And treat and extend, is that the same type of

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1 protocol that's currently used today?

2 A. I believe that that's the most commonly used
3 treatment protocol today, yes.

4 Q. And does treat and extend involve individualized
5 assessments?

6 A. It does. The -- one of the concepts of treat and
7 extend is to try to determine what a dosing interval is that's
8 required for a particular patient and then to stick to that
9 interval. So some patients are seen as patients who require
10 injections every four weeks, some every six weeks, some every
11 eight weeks, and so on. And that's determined through trial
12 and error for each individual patient.

13 Q. Were you using prn dosing as well in the pre-2010
14 time period?

15 A. Yes, I was.

16 Q. And that involved -- that was a regimen that would
17 allow you to administer fewer injections to patients compared
18 to a monthly dosing regimen, a fixed monthly dosing regimen,
19 correct?

20 A. Yeah, that's true. And what I recall happening is
21 that, as patients were coming in -- some patients, not all --
22 but as some patients came in for their, let's say, third month
23 visit and there was no fluid seen and then they came in for
24 their fourth month visit and there was no fluid seen, then it
25 was a natural progression to say, "You know what? You don't

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1 have to come in next month. Come in in six weeks. Let's see
2 you then." And then if there was no fluid -- so treat and
3 extend kind of built out of prn in a very natural way for a lot
4 of us.

5 Q. And treat and extend was an individualized dosing
6 regimen that would allow not only an extension of time between
7 injections but also an extension of time between office visits;
8 is that right?

9 A. That's correct.

10 Q. Now, I'd like to ask you about a -- that 2008
11 presentation that you were shown earlier.

12 If I could ask to be put up on the screen, side by
13 side, both DTX 0204 as well as that 2008 presentation. I
14 believe it's DTX 3173.

15 Actually, while they're doing that, I wanted to ask
16 you -- I'll jump ahead and ask you something else while they're
17 finding those documents.

18 You were also asked about isotonicity by counsel?

19 A. That's correct.

20 Q. And your view of the injections of potentially
21 nonisotonic formulations.

22 A. That's correct. I was asked about that, yes.

23 Q. Do you have a sense -- actually let me back up.

24 You were asked about the confidentiality of the Eylea
25 formulation and what was known about it prior to 2011; is that

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1 right?

2 A. That's correct.

3 Q. And you were asked about whether you were aware of
4 any public disclosure of that formulation?

5 A. I was, yes.

6 Q. And you were asked about whether that formulation was
7 confidential or not?

8 A. That's true. As you're asking me this question now,
9 I'm realizing that there were certainly elements of that
10 formulation that may not have been confidential that were
11 known. So I maybe shouldn't have answered that as a blanket
12 that it was not known. Some parts of the formulation I think
13 probably were readily available and certainly could have been
14 tested by anyone who bought the drug.

15 Q. Let me ask you this: Are you aware that in this
16 litigation Regeneron is also asserting a formulation patent?

17 A. Yes, I'm aware of that.

18 Q. And I will represent to you that that formulation
19 patent lists on its face an earliest application date of 2006,
20 and I will also represent to you that Regeneron has represented
21 the '865 patent covers Eylea.

22 Would that knowledge have been important to you in
23 answering counsel's questions about the confidentiality and
24 public nature of the Eylea formulation?

25 A. Yeah. Yes. Obviously, yes, it would have been. And

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1 I'm sorry that I may have not answered that in the best
2 possible way.

3 Q. No need to apologize, Dr. Albin.

4 A. I did not know that they had patented the
5 formulation. I still don't know, sitting here now, whether
6 the -- all the exact attributes of the formulation are
7 available in this patent; but, again, certainly some components
8 of the formulation would have been available, and some
9 components of the formulation are disclosed in Dixon, as we've
10 described earlier today.

11 Q. You were asked about the induction versus loading
12 doses.

13 In your view, is there any real difference between
14 induction doses and loading doses as the terms are used in
15 practice?

16 A. I don't think that there was much use of the term
17 "induction doses," and I certainly can't think of any loading
18 doses that would not be induction doses. So I think there's a
19 lot of overlap in those terms, and I don't know that there's
20 any meaningful distinction in clinical practice -- or there is
21 no meaningful distinction in clinical practice.

22 Q. Now that we have these documents up, let me go back
23 to Dixon. That's 0204.

24 Now, you recall you were asked questions about the
25 availability of this presentation. I believe in your earlier

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1 testimony, you confirmed that this presentation was cited in
2 the references section of Dixon?

3 A. That's correct.

4 Q. And if we can go to that and take a look at that.

5 Let's go to the references portion of this article.

6 Should be the second-to-last page. If we pull up Reference

7 Number 45. If we can put it so that Dr. Albinini can still see
8 the image on the right.

9 It's the same title that we're looking at here?

10 A. Yes.

11 Q. Is that the same date?

12 A. Yes.

13 Q. If we go back to 0204, page 4, and if we move to
14 page 12 of the document on the right.

15 So if we can look at Dixon, left-hand column towards
16 the bottom, where it says, "Patients initially dosed on a
17 2-milligram schedule received an average of 1.6 more injections
18 over the course of the treatment phase," is that consistent
19 with the data shown to the right with respect to that dosing
20 arm in the CLEAR-IT 2 clinical trial shown at Slide 12 where it
21 says 1.55?

22 A. In here it says -- I'm sorry; I'm just confused.
23 Here it says 1.6, and here it says 1.55. I would say those are
24 consistent.

25 Q. And the 2 mg q4 regimen, do you understand that to be

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1 the one with the every-four-month loading doses following by
2 prn dosing?

3 A. That's right.

4 Q. Then if we flip to page 13 of this -- of the document
5 on the right. What does it tell you about the time to
6 reinjection in all patients in the CLEAR-IT 2 trial?

7 A. Somewhere it discloses the median time to
8 reinjection. Just a minute here.

9 "The median time to first reinjection in all groups
10 was 110 days," and that does look to be the exact same data
11 that's reported in the slide on the right.

12 Q. Okay. Thank you.

13 We can take that down now.

14 Actually, one more thing. Can we just go back to
15 3173 and go to Slide 16.

16 Can you describe what's shown in this data here on
17 Slide 16 of 3173?

18 A. This is mean change in visual acuity over time in two
19 arms of the study, the 2-milligram dosing group that started
20 off with the four monthly loading doses and then
21 the .5 milligram dose with the four monthly loading doses and
22 then prn treatment thereafter.

23 And do you see that there's -- in the 2-milligram
24 group, there is a better visual acuity outcome of nine letters
25 compared to 5.4 letters in the .5-milligram group.

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1 Q. Thank you. We can put that away now.

2 And if you recall, you were also asked about -- going
3 back to isotonicity and your experience in injecting isotonic
4 solutions, did the questions that were asked by counsel, did
5 that change your opinion that a POSA clinician like yourself
6 would accept that the aflibercept formulated for comfortable,
7 nonirritating injection was inherently isotonic?

8 A. Especially after considering the teachings of a
9 formulation expert like Dr. Rabinow, I don't think that the
10 POSA would have -- that there's nothing in the
11 cross-examination here today that would change anybody's mind
12 about that.

13 Q. Okay. Do you recall you were also asked about the
14 '747 patent by counsel?

15 A. That's correct.

16 Q. Specifically Example 17?

17 A. That's correct.

18 Q. That Example 17 is an example of a method of treating
19 angiogenic eye disorder, like AMD?

20 A. That's correct.

21 Q. Is there anything that would have prevented somebody
22 from also trying that with the diabetic retinopathy that's also
23 disclosed in the '747 patent?

24 A. I think no. And, again, as an argument for the
25 rationality of looking across diseases, we have the internal

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1 communications of Regeneron showing that they based some of
2 their study design in the DME trials based on AMD trial data.

3 So I think people did use information from one
4 disease space to guide their therapeutic approaches in another
5 disease with these anti-VEGF agents.

6 Q. If we can pull up DTX 2198.

7 Just like to ask you a question that you were asked
8 about that document with respect to RVO.

9 A. Sure.

10 Q. If we could go to page 2 of this document, top
11 paragraph.

12 This is the paragraph that you were shown by counsel?

13 A. Yes.

14 Q. And this discloses that patients in both studies will
15 receive six monthly intravitreal injections via the VEGF
16 Trap-Eye at a dose of 2 milligrams or sham-controlled
17 injections.

18 Do you see that?

19 A. Yes.

20 Q. But then this section also continues, doesn't it? At
21 the end it says, "At the end of the initial six months,
22 patients will be dosed on a prn, as-needed basis for another
23 six months."

24 Do you see that?

25 A. Yeah. You know, I recalled that, but I couldn't find

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1 the text. I don't know what I was shown. But, yes, I see that
2 now, yes.

3 Q. Does that help clarify whether or not the person of
4 ordinary skill in the art reading this would have thought those
5 six monthly intravitreal injections to be loading injections or
6 not?

7 A. I think they would be interpreted to be those first
8 loading injections, followed by prn dosing, just like in so
9 many of the other trials that we've seen.

10 Q. You were asked questions about the formulation of
11 Eylea and whether it can contribute to the commercial success
12 of the product.

13 Ask you a question. Would you buy Eylea for your
14 practice if it didn't have aflibercept in it?

15 A. No.

16 MR. McLAUGHLIN: Nothing further. Thank you.

17 THE COURT: Counsel, recross?

18 MS. OBERWETTER: Briefly, Your Honor.

19 RECROSS-EXAMINATION

20 BY MS. OBERWETTER:

21 Q. Dr. Albin, Mr. McLaughlin had questions for you
22 about PTX 0002, the '865 patent that he directed your attention
23 to briefly.

24 If we could just put that up on the screen.

25 I just want to be clear for the record. You have not

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1 undertaken any exercise to determine what this patent does or
2 does not disclose as it relates to the Eylea formulation,
3 correct?

4 A. I was not -- as we've said multiple times, I was not
5 engaged here as an expert on formulation and my efforts were
6 not focused on the formulation patent as a consequence of that.

7 MS. OBERWETTER: Nothing further.

8 THE COURT: Thank you.

9 Reredirect then, Counsel?

10 MR. McLAUGHLIN: Nothing further, Your Honor.

11 THE COURT: Doctor, I have wonderful news for you.
12 You can step down, sir.

13 THE WITNESS: Fantastic.

14 THE COURT: Outside, you're fair game.

15 THE WITNESS: That was a lot of fun. Thank you.

16 THE COURT: I'm sure it was. Thank you very much. I
17 appreciate it, but you're now fair game. Folks can talk to you
18 again.

19 THE WITNESS: Oh, great.

20 THE COURT: Thank you, sir.

21 MR. McLAUGHLIN: Your Honor.

22 THE COURT: Doctor, hold on one second. Let's go
23 ahead and --

24 MR. McLAUGHLIN: Read into the record the exhibits.

25 THE COURT: You may do so, slowly.

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1 MR. McLAUGHLIN: This would include DTX 204,
2 DTX 2034, DTX 2035, DTX 3173, DTX 2040, DTX 2062, DTX 2730,
3 DTX 2731, DTX 2733, DTX 2745, DTX 3102, DTX 3105, DTX 3115,
4 DTX 3131, DTX 3198, DTX 3215, DTX 4008, DTX 4013, DTX 4056,
5 DTX 4061, DTX 4113, DTX 4116, DTX 4120, DTX 4129.

6 THE COURT: A little bit slower, Counsel.

7 MR. McLAUGHLIN: Sorry. DTX 4192, DTX 4194,
8 DTX 4900, DTX 4903, DTX 8190. And I believe we've already
9 moved this one in, but just in case, DTX 8205.

10 And if I could just get clarity from my cocounsel on
11 three remaining ones.

12 THE COURT: Certainly.

13 MR. McLAUGHLIN: There will be two more. Thank you.
14 DTX 3144 and DTX 3316.

15 THE COURT: Any objection to any of those?

16 MS. OBERWETTER: No, Your Honor.

17 THE COURT: Without objection, the aforementioned
18 list are all hereby deemed admitted.

19 (DTX 204, DTX 2034, DTX 2035, DTX 3173,
20 DTX 2040, DTX 2062, DTX 2730, DTX 2731, DTX 2733,
21 DTX 2745, DTX 3102, DTX 3105, DTX 3115, DTX 3131,
22 DTX 3198, DTX 3215, DTX 4008, DTX 4013, DTX 4056,
23 DTX 4061, DTX 4113 ,DTX 4116, DTX 4120, DTX 4129,
24 DTX 4194, DTX 4900, DTX 4903, DTX 8190, DTX 8205,
25 DTX 3144 and DTX 3316 were admitted.)

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1 MR. McLAUGHLIN: Thank you, Your Honor.

2 THE COURT: Ms. Oberwetter?

3 MS. OBERWETTER: I have just a few more that I did
4 not do during the course of cross.

5 I think I heard DTX 3105 on Mr. McLaughlin's list.
6 We move to admit that. DTX 4099, DTX 4209, DTX 8151-A.

7 THE COURT: Any objection to those?

8 MR. McLAUGHLIN: No objection, Your Honor.

9 THE COURT: Without objection, Ms. Oberwetter's list
10 is hereby deemed admitted.

11 (DTX 4099, DTX 4209, and DTX 8151-A were
12 admitted.)

13 THE COURT: Everyone satisfied their respective lists
14 have all been checked off? Okay. Great.

15 Doctor, now you can exhale.

16 I do need to ask counsel about any exhibits from our
17 video experts.

18 MS. MAZZOCHI: I think that --

19 THE COURT: Video witnesses.

20 MS. MAZZOCHI: Yes. My understanding is that thus
21 far, everything has been moved in. I know our court reporter
22 has copies, I think, of all the PTX/DTX exhibits
23 electronically; so she should have those. And, obviously, at
24 the end of the proceedings, I'm assuming Your Honor will want a
25 flash drive complete with everything on it.

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1 THE COURT: Please.

2 MS. MAZZOCHI: Maybe you want to keep the paper; but
3 as a general rule, you know, I think people might let that go
4 by the wayside.

5 But I think we've been keeping track of which ones
6 are which. Teagan had a few things he wanted to reconcile from
7 yesterday, but otherwise, with that, I think we'll be up to
8 date.

9 THE COURT: Counsel.

10 MR. GREGORY: Ms. Mazzochi is correct.

11 We have a little bit of housekeeping from the video
12 testimony from Vanessa Smith and Parag Goyal yesterday. I
13 believe we can read into the record and move into evidence the
14 following, which I believe we have consent on: PTX 0353,
15 PTX 0354, PTX 0364, PTX 0472, and PTX 0478.

16 MS. MAZZOCHI: And my understanding is, if that's a
17 list that came out of meet-and-confer, then those are the ones
18 that are agreed to.

19 THE COURT: Those are thereby deemed admitted.

20 Who does Mylan intend to call next?

21 MS. MAZZOCHI: So, Your Honor, we had -- again, we
22 would like to call Karen Chu at some point as the Regeneron
23 30(b)(6) witness. I don't know if you want to do that now or
24 wait till later.

25 Or we could -- we have roughly another 45-ish

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1 minutes, maybe 50 minutes of two of our last -- basically, the
2 last two ones of ours going in by designation. Then our plan
3 would be we would start with Dr. Rabinow tomorrow, followed by
4 Dr. Stewart. If you'd rather kick the Chu issue till tomorrow,
5 we could do that. The only thing is we might not have clip
6 reports in time. That's the one concern on that.

7 THE COURT: Let's go ahead, and we can do the other
8 two videos first. We'll discuss the Chu issue so we can have
9 that ready to go going forward.

10 MS. MAZZOCHI: And then, Your Honor, I also wanted to
11 make clear, our next and, I believe, last live witness as part
12 of our case in chief will be Dr. MacMichael. Plaintiffs have
13 been aware he is not available until Tuesday. So I don't know
14 how long plaintiff's crosses are going to go tomorrow. So they
15 may actually start putting on their rebuttal case. And then
16 our last live witness will be Dr. Hofmann, but he has to come
17 in response to their expert Dr. Manning. So I suspect that
18 will happen next week.

19 THE COURT: Understood.

20 Any disagreement with that projected plan?

21 MR. BERL: Well, that's the first I've heard of it.
22 We're fine with Dr. MacMichael, who apparently has some health
23 issue, not coming till Tuesday. I suspect their case will take
24 most if not all of the day tomorrow. I don't think it makes
25 any sense for us to start our rebuttal case until they finish

THOMAS A. ALBINI, MD - RECROSS

1 their case in chief. So we were planning to do that after
2 Dr. MacMichael testifies on Tuesday. That's one thing.

3 The second thing is before the end of court today, I
4 think it would be wise to address another issue that has arisen
5 with respect to Dr. Rabinow. We just received their amended
6 slides in view of Your Honor's ruling, and let's say we don't
7 think it complies with Your Honor's ruling, to put it mildly.

8 THE COURT: We're going to put a pin in that.

9 Let's go ahead and receive the next two videos we
10 discussed, Counsel. Then we'll take up the issue with Ms. Chu,
11 and then we'll get to that when we get to that.

12 MS. MAZZOCHI: All right. Thank you, Your Honor.

13 Defendants next call by video deposition Ms. Abby
14 Cahn, a Regeneron employee.

15 THE COURT: Thank you so much.

16 MS. MAZZOCHI: Your Honor, I think we may have the
17 exhibits for Cahn. I don't know if you want a paper copy or if
18 you would like them up on the screen and then we just submit
19 them.

20 THE COURT: Are they synced on the screen?

21 MS. MAZZOCHI: Yes.

22 THE COURT: I can just watch them from there. That's
23 fine. I'm going to work on, hopefully this evening, clearing
24 out some space for any additional binders that might be
25 necessary.

(Video deposition of Abby Cahn)

1 VIDEO DEPOSITION OF ABBY CAHN

2 Q. Good morning, Ms. Cahn. If you could please state
3 your full name and your home address for the record.

4 A. My name is Abby Margo Cahn. I live at 209 East 56th
5 Street, New York, New York 10022.

6 Q. You understand that you're appearing here and
7 providing testimony in your personal capacity?

8 A. Yes, I understand.

9 Q. And do you also understand that Regeneron has
10 designated you as a witness to speak on behalf of marketing
11 subject matter with respect to Mylan's 30(b)(6) notice?

12 A. Yes, I understand and am aware.

13 Q. This is DX 802. It is plaintiff's Regeneron, their
14 second supplemental Rule 26(a) initial disclosures.

15 Have you seen this document before, Ms. Cahn?

16 A. Yes. I was shown this document by my lawyers during
17 preparation.

18 Q. Are you aware that Regeneron identified you as a
19 person with knowledge about the marketing and commercial
20 success of Eylea?

21 A. Yes, I am aware.

22 Q. Okay. What is your current title at Regeneron?

23 A. My current title at Regeneron is executive director,
24 marketing and customer engagement, as of January 3rd.

25 Q. So Regeneron, with respect to Eylea, provides both

(Video deposition of Abby Cahn)

1 tabletops and booths at conferences where appropriate?

2 A. If that is part of the tangible method of a
3 sponsorship, then Regeneron would be able to exhibit at that
4 medical conference.

5 Q. Okay. And then another thing you mentioned was
6 providing ads at conferences. What did you mean by ads?

7 A. Depending upon each meeting's prospectus, which is
8 submitted to the sponsorship portal, there are very specific --
9 there's a specific outline of benefits. That would include,
10 for example, a banner, and that would be placed in either a
11 certain location or potentially, if it's a virtual conference,
12 on the meeting website.

13 Q. When Regeneron has podium time that you referred to,
14 who speaks on behalf of Regeneron?

15 A. Depending upon the availability of individuals as
16 well as the meeting, the Regeneron employees would be able to
17 give an approved presentation at the meeting. So that, yeah.

18 Q. Does Regeneron ever sponsor talks given by physicians
19 or clinicians or health care professionals?

20 A. So at medical conferences in general, there's a
21 number of ways that physicians are able to appropriately
22 educate their peers at the conference. As a marketer, I am
23 aware of one of those -- one of those opportunities, which is
24 referred to, essentially, as a product theater.

25 Q. And what is a product theater?

(Video deposition of Abby Cahn)

1 A. As part of the meeting prospectus, the product
2 theater would be part of the request for support. If the
3 sponsorship is approved, the marketing team would have the
4 ability to work with a physician to give the on-label approved
5 educational speaker program presentation at that meeting or
6 convention.

7 Q. You used the word "thought leader liaison." What is
8 that?

9 A. So at Regeneron a thought leader liaison is a
10 field-based marketing role, and the main responsibility of that
11 field-based marketing thought leader liaison is to gain insight
12 into the evolving retina landscape through engagement with
13 thought leaders in the retina community.

14 Q. Does Regeneron provide compensation for thought
15 leaders?

16 A. Regeneron, and specific to Eylea and my role in the
17 marketing team, we contract with advisers for -- in
18 insight-gathering settings, such as advisory boards. We also
19 have contracts with retina specialists who are part of the
20 Eylea educational speaker bureau.

21 Q. What is Eylea educational speaker bureau?

22 A. The Eylea educational speaker bureau is a program
23 that enables physicians to give approved on-label presentation
24 of Eylea to other health care professionals.

25 Q. In your opinion, is it important for Regeneron to

(Video deposition of Abby Cahn)

1 enable physicians to give presentations concerning Eylea?

2 A. It is my opinion that it is important for physicians
3 to be educated about the on-label -- the on-label information
4 for Eylea when making treatment decisions for their patients.

5 Q. What are the ways that you're aware of?

6 A. So from the -- within the marketing organization, there
7 is a team that is responsible for scientific marketing. They
8 are responsible for the Eylea educational speaker program,
9 which is the presentations that physicians give to other health
10 care professionals around the on-label use of Eylea.

11 The patient marketing or consumer marketing team is
12 responsible for providing educational materials about Eylea as
13 well as education around the diseases that Eylea is indicated
14 for. And the promotional marketing team is responsible for
15 developing the sales materials which our sales team uses to
16 educate physicians and their offices about the on-label use of
17 Eylea.

18 Oh, it's aligned to the regional directors. Under
19 each regional director are medical specialists or diabetic eye
20 medical specialists.

21 Q. So Eylea4U program has been active since the launch
22 of Eylea and it continues today; is that correct?

23 A. So a version of Eylea4U patient assistance programs
24 were available at launch. I would not be able to speak to the
25 difference in the program between launch and today.

(Video deposition of Abby Cahn)

1 Q. But a program Eylea4U has existed within -- the name
2 Eylea4U has existed continuously since Eylea's launch and is
3 ongoing today?

4 A. A program called Eylea4U has existed since launch and
5 does exist today.

6 Q. Do you know, what insights have you gained on why
7 physicians express an interest for a prefilled syringe?

8 A. So based on my conversations with physicians around
9 the availability of treatment options for patients, there is a
10 perception that administering intravitreal injections with a
11 prefilled syringe may have an improved -- is an improvement on
12 the -- sort of the safety of and decreasing the risks
13 associated with the intravitreal injections.

14 Q. And based on the sales numbers, do you agree that
15 there is a preference for the prefilled syringe over the vial
16 of Eylea?

17 A. So my understanding of preference comes from insights
18 from physicians in different settings, and based on my personal
19 conversations with some physicians, there is a preference for a
20 prefilled syringe.

21 Q. Ms. Cahn, before the lunch break I recall you
22 mentioned a promotional marketing team for Eylea. Is my
23 recollection correct that Regeneron has a promotional marketing
24 team for Eylea?

25 A. So Regeneron has a marketing team, and there are

(Video deposition of Abby Cahn)

1 individuals on that marketing team who are responsible for
2 promotion.

3 Q. Ms. Cahn, are you familiar with the acronym ATU?

4 A. I am familiar with the ATU market research surveys.
5 I do not recall what the letters ATU stand for.

6 Q. DX 514 was marked as a previous deposition. The
7 first page includes the Bates numbers RGN-EYLEA-MYLAN-701395.
8 It's a Q3 2020 ATU combined full report.

9 Is this the type of document that you review in your
10 marketing role at Regeneron?

11 A. So I am part of the marketing team and get invited to
12 the market research meetings where these types of reports are
13 shared with the marketing team.

14 Q. What is your understanding of the phrase
15 "out-of-pocket costs"?

16 A. My understanding of "out-of-pocket costs" would be
17 the portion of the cost that is not covered by insurance.

18 Q. With that understanding of out-of-pocket costs, is it
19 your opinion that physicians might not prescribe a drug if the
20 out-of-pocket costs for that drug are unaffordable to the
21 patient?

22 A. So although I'm not a physician, it is my
23 understanding that physicians have conversations with their
24 patients around all of the treatment options that are available
25 to them and make decisions together based on a number of

(Video deposition of Abby Cahn)

1 factors, including out-of-pocket costs based on their
2 insurance.

3 Q. This is the current August 2022 label, and it's been
4 labeled DX 520-A because it now has Bates numbers on it. The
5 prior version used at another deposition did not have Bates
6 numbers.

7 Ms. Cahn, based on your testimony, you're familiar
8 with this package insert -- or I refer to it as a label -- this
9 package insert for Eylea?

10 A. Yes, I am.

11 Q. You've seen this document before?

12 A. Yes, I have.

13 Q. Does the dosing and administration instructions for
14 wet AMD provide flexibility for a clinician to dose Eylea?

15 A. Yes, the wet AMD dosing administration section does
16 provide flexibility for physicians who choose to treat with
17 Eylea.

18 Q. And that flexibility is with respect to the dosing
19 schedule?

20 A. Yes. It would -- dosing schedule is one way to
21 describe the time between treatments.

22 Q. Okay. And for wet AMD here, the label states that
23 the physician may dose Eylea as frequently as 2 milligrams
24 every four weeks; is that correct?

25 A. Yes. Some patients may need every-four-week dosing

(Video deposition of Abby Cahn)

1 after the first 12 weeks, which is the loading dose phase.

2 Q. And if we go down to the next indication, RVO, are
3 you familiar with RVO?

4 A. The indication is macular edema following retinal
5 vein occlusion, yes.

6 Q. MEfRVO; is that correct?

7 A. Yes.

8 Q. And the recommended dose of Eylea for MEfRVO is once
9 every four weeks; isn't that correct?

10 A. Yes, that is correct.

11 Q. And so for DME and DR, Eylea may be dosed as
12 frequently as 2 milligrams every four weeks; is that correct?

13 A. Yes. Some patients may need every-four-week monthly
14 dosing after the first 20 weeks, which is the first five months
15 of the loading dose in diabetic macular edema and diabetic
16 retinopathy.

17 Q. So I think -- do the dosage administration
18 instructions on the Eylea package insert require a physician
19 dose Eylea every eight weeks?

20 A. No. There is the -- some patients may need
21 every-four-week dosing as indicated in the label in each of the
22 indications we previously reviewed.

23 Q. Ms. Cahn, right before the break I had you pull up
24 DX 514. If you could turn to what is page 90 of 142. The
25 Bates number ends in 484. And then it's pulled up on the

(Video deposition of Abby Cahn)

1 screen share as well.

2 Okay. This slide with Bates number ending 484 is
3 titled "Wet AMD Dosing Update." Do you see that?

4 A. Yes. Yes, I do.

5 Q. And, Ms. Cahn, do you agree that the mean dosing
6 frequency for Eylea that's reflected on this slide is 7.5 weeks
7 for the dosing interval?

8 A. So this is a -- as per the source, a Q3 2020 ATU
9 study of 171 retinal specialists and 30 comprehensive
10 ophthalmologists.

11 This -- under the sentence we just covered, projected
12 percentage of treated eyes receiving dosing schedule with an
13 asterisk, ongoing, following initiation of therapy.

14 So based on this group of physicians projecting
15 intervals of treatment following a loading dose of Eylea for
16 these physicians, their perception is a loading dose of what
17 you -- mean frequency of 7.5 weeks.

18 Q. Okay. And if we could go to two pages down.

19 A. Okay.

20 Q. It's page ending in number 486.

21 A. Okay.

22 Q. And does this slide reflect that the mean frequency
23 for the dosing interval for Eylea with respect to DME is 7.7
24 weeks?

25 A. So for -- again, for based on in this quarter, Q3

(Video deposition of Abby Cahn)

1 2020 ATU, this 164 retinal specialists and 36 comprehensive
2 ophthalmologists, their projected percent of treated eyes
3 receiving dosing schedule, what they project to be true,
4 following a loading dose is the mean frequency of injections is
5 7.7 weeks.

6 Q. Okay.

7 Mike, if we can bring up DX 515.

8 DX 515 was marked at a previous deposition. First,
9 page Bates number is RGN-EYLEA-MYLAN-700292. It is the Q4 2020
10 ATU combined full report.

11 All right. Have you seen this document before?

12 A. So I have reviewed a number of performance updates in
13 my role as -- in marketing. I also reviewed a performance
14 update with my lawyers in preposition for today. I do not
15 recall if it was Q4 2020.

16 Q. If we could turn to what is page 92 of 137 in this
17 document. The Bates number ends in 383.

18 A. 383. Okay. 383. Okay. It's loading.

19 Q. Sure. And does this slide reflect the mean dosing
20 frequency for Eylea of 7.3 weeks?

21 A. So these specific physicians are recalling treatment
22 intervals for their patients, and they are -- on average, the
23 mean frequency of this set of physicians with this recall of
24 their patients is 7.3 weeks.

25 Q. Okay. If we could go two pages down, it ends in 385

(Video deposition of Abby Cahn)

1 in this document.

2 A. Can you repeat your question.

3 Q. Sure. This slide is titled "DME Dosing Update."

4 Can you agree that the data shown here is that on
5 average the mean frequency for Eylea dosing for DME is every
6 7.5 weeks?

7 A. So for this 2020 ATU study of 172 retina specialists
8 and 30 comprehensive ophthalmologists who were recalling
9 treatment intervals for a specific number of patients, the mean
10 frequency for Eylea is 7.5 weeks.

11 Q. Mike, can we pull up DX 516, please.

12 This was previously marked at another deposition as
13 RGN-EYLEA-MYLAN-700931 on the first page. It's on the Q4 2019
14 ATU report.

15 Okay. And if we could turn to page 98 of 153 in this
16 document. The Bates number ends in 028.

17 A. Got it. I'm right there. Hold on. Yep, I do have
18 it up.

19 Q. Okay. And, Ms. Cahn, do you agree that in this
20 Q4 2019 ATU report, the data shows that the mean dosing
21 frequency for Eylea for wet AMD is 7.0 weeks?

22 A. So for these 200 retina specialists surveyed for the
23 Q4 2019 ATU study, their recollection or recall of patients on
24 each of these agents, the mean frequency of Eylea injections is
25 7.0 weeks.

(Video deposition of Abby Cahn)

1 Q. If we can go two pages down, it ends in 030, titled
2 "DME Dosing Update."

3 Ms. Cahn, do you agree that this Q4 2019 ATU report
4 reflects a mean dosing frequency of 6.7 weeks for dosing Eylea
5 for DME?

6 A. So for this -- these 200 retina specialists on
7 Q4 2019 ATU study, they are projecting or recalling that the
8 Eylea treatment interval for their patients, the mean frequency
9 was 6.7 weeks.

10 Q. Okay.

11 Mike, if we could pull up DX 517.

12 DX 517 was marked at a prior deposition. The first
13 page has Bates number RGN-EYLEA-MYLAN-705670. You could go to
14 the pages ending in 689. It is page 20 of this PDF.

15 A. 689. Okay. Thinking. Hold on.

16 Q. Sure.

17 A. 689. Okay. I am on 689.

18 Q. Sure. The slide that -- the page that we're already
19 looking at --

20 A. Okay.

21 Q. -- it reflects that the Eylea mean dosing frequency
22 overall is 6.7 weeks; is that correct?

23 A. So for these physicians recalling their projected
24 dosing intervals for a set of patients which I cannot -- which
25 I have no understanding if they are previously treated or naive

(Video deposition of Abby Cahn)

1 eyes or actually how many eyes -- there we go. Sorry -- of
2 this set of 42,763 eyes, the overall dosing frequency and the
3 mean in the weeks would be 6.7 weeks.

4 Q. DX 518.

5 A. DX 518. Okay. It's open.

6 Q. This is the Q3 2017 ATU report.

7 A. Okay. Its title page is up.

8 Q. If you can turn to page 20 of 35 of the document.

9 A. 20 of 35.

10 Q. Do you agree that this slide reflects that the
11 overall dosing frequency for Eylea for wet AMD has a mean of
12 6.7 weeks?

13 A. So based on this slide from the -- okay -- no source
14 on this. I do not recall which quarter and year this new
15 document is referring to.

16 The physicians who completed this survey recalled
17 that patients were dosed at different dosing frequency,
18 although I cannot comment if these are treatment-naive eyes or
19 those eyes that have been transitioned from another agent.

20 And the mean overall dosing frequency for Eylea on --
21 from this group of physicians recalling based on this number of
22 patients is 6.7 weeks.

23 Q. So we reviewed ATU surveys -- at least one ATU survey
24 from each of 2017, 2018, 2019, and 2020; is that correct?

25 A. Yes, I believe that's correct.

(Video deposition of Abby Cahn)

1 Q. And we discussed a number of mean dosing frequencies
2 for Eylea, correct?

3 A. We discussed the results of ATU surveys from a group
4 of physicians who are recalling their patients' dosing
5 intervals, yes.

6 Q. And do you agree that of the data we looked at, the
7 mean dosing frequency for Eylea was always less than eight
8 weeks?

9 A. So for the results of these surveys where the
10 physicians were asked to recall that their projected dosing
11 frequency of Eylea with the patients that they recall and are
12 projecting according to this, in those patients the dosing
13 frequency of Eylea is less than eight weeks.

14 Q. Sure. It is DX 531a.

15 A. DX 531a. Okay.

16 Q. Okay. But you, in your role, cannot speak to
17 off-label uses of Eylea, correct?

18 A. That is correct. I am unable to -- unable to speak
19 about anything other than the Eylea package insert.

20 Q. That's because that's what the law states, correct?

21 A. Yes.

22 Q. Do you agree that with Dr. Schleifer's comments here
23 that here the availability of Eylea copay assistance is
24 reversing the shift from Avastin back to Eylea?

25 A. My opinion of -- my opinion is that there are a

(Video deposition of Abby Cahn)

1 number of factors that contribute to a physician's treatment
2 decision and that patient access and copay assistance
3 challenges are factors that do affect physicians' abilities to
4 choose medications.

5 Q. Ms. Cahn, once they load, DX 807 is going to be a
6 brief video --

7 A. Okay.

8 Q. -- that will play, and then DX 808 is a transcript of
9 that video.

10 (Video played within deposition.)

11 Q. Once they load, DX 807 is going to be a brief
12 video --

13 A. Okay.

14 Q. -- that will play, and then DX 808 is a transcript of
15 that video.

16 Ms. Cahn, is DX 808 an accurate transcript of the
17 video we watched in DX 807?

18 A. Yes, it is.

19 Q. Did you discuss any trend -- a trend of Eylea was
20 utilized more in areas where "A Beautiful Pair" was run than in
21 areas where it was not run?

22 A. So I can't speak to any trends because I don't have
23 enough information that would make -- that would lead to a
24 trend. But I know from what Mr. Clark told me that in the
25 markets where "A Beautiful Pair" was run compared to in markets

(Video deposition of Abby Cahn)

1 where "A Beautiful Pair" did not run, there was a difference of
2 Eylea utilization in those markets.

3 Q. Mike, if you can mark as Tab 62 Defendant's
4 Exhibit -- mark Tab 62 as Defendant's Exhibit 811, 811.

5 This is, as you can see in the top left, pulled from
6 the hcp.eylea.us website, January 16, 2023.

7 A. Yes, I can see that.

8 Q. Are you familiar with the hcp.eylea.us website?

9 A. So I am not familiar specifically on the website.
10 This is the HCP website. I am not responsible for updating or
11 producing content for this website.

12 Q. The first page, DX 811, at the top it says "Wet AMD:
13 Dosing Flexibility."

14 Do you see that?

15 A. Yes, I do.

16 Q. Okay. And it recites, "Flexibility to choose from
17 three FDA-approved dosing regimens for wet AMD."

18 Do you see that?

19 A. Yes, I do.

20 Q. So do you agree that clinicians have flexibility to
21 choose a dosing regimen for wet AMD, according to the current
22 package insert for Eylea?

23 A. Yes. According to the package insert for Eylea,
24 physicians may choose the dosing paradigms that are listed in
25 the package insert.

(Video deposition of Abby Cahn)

1 Q. Okay. If we can scroll down to page 4 of 12, on the
2 top it says "DME:Dosing Flexibility."

3 A. In the same -- oh, I see it, yes.

4 Q. Okay. So you agree that physicians have flexibility
5 with respect to DME dosing?

6 A. I do agree that physicians have flexibility to treat
7 their DME patients based on the patient's need for treatment.

8 Q. Defendants' Exhibit 815 has the Bates number on the
9 first page of RGN-EYLEA-MYLAN-314737.

10 Ms. Cahn, does this appear to be print advertisements
11 that Regeneron ran in *Time* magazine promoting Eylea?

12 A. Yes, it does.

13 Q. And is this a different ad campaign for Eylea other
14 than "A Beautiful Eye"?

15 A. Yes, this is.

16 Q. Mike, if you can scroll to the last page of this
17 document ending in Bates Number 707.

18 Ms. Cahn, does this page of Defendant's Exhibit 817
19 refresh your memory that this was mailed directly to Eylea
20 patients?

21 A. So this looks like a direct mail to Eylea patients
22 once patients were enrolled in Eylea4U.

23 Q. And, Ms. Cahn, if you'd like to review this document,
24 you can ask Mike to page through it at the appropriate page.

25 A. Can I see the front cover, please, Mike? I can't

(Video deposition of Abby Cahn)

1 really see it.

2 So this is another "A Beautiful Pair" print
3 advertisement.

4 Q. Have you seen -- when you say another version, you
5 mean this is a print ad that was part of the "Beautiful Pair"
6 ad campaign?

7 A. Yes, that is correct.

8 MS. MAZZOCHI: And that's the conclusion of that
9 video. And then for administrative purposes, I believe all of
10 these exhibits are agreed to.

11 The defendants would like to rule in -- move into
12 evidence DTX 514, 515, 516, 517, 518, 520-A, 531-A, 802, 807,
13 808, 811, 815, 817, and 818.

14 THE COURT: Any objection to any of those?

15 MS. OBERWETTER: No objection, Your Honor.

16 THE COURT: Without objection, those are hereby
17 admitted.

18 (DTX 514, DTX 515, DTX 516, DTX 518, DTX
19 520-A, DTX 531-A, DTX 802, DTX 807, DTX 808, DTX
20 811, DTX 815, DTX 817, DTX 818 were admitted.)

21 MS. MAZZOCHI: Great. Thank you, Your Honor.

22 The next video deposition we have is 21 minutes. And
23 this will be Jennifer Colyer, who is part of Regeneron's
24 finance and marketing, and I believe she was also designated as
25 a 30(b)(6) witness.

(Video deposition of Jennifer Colyer)

1 THE COURT: Understood.

2 VIDEO DEPOSITION OF JENNIFER COLYER PLAYED

3 Q. Mrs. Colyer, could you please state your full name
4 and your home address for the record.

5 A. Sure. Jennifer Colyer, 37 Shady Lane, Dobbs Ferry,
6 New York 10522.

7 Q. And the second is a document, "Jennifer Colyer
8 30(b)(6) Deposition Topics," which will be DX 501.

9 Do you have both those documents, Ms. Colyer?

10 A. Yes, I do.

11 Q. Okay. You can set that document aside.

12 Do you also understand that you're here testifying
13 today as a corporate representative of Regeneron to speak on
14 behalf of the topics listed in DX 501?

15 MR. GOLDSMITH: I object to the Exhibit DX 501 to the
16 extent it's not consistent with Regeneron's December 12, 2022,
17 letter. But the witness can answer the question.

18 THE WITNESS: What my lawyer just said, yes.

19 Q. Well, factually then, what is driving the sales of
20 Eylea?

21 A. Successful scientific research.

22 Q. And what is that research referring to?

23 A. The research that was done to develop the molecule
24 that became Eylea, aflibercept.

25 Q. When you say Eylea drug, you're referring to the

(Video deposition of Jennifer Colyer)

1 active ingredient aflibercept?

2 A. I'm referring to Eylea.

3 Q. When you say Eylea, what are you referring to?

4 A. I'm referring to Eylea, the brand name as licensed by
5 Regeneron.

6 Q. What is encompassed by the brand name Eylea?

7 A. I'm afraid I don't fully understand. What do you
8 mean by "encompassed"?

9 Q. You mentioned that when you used the word Eylea,
10 you're referring to the brand name. And I'm trying to
11 understand what is included, what is different between Eylea
12 and the brand name. Is there a difference?

13 A. I'm afraid you're trying to make a distinction that
14 I'm not really familiar with. To me, Eylea is a brand name
15 that is licensed by Regeneron somewhere legally, and that is
16 Eylea.

17 Q. Is the safety and efficacy of Eylea a factor that
18 drives sales?

19 A. I freely admit I am no scientist. I have not been
20 involved in clinical trial research. The safety and efficacy
21 of Eylea would be considered a benefit absolutely in the use of
22 Eylea.

23 Q. Are there any other benefits that Eylea imparts to
24 patients?

25 A. As a finance person, I'm not too familiar with the

(Video deposition of Jennifer Colyer)

1 detail behind Eylea and the clinical research and what it has
2 proven over the past many years.

3 Q. Does Regeneron advertise Eylea directly to health
4 care providers?

5 A. Regeneron advertises Eylea, yes, to health care
6 providers.

7 Q. And does Regeneron advertise Eylea to the public?

8 A. Over the years Regeneron has advertised Eylea
9 directly to the public.

10 Q. Does Regeneron undertake market research for Eylea?

11 A. Yes, it does.

12 Q. Are you familiar with that market research?

13 A. I do not work directly with that market research, no.

14 Q. Your current job title, is it correct that you're the
15 executive director of commercial finance and business planning?

16 A. Yes.

17 Q. Does Regeneron have medical specialists for Eylea
18 currently?

19 A. Yes, we do.

20 Q. And what is a medical specialist?

21 A. That would be a -- I guess layman term, a rep, a
22 representative, customer representative, salesperson.

23 Q. Salesperson. Do those people have medical degrees?
24 Do you know?

25 A. I'm not familiar with each and every one of them, but

(Video deposition of Jennifer Colyer)

1 they certainly can have a medical degree.

2 Q. Do you know how many medical specialists Regeneron
3 has for Eylea, approximately?

4 A. I'll stick with roughly 90.

5 Q. And those medical specialists, do they report to the
6 regional sales directors?

7 A. Yes.

8 Q. Does Regeneron have reimbursement and managed market
9 specialists for Eylea?

10 A. Regeneron has regional business managers.

11 Q. Are those regional business managers, are any
12 specifically assigned to Eylea?

13 A. There is a specific team of Eylea regional business
14 managers.

15 Q. Do you know how many regional business managers
16 Regeneron has for Eylea, approximately?

17 A. As of today, I believe there are 30.

18 Q. What is Eylea4U?

19 A. Eylea4U is the reimbursement support program
20 utilized.

21 Q. What type of reimbursement support does Regeneron
22 provide for Eylea under this Eylea4U program?

23 A. Copay assistance.

24 Q. Any other type of assistance that you're aware of?

25 A. The core is copay assistance.

(Video deposition of Jennifer Colyer)

1 COURT REPORTER: Say it again?

2 THE WITNESS: The core is copay assistance, yes.

3 Q. What is a regional science manager?

4 A. That is typically -- how to phrase it? -- a medical
5 science liaison. These are field-based folks that are
6 authorized to speak about the science as opposed to --
7 separating them from a medical specialist, which would be a
8 rep.

9 Q. Do these individuals have medical degrees?

10 A. I assume many of them do. I do not know the
11 composition of the team.

12 Q. Do you know how many regional science managers
13 Regeneron employs for Eylea?

14 A. I'm taking a second to recall that because it's not
15 something I work with too frequently.

16 I want to say mid teens, mid teens meaning somewhere
17 between 12 to 19, give or take. I'm just not recalling exact
18 number.

19 Q. That's fine. That's fine.

20 Do you know why Regeneron provides copay assistance?

21 A. Similar to most other pharmaceutical companies,
22 Regeneron provides copay assistance to help commercial patients
23 pay the copay.

24 Q. Do you have an opinion whether rebates drive sales of
25 Eylea?

(Video deposition of Jennifer Colyer)

1 A. Sales of Eylea are derived from the clinical benefit
2 of the drug for patients.

3 Q. What is the clinical benefit you're referring to?

4 A. Why doctors prescribe it to patients.

5 Q. Do you know why doctors prescribe it to patients?

6 A. To improve their lives.

7 Q. Are bonuses for Eylea sales representatives related
8 to any sales targets?

9 A. Field forces are paid bonuses based on achievement of
10 targets.

11 Q. Do you know why Regeneron is developing a high-dose
12 version of Eylea?

13 A. The benefit of a high dose would be about a longer
14 dose -- a dosing regimen, greater weeks between injections.

15 Q. Is that a benefit, a longer dose duration?

16 A. I think personally, if I could have fewer injections
17 directly into my eye, I would choose to do so.

18 Q. What has been discussed in terms of how to handle the
19 8-milligram high-dose version of Eylea?

20 A. To be fair, it hasn't gone -- it certainly hasn't
21 left any rooms. It's not -- I freely admit, it's not
22 necessarily something I'm comfortable discussing.

23 Q. Why are you not comfortable discussing it?

24 A. Because there is no approved plan yet. It's in
25 active -- it's different than a lot of what we've discussed

(Video deposition of Jennifer Colyer)

1 here, which are things that have gone on in the past. It's not
2 public knowledge. It's up for active what do we want to do? I
3 wouldn't say we have something I could declare is a plan.

4 Q. What have individuals expressed they want to do with
5 respect to a high-dose version of Eylea?

6 A. Make an 8-milligram version of Eylea available to the
7 public to hopefully improve the dosing timeline so people would
8 have to get their injections into their eye with a greater time
9 period between them.

10 Q. Does Regeneron track these sales of Eylea with
11 respect to each indication?

12 A. You cannot track sales based on indication.

13 Q. So the sales that Eylea tracks in the financial
14 documents we looked at earlier are independent of what that
15 Eylea is being prescribed for, what condition?

16 A. That is true from a sales perspective.

17 Q. In what context, then, have you come to learn about
18 the indications for Eylea?

19 A. Sales are not tracked by indication, but certainly
20 want -- percentage of the Eylea sales could be allocated to the
21 indications is a separate source of analysis.

22 Q. Do you know who at Regeneron is responsible for
23 approving the Eylea4U program?

24 A. There's a chain of approvals, authorized signature
25 levels, and so on. If the budget exceeds a certain amount, as

(Video deposition of Jennifer Colyer)

1 it typically does with Eylea4U, then Len Schleifer is the final
2 approval, our CEO.

3 Q. What type of data does your department provide with
4 respect to Eylea4U to this decision process?

5 A. If it is within the budget that was planned for the
6 year and approved by Len for spend on Eylea, then we would
7 confirm that this is within the approved budget.

8 Q. I believe you testified -- I just want to confirm --
9 does Regeneron have to approve all costs with respect to Eylea
10 on an annual basis or is there an annual review?

11 A. Regeneron approves all budgets for all brands on an
12 annual basis, not specific to Eylea, not specific to Eylea4U.

13 Q. Does Regeneron today consider Lucentis and Avastin
14 competitors to Eylea?

15 A. As previously discussed, we talked about Lucentis as
16 indeed competition and Avastin to be an off-label use in the
17 anti-VEGF market.

18 Q. Have you seen -- are these the ads that ran in *People*
19 for Eylea that you were referring to?

20 A. Most likely.

21 Q. If you could turn to the page that says Cover 1 on
22 the bottom left. It's got 535 as the ending Bates number.

23 A. Yes.

24 Q. Do you know if this was an insert in *People* magazine?

25 A. I don't know. This does say at the bottom it was a

(Video deposition of Jennifer Colyer)

1 cover wrap, but I don't recall. I've read a lot of *People*
2 magazines over the years.

3 Q. On this page here do you see any discussion of Eylea
4 dosing on this advertisement page?

5 A. I do not see anything about dosing on this page.

6 Q. You can go to the next page. It's got Gate 1, lower
7 left-hand corner.

8 A. Yes.

9 Q. Does this advertisement page state anything with
10 respect to the dosing schedule for Eylea?

11 A. As I read through it, I do not see anything related
12 to dosing.

13 Q. If we can go to the next page, Bates number ending in
14 537. Do you see the bold heading that's approximately four
15 down in the left-hand column that says "How Is Eylea Given?"

16 A. Yes.

17 Q. And this states, "Depending on your condition, Eylea
18 injections are given on different schedules. Consult your eye
19 doctor to confirm which Eylea schedule is appropriate for you."

20 Do you see that?

21 A. Yes, I do.

22 Q. Does that statement state anything concerning an
23 eight-week dosing schedule?

24 A. It does not use the number eight at all.

25 Q. Does it talk about how many weeks between doses of

(Video deposition of Jennifer Colyer)

1 Eylea?

2 A. It doesn't say anything about weeks.

3 Q. On the rest of this page is there any other
4 discussion on this page concerning dosing schedules for Eylea?

5 A. I've not had an opportunity to read every word on the
6 page. I'm happy to do so.

7 Q. Sure. Go ahead.

8 A. I'd like a Ctrl-F.

9 I do not see anything about dosing schedules on my
10 read through this document.

11 Q. Okay. You can go to the next page, Cover 2.

12 Is there any discussion concerning Eylea dosing
13 schedules on this page ending in Bates Number 538?

14 A. No, there is not.

15 Q. If you go to the next page, Cover 3 is in the lower
16 left-hand corner as Bates Number 539.

17 If you could take a second and review the text on
18 this page and confirm that there is no discussion of an Eylea
19 dosing schedule on this advertisement page.

20 A. I do not see anything related to dosing schedules on
21 this page.

22 Q. And if you could turn to the next page ending in
23 Bates Number 540.

24 Can you confirm there's no discussion of an Eylea
25 dosing schedule in this advertisement for Eylea?

(Video deposition of Jennifer Colyer)

1 A. It does not say anything about a dosing schedule on
2 this page either.

3 Q. If I can have the court reporter mark as DX 529 a
4 document that does not have any Bates numbers. It is Eylea
5 advertisements that ran in *Good Housekeeping* in 2022.

6 Ms. Colyer, if you could look at pages 2 and 3 of
7 this document. Have you ever seen these advertisements that
8 Regeneron has run in *Good Housekeeping*?

9 A. I have never read *Good Housekeeping* before.

10 Q. Have you ever seen these advertisements before?

11 A. I mean, I've seen similar advertising.

12 Q. Where have you seen similar advertising?

13 A. These ads tend to be fairly consistent; so this is a
14 fairly standard set of data.

15 Q. Does it appear to be the same ad that ran in all
16 three magazines that are included here in DX 529?

17 A. Without comparing word for word, at a glance it does
18 appear to be a similar ad, yes.

19 Q. If you could look at the ad that is the -- the first
20 page of the advertisement that appears on page 2 of DX 529. It
21 is entitled "Keep living life through your eyes."

22 Do you see that?

23 A. Yes.

24 Q. Do you see any discussion of the Eylea dosing
25 schedule on this page of this advertisement?

(Video deposition of Jennifer Colyer)

1 A. I do not see anything on that page related to dosing
2 regimens.

3 Q. If you could turn to the next page of the ad, it has
4 a picture of a woman in a pink sweater.

5 A. Yes.

6 Q. Do you see any discussion of Eylea dosing schedule on
7 this page of the Eylea ad?

8 A. I do not.

9 Q. If we could turn to the next page, which is the last
10 page of this advertisement, and if you need to, take a moment
11 to review it.

12 Does this page include any discussion concerning the
13 Eylea dosing schedule?

14 A. It does not.

15 Q. Are you aware that Regeneron won awards for the
16 "Beautiful Pair" ad campaign?

17 A. Yes, I am.

18 Q. How are you aware of that?

19 A. Because it was all over the place for a while. I
20 follow LinkedIn.

21 Q. It was all over the place; you mean the advertising
22 campaign was very popular?

23 A. No. Who I worked for, Regeneron at the time, and the
24 team was recognized as having won awards. And I saw it posted
25 on LinkedIn in different ways.

(Video deposition of Jennifer Colyer)

1 Q. So we looked at some print that Regeneron had for the
2 "A Beautiful Eye" campaign that ran in *People* magazine,
3 correct?

4 A. Yes, we did.

5 Q. Are you aware of what other media the "A Beautiful
6 Pair" ad campaign appeared in?

7 A. Yes, I am.

8 Q. What are those sources?

9 A. Television.

10 Q. I'm going to have the court reporter mark as DX 530 a
11 transcript of an advertisement that Regeneron ran for "A
12 Beautiful Pair".

13 Do you have that transcript?

14 A. Yes, I do.

15 Q. And do you see at the top of this document it has a
16 URL link for YouTube?

17 A. Yes.

18 Q. I'm going to play that advertisement for you that's
19 available at that URL. If you can follow the transcript and
20 make sure that the transcript accurately reflects what's
21 provided in the ad.

22 A. Okay.

23 Q. Did the transcript track the video?

24 A. Yes, it did.

25 Q. And was there any discussion in this advertisement

(Video deposition of Jennifer Colyer)

1 concerning the dosing schedule for Eylea?

2 A. The YouTube channel did not talk about dosing
3 schedule, no.

4 Q. Was the video that I played the type of ad that would
5 have run on TV?

6 A. Yes, I believe it would have been similar to what
7 would have been on TV.

8 MS. MAZZOCHI: And, Your Honor, that concludes the
9 Jennifer Colyer deposition.

10 THE COURT: Understood. Thank you, Counsel.

11 MS. MAZZOCHI: In association with this, we'd like
12 the administrative matters of entering additional exhibits into
13 evidence. Defendants move into evidence DTX 501, 528, 529,
14 529-A, and 530.

15 THE COURT: Any objection to any of those?

16 MS. OBERWETTER: No objection, Your Honor.

17 THE COURT: Without objection, those are hereby
18 admitted.

19 (DTX 501, DTX 518, DTX 529, DTX 529-A and
20 DTX 530 were admitted.)

21 MS. MAZZOCHI: With that, then our next topic, I
22 guess, Your Honor, is Ms. Chu.

23 THE COURT: Yeah. I'll cut to the chase on that.

24 After giving it some thought, as I indicated
25 yesterday, I do think Mylan's entitled under Rule 32 to play

1 the portions designated as 30(b)(6) testimony.

2 Upon further -- I didn't say anything further past
3 that, having wanted to research it additionally. The Court
4 believes Mylan's likewise entitled to play other testimony from
5 Ms. Chu outside of her 30(b)(6) role. Again, she's unavailable
6 under Rule 32(a)(4)(B) in that she is more than 100 miles from
7 Clarksburg, West Virginia. So there would be no limitations
8 under the rules for using that transcript.

9 I'm aware the parties agreed to something to the
10 contrary in their joint memo applying to this trial, but in all
11 candor, we've blown through that a couple times today -- I'm
12 sorry -- a couple times already. I know paragraph 4 indicates
13 witnesses who are going to testify live, the parties agreed are
14 not be permitted to play deposition testimony. I would not
15 apply that to the 30(b)(6) designations.

16 But, again, the rules are what they are. The parties
17 can agree as they like, but the rules, in all candor, trump.
18 And from the category of what's good for the goose is likewise
19 good for the gander, paragraph 39 dealt with the agreement that
20 impeachment exhibits not previously disclosed would not be
21 admitted into evidence absent good cause.

22 So we've already done that once today. Ms. Chu, I
23 understand, is going to testify live as part of -- is it
24 Regeneron's rebuttal case?

25 MR. GREGORY: Yes, Your Honor.

1 THE COURT: Rebuttal case. But under Rule 32, I
2 think Mylan is entitled to use that transcript regardless of
3 which hat Ms. Chu is wearing at the time, her 30(b)(6) designee
4 hat or her fact witness personal capacity hat. So they'll be
5 permitted to play it as designated.

6 I would note, however, given this kerfuffle over it,
7 Regeneron will have some leeway when Ms. Chu is here in person
8 with respect to what areas they're permitted to cover.

9 So that's how we'll deal with Ms. Chu's testimony.

10 I'll direct the parties to get together this evening
11 to review and discuss the updated slide deck of Dr. Rabinow to
12 see what remaining issues there are.

13 Would that be the first witness Mylan anticipates
14 calling in the morning?

15 MS. MAZZOCHI: Yes, Your Honor.

16 THE COURT: We'll take that up first thing, but y'all
17 need to get together and talk about that this evening to see
18 what, if any, disputes may remain in light of the Court's
19 granting of Regeneron's motion to exclude those particular --
20 that particular opinion, I should say, of Dr. Rabinow with
21 respect to obviousness.

22 Anything else we need to take up at this point of the
23 day, then, from plaintiff's perspective?

24 MS. OBERWETTER: Not today, Your Honor.

25 MS. MAZZOCHI: Nothing from us, Your Honor.

1 THE COURT: We'll see everyone in the morning.
2 Everyone have a pleasant enough evening. Thank you all very
3 much.

4 (Proceedings concluded at 5:13 p.m.)
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CERTIFICATE

I, Cindy L. Knecht, Registered Professional Reporter and Official Reporter of the United States District Court for the Northern District of West Virginia, do hereby certify that the foregoing is a true and correct transcript of the proceedings had in the above-styled action on June 15, 2023, as reported by me in stenotypy.

I certify that the transcript fees and format comply with those prescribed by the Court and the Judicial Conference of the United States.

Given under my hand this 15th day of June 2023.

/s/Cindy L. Knecht

Cindy L. Knecht, RMR/CRR
Official reporter, United States
District Court for the Northern
District of West Virginia