

Exhibit 24

1 IN THE UNITED STATES DISTRICT COURT
2 FOR THE NORTHERN DISTRICT OF WEST VIRGINIA
3 AT CLARKSBURG

4 ----- x
5 REGENERON PHARMACEUTICALS, INC.,

6 Plaintiff,

7 Case No.

8 -versus-

9 1:22-cv-00061-TSK

10 MYLAN PHARMACEUTICALS INC.,

11 Defendant.
12 ----- x

13 ***HIGHLY CONFIDENTIAL***

14 January 18, 2023
15 9:12 a.m.

16 VIDEOTAPED DEPOSITION of GEORGE D.
17 YANCOPOULOS, taken pursuant to Notice, held at
18 Westchester Marriott, 670 White Plains Road,
19 Tarrytown, New York, before Fran Insley, a
20 Notary Public of the States of New York and New
21 Jersey.
22
23
24
25

Page 2	Page 4
1 APPEARANCES: 2 WILLIAMS & CONNOLLY 3 Attorneys for Plaintiff and 4 Witness 5 680 Maine Avenue, S.W. 6 Washington, D.C. 20024 7 BY: DAVID BERL, ESQ. 8 ELLEN OBERWETTER, ESQ. 9 -and- 10 KATHRYN KAYALI, ESQ. 11 12 CAREY DOUGLAS KESSLER & RUBY PLLC 13 Attorneys for Plaintiff 14 707 Virginia Street East 15 901 Chase Tower 16 Charleston, West Virginia 25301 17 BY: DAVID R. POGUE, ESQ. 18 (via teleconference) 19 drpogue@cdkrlaw.com 20 21 22 23 24 25	1 -----INDEX----- 2 WITNESS EXAMINATION BY PAGE 3 GEORGE YANCOPOULOS MS. MAZZOCHI 7 4 5 -----EXHIBITS----- 6 DEPOSITION DESCRIPTION PAGE 7 Exhibit 900 Objections to Interrogatories 51 8 Exhibit 901 RGN-EYLEA-MYLAN00487461 to 503 54 9 Exhibit 902 RGN-EYLEA-MYLAN0054862 to 863 68 10 Exhibit 903 MYL-AFL5190 through 5215 75 11 Exhibit 904 MYL-AFL5216 through 5241 75 12 Exhibit 905 Patent 61/432245 application 87 13 14 (The following exhibits were not referred to in 15 the deposition: 16 Exhibit 906 MYL-AFL90927 through 953 17 Exhibit 907 MYL-AFL90954 through 980 18 Exhibit 908 MYL-AFL91108 19 Exhibit 909 RGN-EYLEA-MYLAN13557 through 20 13602) 21 Exhibit 910 RGN-EYLEA-MYLAN13909 to 917 119 22 Exhibit 911 RGN-EYLEA-MYLAN13628 to 629 121 23 Exhibit 912 RGN-EYLEA-MYLAN13918 to 929 125 24 Exhibit 913 RGN-EYLEA-MYLAN525081 TO 083 135 25 Exhibit 914 MYL-AFL91250 to 273 139
Page 3	Page 5
1 APPEARANCES: (Continued) 2 RAKOCZY MOLINO MAZZOCHI SIWIK LLP 3 Attorneys for Defendant 4 6 West Hubbard Street 5 Suite 500 6 Chicago, Illinois 60654 7 BY: DEANNE MAZZOCHI, ESQ. 8 LAUREN LESKO, ESQ. 9 -and- 10 JEFFREY A. MARX, ESQ. 11 (via teleconference) 12 jmarx@rmmlegal.com 13 AND 14 STEPTOE & JOHNSON, LLP 15 400 White Oaks Boulevard 16 Bridgeport, West Virginia 26330 17 BY: WILLIAM J. O'BRIEN, ESQ. 18 (via teleconference) 19 jamie.obrien@steptoe-johnson.com 20 21 ALSO PRESENT: 22 LARRY COURY, ESQ., Regeneron 23 MATTHEW CHIN-QUEE, Videographer 24 25	1 DEPOSITION DESCRIPTION PAGE 2 Exhibit 915 RGN-EYLEA-MYLAN501236 to 248 153 3 Exhibit 916 RGN-EYLEA-MYLAN493989 to 994 179 4 Exhibit 917 RGN-EYLEA-MYLAN504690 to 693 187 5 Exhibit 918 RGN-EYLEA-MYLAN495807 to 852 203 6 Exhibit 919 RGN-EYLEA-MYLAN539067 to 068 206 7 (EXHIBITS PRODUCED.) 8 Exhibit 520A Previously marked 197 9 Exhibit 4 '601 Patent 24 10 Exhibit 5 '572 Patent 24 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25

Page 6

1 THE VIDEOGRAPHER: Good morning. We 9:12:18AM
 2 are going on the record at 9:12 a.m. on 9:12:19AM
 3 January 18, 2023. 9:12:23AM
 4 This is media unit one of the 9:12:26AM
 5 videotaped deposition of George 9:12:29AM
 6 Yancopoulos in the matter Regeneron 9:12:31AM
 7 Pharmaceuticals Inc. v Mylan 9:12:35AM
 8 Pharmaceuticals Inc. et. al. Case number 9:12:38AM
 9 1:22-CV-00061-TSK. The deposition is 9:12:42AM
 10 being held at 670 White Plains Road, 9:12:52AM
 11 Tarrytown, New York. 9:12:57AM
 12 My name is Matthew Chin-Quee from 9:13:01AM
 13 Veritext and I'm the videographer. The 9:13:04AM
 14 court reporter is Fran Insley from the 9:13:07AM
 15 firm Veritext. 9:13:09AM
 16 Will all counsel please state your 9:13:11AM
 17 appearances. 9:13:13AM
 18 MS. MAZZOCHI: Good morning. My 9:13:14AM
 19 name is Deanne Mazzochi from the law firm 9:13:15AM
 20 of Rakoczy Molio Mazzochi Siwik, LLP. 9:13:17AM
 21 Also with me is Lauren Lesko. 9:13:19AM
 22 MR. BERL: David Berl, Williams & 9:13:23AM
 23 Connolly on behalf of Regeneron and the 9:13:24AM
 24 witness. With me are Ellen Oberwetter 9:13:27AM
 25 from Williams & Connolly and Kathryn 9:13:30AM

Page 7

1 Kayali from Williams & Connolly and Larry 9:13:32AM
 2 Coury from Regeneron. 9:13:37AM
 3 THE VIDEOGRAPHER: Will the court 9:13:39AM
 4 reporter please swear in the witness. 9:13:40AM
 5 GEORGE YANCOPOULOS, the 9:13:41AM
 6 Witness herein, having first been duly sworn by 9:13:41AM
 7 the Notary Public, was examined and testified 9:13:41AM
 8 as follows: 9:13:41AM
 9 EXAMINATION BY MS. MAZZOCHI: 9:13:49AM
 10 Q. Good morning, Dr. Yancopoulos. Can 9:13:50AM
 11 you please state your full name and address for 9:13:52AM
 12 the record? 9:13:54AM
 13 A. George Damis Yancopoulos. 9:13:54AM
 14 Q. Address? 9:13:57AM
 15 A. Home address? 9:13:59AM
 16 Q. Sure. 9:14:00AM

Regeneron Protected Material

 19 Q. Have you given testimony under oath 9:14:09AM
 20 before? 9:14:11AM
 21 A. No. 9:14:13AM
 22 Q. Are you aware of the US Department 9:14:14AM
 23 of Justice lawsuit against Regeneron involving 9:14:16AM
 24 EYLEA? 9:14:20AM
 25 A. Yes, I am. 9:14:25AM

Page 8

1 Q. Have you given any statements or 9:14:26AM
 2 sworn testimony in any matter involving the US 9:14:30AM
 3 government and EYLEA? 9:14:33AM
 4 A. No, I have not. 9:14:40AM
 5 Q. Have you given any statements or 9:14:41AM
 6 testimony involving any claims involving a 9:14:44AM
 7 state government relating to kickback 9:14:47AM
 8 allegations involving EYLEA? 9:14:49AM
 9 A. No, I have not. 9:14:55AM
 10 Q. Have you received any subpoenas to 9:14:56AM
 11 appear before a state or federal grand jury? 9:14:58AM
 12 A. No, I have not. 9:15:04AM
 13 Q. Have you had any discussions 9:15:05AM
 14 internally regarding the US Government's 9:15:06AM
 15 kickback lawsuit against Regeneron involving 9:15:09AM
 16 EYLEA? 9:15:12AM
 17 MR. BERLE: Objection. You can 9:15:13AM
 18 answer that yes or no. 9:15:15AM
 19 A. I am not sure if I heard of anything 9:15:22AM
 20 referred to in the manner in which you just 9:15:24AM
 21 described it. 9:15:27AM
 22 Q. Are you aware of or have you spoken 9:15:29AM
 23 to anyone internally within Regeneron involving 9:15:31AM
 24 allegations by the US Government that of 9:15:35AM
 25 Regeneron's misuse of the Chronic Disease Fund 9:15:39AM

Page 9

1 or improper payments by Regeneron to the 9:15:43AM
 2 Chronic Disease Fund? 9:15:45AM
 3 MR. BERL: Objection. You can 9:15:49AM
 4 answer that yes or no. 9:15:49AM
 5 A. I'm not sure that anything that I'm 9:15:55AM
 6 aware of has been referred to in that way that 9:15:57AM
 7 you referred to it. 9:16:00AM
 8 Q. What is your understanding of the 9:16:02AM
 9 Chronic Disease Fund? 9:16:03AM
 10 A. I'm not an expert in this matter. 9:16:10AM
 11 Q. It doesn't matter. I'm not asking 9:16:11AM
 12 for your expertise. I'm just asking for your 9:16:13AM
 13 factual knowledge about the Chronic Disease 9:16:16AM
 14 Fund. 9:16:17AM
 15 A. Factual knowledge? 9:16:21AM
 16 Q. Right. 9:16:23AM
 17 A. I'm not sure if I understand. 9:16:25AM
 18 Q. Do you know what the Chronic Disease 9:16:28AM
 19 Fund is? 9:16:29AM
 20 A. I believe the Chronic Disease Fund 9:16:40AM
 21 is a foundation that pays for the co-payments 9:16:42AM
 22 for certain medicines when patients cannot 9:16:49AM
 23 afford to pay for them. 9:16:58AM
 24 Q. Are you aware of payments that 9:17:00AM
 25 Regeneron made to the Chronic Disease Fund or 9:17:02AM

Page 10		
1	the foundation that operates it?	9:17:06AM
2	MR. BERL: Objection.	9:17:08AM
3	A. I'm not personally aware of	9:17:15AM
4	payments. That is not my side of the business.	9:17:16AM
5	I believe that we provide donations to that	9:17:22AM
6	foundation.	9:17:29AM
7	Q. Do you know the size and scope of	9:17:30AM
8	the donations that Regeneron has provided to	9:17:33AM
9	that foundation?	9:17:35AM
10	A. No, I do not.	9:17:37AM
11	Q. Do you know why Regeneron made	9:17:38AM
12	donations to that foundation?	9:17:39AM
13	A. My understanding is so that the	9:17:44AM
14	foundation can help pay the co-payments for	9:17:47AM
15	patients below a certain poverty level who	9:17:53AM
16	cannot afford to pay for the co-payments for	9:17:57AM
17	those medicines themselves.	9:18:00AM
18	Q. Do you have an understanding that	9:18:05AM
19	Regeneron spent tens of millions of dollars in	9:18:06AM
20	grants to that foundation?	9:18:11AM
21	A. I really do not know the amounts	9:18:15AM
22	that we have donated to that foundation.	9:18:17AM
23	Q. Who are the individuals you most	9:18:20AM
24	closely associate with Regeneron as	9:18:22AM
25	understanding Regeneron's interaction with the	9:18:24AM

Page 11		
1	Chronic Disease Fund and the foundation that	9:18:30AM
2	operates it?	9:18:33AM
3	A. Well, I would -- so I believe the	9:18:35AM
4	case that you are referring to is referring to	9:18:43AM
5	issues back in 2013. I do not know who at	9:18:46AM
6	Regeneron was largely responsible for	9:18:54AM
7	interactions. I assume it would be somebody in	9:19:00AM
8	our commercial group.	9:19:04AM
9	Q. Like Robert Terifay?	9:19:06AM
10	A. I do not know.	9:19:10AM
11	Q. When was the last time you spoke	9:19:12AM
12	with Robert Terifay?	9:19:13AM
13	A. I don't know.	9:19:22AM
14	Q. Are you aware of the reasons why	9:19:24AM
15	Mr. Terifay left the company?	9:19:26AM
16	A. I am aware of some of the reasons.	9:19:32AM
17	Q. What are some of the reasons you're	9:19:34AM
18	aware of?	9:19:36AM
19	A. I know that he had a number of	9:19:40AM
20	catastrophic medical events such as multiple	9:19:42AM
21	strokes that affected his ability to come to	9:19:48AM
22	work.	9:19:54AM
23	Q. Any others you're aware of?	9:19:55AM
24	A. I know that he was tangentially or	9:19:59AM
25	somehow involved with the foundation issues and	9:20:06AM

Page 12		
1	the lawsuits, but I don't know if that was	9:20:09AM
2	involved in his leaving from the company.	9:20:12AM
3	Q. Do you have an understanding that	9:20:16AM
4	Murray Goldberg was involved with some of these	9:20:18AM
5	foundation issues?	9:20:20AM
6	A. I do not.	9:20:22AM
7	Q. How about your CEO Len Schleifer?	9:20:23AM
8	A. I do not.	9:20:28AM
9	Q. Can you state your educational	9:20:30AM
10	background post high school?	9:20:31AM
11	A. I received an undergraduate degree	9:20:39AM
12	from Columbia College. I received medical and	9:20:41AM
13	Ph.D. degrees from Columbia as well.	9:20:49AM
14	Q. How is it that you came to be	9:20:54AM
15	involved with Regeneron around the 1989 time	9:20:57AM
16	period I think?	9:21:01AM
17	A. I was approached by Leonard	9:21:04AM
18	Schleifer who had interacted with my Ph.D.	9:21:10AM
19	mentor about the possibility of helping start	9:21:16AM
20	this new company.	9:21:23AM
21	Q. Who was your Ph.D. mentor?	9:21:24AM
22	A. Fred Alt.	9:21:29AM
23	Q. What was the subject of your Ph.D.	9:21:30AM
24	thesis?	9:21:34AM
25	A. The molecular biology of lymphocyte	9:21:45AM

Page 13		
1	cell development.	9:21:49AM
2	Q. What about your educational and	9:21:52AM
3	Ph.D. work caused Mr. Schleifer to think you	9:21:56AM
4	would be a good fit for what he was trying to	9:22:03AM
5	do with Regeneron?	9:22:05AM
6	MR. BERL: Objection.	9:22:06AM
7	A. At the time the field of cloning	9:22:10AM
8	genes was in its infancy and the idea was that	9:22:25AM
9	would be a major component of what the company	9:22:36AM
10	would be trying to do, particularly clone nerve	9:22:40AM
11	growth factors that control nerve growth and	9:22:46AM
12	could be used to fight back against	9:22:54AM
13	neurodegenerative diseases and to that point in	9:22:57AM
14	time there had only been a single nerve growth	9:23:04AM
15	factor identified and the dream was to try to	9:23:07AM
16	clone many more and then use them to help	9:23:15AM
17	either grow or sustain neurons that were dying	9:23:22AM
18	in neurodegenerative diseases.	9:23:27AM
19	In order to do that, one would have	9:23:31AM
20	to bring gene cloning in a big way into the	9:23:33AM
21	field of neurobiology. There were not that	9:23:37AM
22	many gene cloners and there were not that many	9:23:41AM
23	gene cloners in that field. Most of them were	9:23:44AM
24	in immunology, which is where I had been, and	9:23:48AM
25	his idea or plan was to bring somebody from a	9:23:56AM

Page 14		Page 16		
1	different field, but I had had a longstanding	9:24:01AM	1 Q. And they eventually wound up using I	9:27:27AM
2	interest for various reasons into	9:24:05AM	2 believe Macugen I believe initially in some of	9:27:30AM
3	neurodegenerative diseases and so it was a very	9:24:09AM	3 their clinical work?	9:27:33AM
4	natural fit that I, as a gene cloner, would	9:24:14AM	4 A. No.	9:27:35AM
5	move to this new company that was going to try	9:24:17AM	5 Q. Well, what molecules were they	9:27:40AM
6	to use gene cloning as a way to fight back	9:24:20AM	6 injecting into the eye?	9:27:43AM
7	against neurodegenerative diseases.	9:24:26AM	7 MR. BERLE: Objection. Vague as to	9:27:45AM
8	Q. Before you get to Regeneron, did you	9:24:29AM	8 time.	9:27:46AM
9	have any training in the field of	9:24:31AM	9 A. I contacted them about injecting	9:27:51AM
10	ophthalmology?	9:24:33AM	10 BDNF neurotrophin 3 and ciliary neurotrophic	9:27:56AM
11	A. During medical training you do	9:24:46AM	11 factors and those were the factors they were	9:28:02AM
12	required rotations in the various areas,	9:24:50AM	12 injecting into the eye.	9:28:04AM
13	including ophthalmology.	9:24:56AM	13 Q. Now, the initial neurodegenerative	9:28:06AM
14	Q. About how much time do you think you	9:24:58AM	14 product that Regeneron tried to bring to market	9:28:09AM
15	spent doing the rotation in ophthalmology when	9:25:01AM	15 that went to Phase III trials, it never got to	9:28:12AM
16	you were in med school?	9:25:04AM	16 market, right?	9:28:15AM
17	A. I don't remember exactly.	9:25:07AM	17 A. That is correct.	9:28:16AM
18	Q. More than six months?	9:25:08AM	18 Q. Who was that in collaboration with?	9:28:17AM
19	A. Probably not.	9:25:10AM	19 A. That was in -- I'm not --	9:28:20AM
20	Q. What training did you acquire while	9:25:12AM	20 Q. Sanofi?	9:28:37AM
21	you were at Regeneron in the field of	9:25:15AM	21 A. It wasn't Sanofi. What I'm	9:28:38AM
22	ophthalmology or diseases involving	9:25:20AM	22 struggling with is we had multiple things of	9:28:40AM
23	ophthalmology?	9:25:23AM	23 neurodegenerative diseases, multiple of which	9:28:43AM
24	MR. BERL: Objection. Vague.	9:25:24AM	24 we put into Phase III trials which didn't	9:28:47AM
25	A. When I helped lead our efforts to	9:25:33AM	25 succeed and I don't know which was the first.	9:28:48AM

Page 15		Page 17		
1	clone a variety of nerve growth factors, I	9:25:40AM	1 I can't remember which was the first one to	9:28:50AM
2	realized that there were also essentially the	9:25:47AM	2 have failed. Some of whom -- some of these we	9:28:52AM
3	equivalent of neurodegenerative diseases of the	9:25:53AM	3 brought forth with partners and some of which	9:28:56AM
4	eye.	9:25:57AM	4 we brought forth by ourselves.	9:29:00AM
5	So just retinal deterioration	9:26:00AM	5 Q. When did Regeneron start making the	9:29:03AM
6	degenerative conditions and so forth. So I had	9:26:03AM	6 switch or adding the focus on ophthalmology in	9:29:07AM
7	the idea that perhaps we could just like we	9:26:08AM	7 developing molecules for ophthalmic uses?	9:29:12AM
8	were trying to help neurons that were dying in	9:26:13AM	8 A. As I said, we first started	9:29:29AM
9	neurodegenerative diseases in the brain, such	9:26:17AM	9 exploring this possibility with LaVail and	9:29:33AM
10	as an Alzheimer's disease or in the spinal	9:26:20AM	10 Steinberg in the early 1990s.	9:29:38AM
11	cord, such as in Lou Gehrig's disease, that we	9:26:23AM	11 Q. When was the first time -- well, did	9:29:44AM
12	could also maybe use nerve growth factors to	9:26:30AM	12 anything come of those initial efforts with Dr.	9:29:47AM
13	help the neurons in the eye survive in retinal	9:26:33AM	13 Steinberg and others involving the -- I think	9:29:52AM
14	degeneration diseases as the retina is an	9:26:39AM	14 you called it BDNF and other neurotropic	9:29:57AM
15	outcropping of the brain.	9:26:43AM	15 factors?	9:30:03AM
16	So I contacted at the time some	9:26:47AM	16 MR. BERL: Objection.	9:30:04AM
17	scientists who I felt were leaders in this	9:26:53AM	17 A. We built internal expertise and	9:30:06AM
18	field and I suggested that we work together to	9:26:59AM	18 knowledge and created a group among several	9:30:13AM
19	inject nerve growth factors into the eye,	9:27:02AM	19 other groups that we had that studied the eye	9:30:18AM
20	starting with animal models to try to protect	9:27:08AM	20 and eye diseases and generated a lot of	9:30:23AM
21	them against these models of neurodegenerative	9:27:12AM	21 expertise and knowledge.	9:30:28AM
22	disease.	9:27:18AM	22 Q. Who were those internal experts that	9:30:29AM
23	Q. Those individuals you initially	9:27:19AM	23 you had at Regeneron relating to the ophthalmic	9:30:32AM
24	contacted, who were they?	9:27:21AM	24 field?	9:30:38AM
25	A. Math LaVail and Roy Steinberg.	9:27:24AM	25 A. It depends on your definition of	9:30:44AM

Page 18

1 experts. 9:30:46AM
2 Q. The way in which you just used the 9:30:48AM
3 term, what you referred to as your internal 9:30:50AM
4 expertise, the people involved in building that 9:30:52AM
5 internal expertise and knowledge you referred 9:30:55AM
6 to? 9:30:57AM
7 A. I would say it would be primarily 9:30:58AM
8 myself and an individual known as Stan Wiegand. 9:30:59AM
9 Q. Well, you didn't have any formal 9:31:11AM
10 training in eye diseases. Did Stan Wiegand 9:31:12AM
11 have any training in eye diseases? 9:31:16AM
12 MR. BERL: Objection. Lack of 9:31:18AM
13 foundation. 9:31:19AM
14 A. In science I'm not sure what formal 9:31:28AM
15 training really means. 9:31:33AM
16 Q. Well, you didn't -- I mean I think 9:31:37AM
17 you said that your experience before you 9:31:39AM
18 started working on these projects was limited 9:31:42AM
19 to a rotation during medical school. So you 9:31:45AM
20 never worked as an ophthalmologist, never did a 9:31:47AM
21 residency in ophthalmology, didn't have a 9:31:52AM
22 post-doc or a fellowship on ophthalmology, 9:31:55AM
23 never treated patients, right? 9:31:59AM
24 MR. BERL: Objection. Compound. 9:32:01AM
25 Q. Was Mr. Wiegand somebody who had 9:32:04AM

Page 19

1 that kind of experience? 9:32:06AM
2 MR. BERL: Objection. Vague, 9:32:07AM
3 compound. 9:32:08AM
4 A. Ph.D. training, science training is 9:32:13AM
5 largely learning by doing and asking and 9:32:16AM
6 exploring questions that have not been asked 9:32:22AM
7 before and that's how one learns and that is 9:32:26AM
8 arguably how most of us, including me, as 9:32:33AM
9 scientists have gotten most of your training, 9:32:39AM
10 including in eye diseases or in allergic 9:32:42AM
11 diseases or in inflammatory diseases or in 9:32:49AM
12 muscular diseases. That's where most of the 9:32:55AM
13 training happens. 9:33:02AM
14 Q. When did you bring Jesse Cedarbaum 9:33:06AM
15 on board? 9:33:08AM
16 MR. BERL: Is that when or why? 9:33:10AM
17 MS. MAZZOCHI: When. 9:33:12AM
18 A. I did not bring Jesse Cedarbaum on 9:33:14AM
19 board. 9:33:18AM
20 Q. Who did? 9:33:19AM
21 A. I don't know for sure. 9:33:24AM
22 Q. Who brought Avner Ingerman on board? 9:33:29AM
23 A. I'm not sure. 9:33:37AM
24 Q. Did Regeneron ever have anyone on 9:33:52AM
25 staff who had actually worked as an 9:33:55AM

Page 20

1 ophthalmologist or treated patients with eye 9:33:58AM
2 diseases? 9:34:03AM
3 MR. BERL: Objection. Vague as to 9:34:04AM
4 times. 9:34:06AM
5 Q. Say prior 2005. 9:34:10AM
6 A. I don't know. 9:34:21AM
7 Q. When, in what time period was it 9:34:27AM
8 decided to test the VEGF compound in the eye? 9:34:30AM
9 A. I don't remember exactly. 9:34:48AM
10 Q. Well, was VEGF tried first for 9:34:50AM
11 cancer and then it led into the eye or the eye 9:34:54AM
12 came first and that led into the cancer 9:34:57AM
13 indications? 9:35:00AM
14 MR. BERL: Objection. Vague. 9:35:02AM
15 A. It's hard to remember. I think that 9:35:17AM
16 I may have been thinking of them somewhat 9:35:20AM
17 simultaneously. Maybe cancer first. Hard to 9:35:31AM
18 remember. 9:35:37AM
19 Q. Is it fair to say that Regeneron has 9:35:44AM
20 been at the center of your professional career 9:35:46AM
21 for the last 30 years? 9:35:49AM
22 A. It's been my entire career for the 9:35:56AM
23 last 30 plus years. 9:36:01AM

Regeneron Protected Material

Regeneron Protected Material

Page 22

Regeneron Protected Material

6 Q. Would it be fair to say that the 9:37:42AM
7 bulk of payers for the aflibercept in some way, 9:37:43AM
8 shape or form are state and federal 9:37:49AM
9 governments? 9:37:52AM
10 A. Can you say that again? 9:37:56AM
11 Q. Sure. Would it be fair to say that 9:37:58AM
12 the largest number of dollars in sales for 9:37:59AM
13 aflibercept come in some way, shape or form 9:38:04AM
14 through state and federal governments such as 9:38:07AM
15 Medicaid and Medicare programs? 9:38:10AM
16 MR. BERL: Objection. 9:38:13AM
17 A. I'm primarily in charge of the 9:38:22AM
18 science. I don't know that much believe it or 9:38:23AM
19 not about those numbers. I believe it's true 9:38:26AM
20 that Medicare does pay for a lot of the use of 9:38:31AM
21 EYLEA in elderly patients. 9:38:39AM
22 Q. Billions of dollars over the years, 9:38:41AM
23 right? 9:38:43AM
24 A. I know that it's a lot of money, 9:38:44AM
25 yes. 9:38:46AM

Page 23

1 Q. So your personal wealth has 9:38:47AM
2 certainly grown significantly as a consequence 9:38:50AM
3 of the taxpayer dollars that have been used to 9:38:53AM
4 fund Medicaid and Medicare purchases of 9:38:56AM
5 aflibercept? 9:38:59AM
6 MR. BERL: Objection. 9:39:00AM
7 A. I don't think of it that way. 9:39:08AM
8 Q. I believe when it comes to worldwide 9:39:16AM
9 sales of aflibercept, Regeneron has gotten half 9:39:20AM
10 of those through its partnership with Bayer; is 9:39:24AM
11 that fair? 9:39:26AM
12 MR. BERL: Objection. 9:39:29AM
13 A. I don't know the exact fraction. 9:39:29AM
14 Q. Were you one of the individuals who 9:39:32AM
15 were involved in negotiating that deal to 9:39:33AM
16 insist that Regeneron would keep a hundred 9:39:36AM
17 percent of the US revenues for itself for 9:39:39AM
18 aflibercept? 9:39:42AM
19 A. Which — what is the question 9:39:47AM
20 exactly? 9:39:49AM
21 Q. When it comes to the Regeneron 9:39:50AM
22 agreements with Bayer, were you one of the 9:39:54AM
23 individuals who insisted on Regeneron keeping a 9:39:57AM
24 hundred percent of the revenues from the US 9:40:01AM
25 market for aflibercept for the ophthalmic 9:40:03AM

Page 24

1 indications? 9:40:09AM
2 A. No, I was not. 9:40:10AM
3 Q. Did you play any role in trying to 9:40:13AM
4 make sure that you were keeping US revenues 9:40:16AM
5 from aflibercept at Regeneron and not in the 9:40:19AM
6 hands of partners? 9:40:23AM
7 A. I wasn't involved in those parts of 9:40:31AM
8 the negotiations. 9:40:34AM
9 Q. Do you remember urging Len Schleifer 9:40:35AM
10 that he should ensure that Regeneron was going 9:40:39AM
11 to keep a hundred percent of the US revenues 9:40:43AM
12 from aflibercept in connection with the Bayer 9:40:46AM
13 deal? 9:40:53AM
14 A. I do not remember doing that. 9:40:53AM
15 Q. I'm going to place before you 9:40:57AM
16 documents that were previously marked as 9:40:59AM
17 Defendant's Exhibit 4 and Defendant's 9:41:01AM
18 Exhibit 5, the '601 and '572 patents in this 9:41:03AM
19 case. 9:41:11AM
20 Feel free to read the whole thing, 9:41:15AM
21 but if you can confirm that you have seen these 9:41:16AM
22 documents before? 9:41:19AM
23 A. (Witness reviewing document.) 9:41:20AM
24 Q. Dr. Yancopoulos, it's taking you 9:55:30AM
25 quite a while to go through these two patents, 9:55:32AM

Page 25

1 the '601 and 572 patents. Have you not seen 9:55:34AM
2 these before? 9:55:38AM
3 MR. BERL: Objection. You said feel 9:55:39AM
4 free to read through the whole thing. 9:55:41AM
5 MS. MAZZOCHI: If he needs to 9:55:43AM
6 identify it. 9:55:44AM
7 MR. BERL: That's not what you said. 9:55:45AM
8 A. Well, I haven't looked at these in 9:55:47AM
9 detail in a very long time and I was, as you 9:55:49AM
10 suggested, I was reviewing the documents. I 9:55:53AM
11 have only gotten through one of them right now. 9:55:55AM
12 Q. Well, the specification is the same 9:55:58AM
13 for both of them, so no need to read it twice. 9:56:00AM
14 Do you recognize these documents as your 9:56:04AM
15 patents? 9:56:06AM
16 A. They look very similar to what I 9:56:07AM
17 believe were my patents. 9:56:08AM
18 Q. When was the last time you actually 9:56:10AM
19 looked at the '601 or '572 patents that you 9:56:12AM
20 recall? 9:56:15AM
21 A. I have looked at copies of them as 9:56:17AM
22 recently as yesterday, but I haven't reviewed 9:56:19AM
23 them carefully in years. 9:56:22AM
24 Q. Do you recall why you decided to 9:56:29AM
25 file for these patents? 9:56:31AM

Page 26			Page 28		
1	MR. BERL: Objection. Vague.	9:56:35AM	1	trial?	10:00:48AM
2	A. I don't recall.	9:56:55AM	2	A. The standard dose escalation Phase I	10:01:56AM
3	Q. If you take a look at the second	9:56:58AM	3	trial, I don't remember who designed this.	10:01:59AM
4	page of these exhibits, there is a reference to	9:57:01AM	4	Q. Further down in column 8 there is a	10:02:03AM
5	related US application data and about	9:57:07AM	5	reference to "Example 2" a "Phase II clinical	10:02:05AM
6	two-thirds of the way down to the left-hand	9:57:14AM	6	trial of repeated doses of intravitreally	10:02:08AM
7	column there is references to provisional	9:57:16AM	7	administered VEGF Receptor-based chimeric	10:02:13AM
8	application number 61/432245 filed on	9:57:18AM	8	molecule (VEGFT) in subjects with neovascular	10:02:19AM
9	January 13, 2011. Do you see that?	9:57:25AM	9	AMD." I believe that was the CLEAR-IT 2 study.	10:02:22AM
10	A. Which patent am I looking at?	9:57:29AM	10	Who designed that clinical trial?	10:02:27AM
11	Q. It doesn't matter. Either the '601	9:57:32AM	11	A. I was involved in designing that	10:02:42AM
12	or the '572.	9:57:34AM	12	trial along with my team.	10:02:43AM
13	A. And where in the patent am I	9:57:37AM	13	Q. Who else on the team?	10:02:45AM
14	looking?	9:57:39AM	14	A. It's so long ago I can't remember.	10:02:51AM
15	Q. Second page of the exhibit. There	9:57:39AM	15	Q. Do you know why any of your other	10:02:53AM
16	you go. Left-hand column about two-thirds of	9:57:44AM	16	team members are not listed on this patent if	10:02:56AM
17	the way down, do you see a reference to	9:57:47AM	17	they helped you with the clinical trial design	10:02:58AM
18	provisional application number 61/432245 held	9:57:50AM	18	or coming up with ideas for the clinical trial	10:03:01AM
19	on January 13, 2011?	9:57:55AM	19	design?	10:03:04AM
20	A. Could you just repeat the number?	9:57:59AM	20	MR. BERL: Objection. Lack of	10:03:05AM
21	Q. 61/432245.	9:58:01AM	21	foundation.	10:03:06AM
22	A. Yes.	9:58:05AM	22	A. This was an exploratory study that	10:03:44AM
23	Q. Now, by the time we had reached	9:58:07AM	23	was used to produce data to inform so as to how	10:03:47AM
24	January 13, 2011, would you have considered	9:58:11AM	24	to design a dosing regimen and I gather that	10:04:01AM
25	yourself to be an ophthalmologist with	9:58:15AM	25	the lawyers didn't think that there was	10:04:17AM
Page 27			Page 29		
1	experience in treating angiogenic eye	9:58:19AM	1	anything inventive here in terms of using this	10:04:19AM
2	disorders?	9:58:23AM	2	to design the ultimate dosing regimen.	10:04:24AM
3	A. I was never an ophthalmologist.	9:58:36AM	3	Q. Take a look at "Example 3: Phase I	10:04:26AM
4	Q. Do you have an understanding as to	9:58:47AM	4	Clinical Trial of Systemically Administered	10:04:29AM
5	why you are listed as the sole named inventor	9:58:49AM	5	VEGF Receptor-Based Chimeric Molecule (VEGFT)	10:04:34AM
6	on these two patents?	9:58:52AM	6	in Subjects with neovascular AMD." Did you	10:04:40AM
7	A. Our legal team would have reviewed	9:59:22AM	7	have any role in designing this clinical trial?	10:04:43AM
8	all the work and effort that is described	9:59:27AM	8	A. I'm sure I played a role in the	10:05:57AM
9	herein and reached that conclusion.	9:59:32AM	9	design of this, but I can't remember the	10:05:59AM
10	Q. Well, let's take a look, for	9:59:40AM	10	details.	10:06:00AM
11	example, in DX4, the '601 patent and let's	9:59:42AM	11	Q. Do you know if you were ever	10:06:01AM
12	start with column 8, example.	9:59:55AM	12	identified as a coauthor on any publication	10:06:02AM
13	One there is a reference to a "Phase	10:00:03AM	13	describing this clinical trial?	10:06:06AM
14	I Clinical Trial of Intravitreally Administered	10:00:05AM	14	A. I couldn't remember.	10:06:12AM
15	VEGF Receptor-Based Chimeric Molecule VEGFT in	10:00:12AM	15	Q. Do you recall whether this trial was	10:06:14AM
16	Subjects with Neovascular AMD." That's in	10:00:21AM	16	one that was done with Dr. Cedarbaum and others	10:06:15AM
17	column 8. Let me know when you are there.	10:00:25AM	17	at Johns Hopkins?	10:06:20AM
18	A. In patent '601?	10:00:28AM	18	A. I would believe that Dr. Cedarbaum	10:06:26AM
19	Q. Yes.	10:00:30AM	19	was involved. I'm not sure with which sites he	10:06:28AM
20	A. I see page numbers.	10:00:31AM	20	collaborated.	10:06:31AM
21	Q. Yes, go to column 8.	10:00:32AM	21	Q. Let's take a look at Example 4 which	10:06:33AM
22	A. Page 8?	10:00:35AM	22	is titled "Phase III Clinical Trials of the	10:06:35AM
23	Q. No, column 8.	10:00:36AM	23	Efficacy, Safety, and Tolerability of Repeated	10:06:39AM
24	A. I see. Yes.	10:00:39AM	24	Doses of Intravitreal VEGFT in Subjects with	10:06:44AM
25	Q. Who designed that Phase I clinical	10:00:46AM	25	Neovascular Age-Related Macular Degeneration."	10:06:50AM

Page 30		Page 32	
1	Do you see that? 10:06:54AM	1	were the first person to come up with the idea 10:11:52AM
2	A. Yes. 10:06:56AM	2	of dosing in an eight week dosing interval with 10:11:56AM
3	Q. What individuals were involved in 10:06:56AM	3	aflibercept, right? 10:12:02AM
4	the design of this clinical trial? 10:06:58AM	4	MR. BERL: Objection. 10:12:04AM
5	A. There were a number of individuals 10:07:32AM	5	Q. Within Regeneron? 10:12:04AM
6	as well as myself involved in the design of 10:07:34AM	6	MR. BERL: Objection. 10:12:08AM
7	this clinical trial. 10:07:37AM	7	A. As I said, there literally were an 10:12:20AM
8	Q. Who do you recall? 10:07:38AM	8	infinite number of potential dosing regimens 10:12:25AM
9	A. Over the years we did so many 10:07:59AM	9	that could be considered with every potential 10:12:29AM
10	clinical trials, just in this space, let alone 10:08:01AM	10	interval imaginable and somebody had to provide 10:12:34AM
11	across other spaces, that I can't remember for 10:08:05AM	11	a rationale and justification to pick what 10:12:44AM
12	any specific trial who would have been involved 10:08:07AM	12	might be dosing intervals that might be able to 10:12:49AM
13	other than — I would remember Neil Stahl. 10:08:12AM	13	offer a benefit and a rationale as to how to 10:12:54AM
14	Q. Do you recall who was the first 10:08:23AM	14	try them and as I just said, to my 10:12:59AM
15	person who suggested aflibercept should be 10:08:25AM	15	recollection, I was the one who did that. 10:13:05AM
16	dosed for wet AMD on an eight week schedule as 10:08:29AM	16	Q. Well, are you saying that you were 10:13:08AM
17	opposed to a twelve week schedule or monthly 10:08:35AM	17	the first person within Regeneron who came up 10:13:09AM
18	schedule? 10:08:39AM	18	with a rationale for dosing on an eight week 10:13:12AM
19	MR. BERL: Objection. 10:08:40AM	19	schedule? 10:13:16AM
20	A. As you might imagine, these 10:09:20AM	20	MR. BERL: Objection. 10:13:17AM
21	injections could incur by almost an infinite 10:09:25AM	21	A. I believe I have answered that 10:13:20AM
22	number of dosing regimens and it's possible 10:09:30AM	22	question. 10:13:21AM
23	that anyone of the infinite regimens were 10:09:36AM	23	Q. No, I'm asking if you believe you 10:13:22AM
24	brought up by different people at different 10:09:40AM	24	were the first person who came up with a 10:13:23AM
25	times, but what I do remember is that there was 10:09:43AM	25	rationale for dosing at the eight week mark; 10:13:25AM
Page 31		Page 33	
1	not a convincing rationale given to drive us to 10:09:53AM	1	yes or no? 10:13:28AM
2	try any one of the infinite potential dosing 10:10:03AM	2	MR. BERL: Objection. 10:13:29AM
3	regimens until I tried to look at the — all 10:10:06AM	3	A. I believe I just answered that 10:13:30AM
4	the available data and decide where I thought 10:10:21AM	4	question. 10:13:32AM
5	the breaking point was in the durability of the 10:10:25AM	5	Q. Well, I'm not clear. Was it yes or 10:13:33AM
6	existing best medicine at the time. 10:10:38AM	6	was it no or you don't know? 10:13:35AM
7	Q. What do you think — 10:10:42AM	7	MR. BERL: Objection. 10:13:38AM
8	MR. BERL: Objection. 10:10:43AM	8	A. As I described, I looked at the 10:13:46AM
9	MS. MAZZOCHI: I'm sorry, I thought 10:10:45AM	9	available data to determine where there was a 10:13:53AM
10	he was finished. 10:10:46AM	10	potential breaking point in the ability or 10:13:58AM
11	Q. Go ahead. 10:10:47AM	11	durability of the best available standard of 10:14:01AM
12	A. And that led me to conclude that the 10:10:48AM	12	care at the time, how long it could last and I 10:14:05AM
13	breaking point or where the existing best 10:10:52AM	13	believe that I calculated that that might be 10:14:11AM
14	standard of care would fail in terms of 10:10:57AM	14	around eight weeks and that provided the 10:14:15AM
15	durability of interval was at the eight week 10:11:00AM	15	rationale to then use an eight week dosing 10:14:19AM
16	point and so to have something that might be 10:11:06AM	16	interval within dosing regimens that we would 10:14:24AM
17	able to have a better benefit to patients 10:11:11AM	17	test in our trial to show that there was a 10:14:29AM
18	predominantly by reducing the treatment burden 10:11:17AM	18	potential benefit to patients to take this 10:14:34AM
19	that that might be an appropriate interval to 10:11:25AM	19	treatment as opposed to the standard of care. 10:14:38AM
20	consider into a dosing regimen and so that was 10:11:30AM	20	Q. Sure, I understand that you are 10:14:40AM
21	the major driver for us considering potential 10:11:34AM	21	saying that you sat down and you thought about 10:14:42AM
22	dosing regimens that included within them an 10:11:39AM	22	a rationale. I'm asking whether you were the 10:14:43AM
23	eight week dosing interval. 10:11:43AM	23	first one at Regeneron to come up with a 10:14:45AM
24	Q. But again, I just want to be clear, 10:11:48AM	24	rationale for using an eight week dosing 10:14:48AM
25	you can't say, sitting here today, that you 10:11:50AM	25	interval with aflibercept? 10:14:51AM

Page 34			Page 36		
1	MR. BERL: Objection.	10:14:54AM	1	MR. BERL: Objection. Vague and	10:18:25AM
2	A. I'm not aware of any other rationale	10:14:59AM	2	compound.	10:18:26AM
3	that I had heard of.	10:15:02AM	3	A. At the time we were a much smaller	10:18:33AM
4	Q. Do you recall whether Robert Terifay	10:15:09AM	4	company and every -- a lot of people knew what	10:18:37AM
5	came up with a marketing rationale for using an	10:15:14AM	5	was going on and there were constant	10:18:41AM
6	eight week dosing interval with aflibercept?	10:15:18AM	6	communications between the small number of	10:18:46AM
7	A. I do not believe that Robert Terifay	10:15:41AM	7	individuals we had in the patent office and the	10:18:51AM
8	would have come up with such a rationale.	10:15:44AM	8	scientists and, in fact, they often attended	10:18:53AM
9	Q. Do you recall having discussions	10:15:48AM	9	meetings.	10:18:56AM
10	within the joint steering committee between	10:15:51AM	10	I can't remember how or when the	10:18:57AM
11	Regeneron and Bayer, what would be an	10:15:53AM	11	exchange occurred, but in a much smaller	10:19:00AM
12	appropriate dose interval to use for	10:15:56AM	12	company, it was much easier for communications	10:19:07AM
13	aflibercept when it came to AMD dosing?	10:16:01AM	13	to happen that way.	10:19:10AM
14	A. There was an ongoing debate with	10:16:08AM	14	Q. Who was your primary person or who	10:19:12AM
15	many individuals arguing for an assortment of	10:16:15AM	15	were the individuals you recall who were within	10:19:14AM
16	the many different potential dosing schedules	10:16:20AM	16	the patent -- your Regeneron's patent	10:19:18AM
17	and it was a source of constant debate.	10:16:23AM	17	department in and around this 2010, 2011 time	10:19:20AM
18	Q. Before you filed this patent	10:16:33AM	18	period that you interacted with on aflibercept?	10:19:24AM
19	application, signing an oath stating that you	10:16:35AM	19	A. It's hard to remember individuals	10:19:41AM
20	were the sole inventor, did you ever go back	10:16:40AM	20	more than ten years later, but I believe Frank	10:19:44AM
21	and look at the historical record to make sure	10:16:43AM	21	Cunningham was one of the key individuals.	10:19:48AM
22	that you were the one and only person who had	10:16:46AM	22	Q. Do you recall whether he reached out	10:19:51AM
23	come up with this dosing regimen, particularly	10:16:49AM	23	to you or you reached out to him about filing a	10:19:53AM
24	the eight week dosing regimen?	10:16:55AM	24	patent application?	10:19:58AM
25	MR. BERL: Objection. Vague and	10:16:57AM	25	MR. BERL: Objection.	10:20:00AM
Page 35			Page 37		
1	compound.	10:16:58AM	1	A. I don't recall.	10:20:04AM
2	A. I lived through the whole experience	10:17:23AM	2	Q. Do you recall whether Bayer ever	10:20:07AM
3	and I relied on my recollection at the time of	10:17:29AM	3	suggested that or any of the investor groups	10:20:09AM
4	the history.	10:17:33AM	4	you were speaking with ever suggested that	10:20:13AM
5	Q. Did you ever file or prepare any	10:17:35AM	5	Regeneron didn't have particularly strong	10:20:15AM
6	invention disclosure statements?	10:17:38AM	6	patent protection for the EYLEA product and	10:20:18AM
7	MR. BERL: Objection. Vague. Are	10:17:42AM	7	ophthalmic indications?	10:20:22AM
8	we talking about with this application?	10:17:45AM	8	MR. BERL: Objection.	10:20:24AM
9	MS. MAZZOCHI: Sure, with regard to	10:17:48AM	9	A. I don't remember that ever coming	10:20:27AM
10	the dosing regimen set forth in the '601	10:17:49AM	10	up.	10:20:29AM
11	or '572 patents.	10:17:52AM	11	Q. Do you know whether your -- whether	10:20:30AM
12	A. More than ten years later, I can't	10:17:55AM	12	Regeneron's agreement with Bayer, whether the	10:20:33AM
13	remember that.	10:17:57AM	13	percentage of dollars that they are sharing	10:20:36AM
14	Q. Was it your custom and practice at	10:17:58AM	14	with Regeneron goes down as your patents	10:20:40AM
15	Regeneron that if you thought you had an	10:18:00AM	15	expire?	10:20:44AM
16	invention, to file an invention disclosure	10:18:01AM	16	A. I would not know whether that is in	10:20:50AM
17	statement?	10:18:04AM	17	the contract or not.	10:20:53AM
18	MR. BERL: Objection.	10:18:05AM	18	Q. Let's take a look at Example 5 at	10:20:57AM
19	A. I can't speak to customary practice	10:18:08AM	19	column 14 of your '601 patent that is referring	10:21:04AM
20	at that time from this vantage point more than	10:18:12AM	20	to the DAVINCI trial. Who did the clinical	10:21:13AM
21	ten years later.	10:18:16AM	21	trial designed for the DAVINCI trial?	10:21:18AM
22	Q. Well, how did the lawyers know to	10:18:17AM	22	A. Just to be clear, I'm talking about	10:21:26AM
23	start drafting a patent application? Who told	10:18:19AM	23	the right example, the one that is labeled	10:21:28AM
24	them? Were you the one who initiated that	10:18:22AM	24	"Phase II Clinical Trial of VEGFT in Subjects	10:21:30AM
25	process?	10:18:25AM	25	with Diabetic Macular Edema?"	10:21:34AM

Page 38		Page 40	
1	Q Yes. 10:21:38AM	1	every eight weeks after three monthly loading 10:27:00AM
2	A Let me take a second here by 10:21:39AM	2	doses; is that fair? 10:27:05AM
3	refreshing my memory by reading this. (Witness 10:21:41AM	3	A Yes, both the continued monthly 10:27:07AM
4	reading document). 10:22:39AM	4	dosing EYLEA arm as well as the so-called PRN 10:27:10AM
5	I was involved in design of this 10:23:22AM	5	or dosing as needed arms numerically behaved 10:27:15AM
6	along with members of my team. 10:23:25AM	6	better than the VEGF-Trip every eight weeks 10:27:21AM
7	Q Who else on the team? 10:23:27AM	7	after the three loading doses. 10:27:28AM
8	A Once again, across so many trials 10:23:30AM	8	Q It was that data that prompted 10:27:30AM
9	across so many years, I wouldn't remember 10:23:33AM	9	Regeneron and Bayer to push for more monthly 10:27:33AM
10	specific individuals other than Neil Stahl. 10:23:35AM	10	loading doses before going to every eight week 10:27:36AM
11	Q Do you recall who made the decision 10:23:38AM	11	dosing, true? 10:27:41AM
12	to use three monthly loading doses? 10:23:40AM	12	MR. BERL: Objection. Vague. 10:27:43AM
13	MR. BERL: Objection. 10:23:51AM	13	Q In the clinical trial design for 10:27:52AM
14	A That, I don't remember. 10:24:12AM	14	Phase III DME? 10:27:54AM
15	Q Do you recall whether any of the 10:24:13AM	15	MR. BERL: Objection. 10:27:56AM
16	Lucentis DME trials used three monthly loading 10:24:15AM	16	A As I said before, there was an 10:27:57AM
17	doses before going on extended interval dosing 10:24:20AM	17	integration of a large amount of data that 10:28:01AM
18	schedule? 10:24:24AM	18	compelled us to design a Phase III trial where 10:28:09AM
19	A Lucentis trials in any-- 10:24:32AM	19	we felt we needed to have more frequent dosing 10:28:13AM
20	Q For DME. 10:24:36AM	20	for a longer period of time until we achieved 10:28:19AM
21	A For DME? That, I can't remember. 10:24:38AM	21	what we thought was a plateau, at which point 10:28:21AM
22	Q The Phase III clinical trials that 10:24:39AM	22	we thought we might be able to switch to less 10:28:25AM
23	Regeneron performed in DME wound up using five 10:24:45AM	23	frequent dosing. 10:28:28AM
24	monthly loading doses before allowing a switch 10:24:49AM	24	Q Well, is there any data that you put 10:28:31AM
25	to every eight weeks dosing. Do you recall why 10:24:53AM	25	in your '601 patent or any rationale about 10:28:34AM
Page 39		Page 41	
1	that was? 10:24:57AM	1	reaching this plateau in the context of DME's 10:28:39AM
2	A I believe after reviewing all the 10:25:14AM	2	therapy that would justify increasing the 10:28:46AM
3	data, it suggested that you continue to accrue 10:25:17AM	3	number of loading doses before switching to the 10:28:50AM
4	benefit by frequently giving injections early 10:25:22AM	4	eight week dosing? 10:28:54AM
5	on and we were trying to achieve a plateau 10:25:30AM	5	MR. BERL: Objection. Counsel, 10:28:56AM
6	stage wherein perhaps you might not need as 10:25:36AM	6	we've been going significantly more than 10:28:57AM
7	frequent dosing to maintain. 10:25:44AM	7	an hour, so if you have a breaking point 10:29:00AM
8	Q In the DAVINCI study data, the three 10:25:49AM	8	soon. 10:29:02AM
9	loading doses, 2 milligrams -- three monthly 10:25:57AM	9	MS. MAZZOCHI: Sure. 10:29:04AM
10	loading doses, 2 milligrams followed by the 10:26:00AM	10	A In my attempt to read the whole 10:29:04AM
11	2-milligram eight week dosing schedule did not 10:26:04AM	11	patent very quickly earlier, I'm not aware of 10:29:20AM
12	perform as well in terms of letter gain as the 10:26:07AM	12	seeing that data shown though it could very 10:29:25AM
13	2-milligram monthly dosing arm; is that fair? 10:26:12AM	13	well be in some of the many references that are 10:29:29AM
14	MR. BERL: Objection. 10:26:17AM	14	included. 10:29:33AM
15	A It's hard to remember the trials by 10:26:20AM	15	Q Well, if you take a look at column 10:29:35AM
16	the names. I don't see the DAVINCI name. 10:26:23AM	16	16 of the '601 patent, starting around line 23, 10:29:38AM
17	Which trial again are we referring to? 10:26:26AM	17	there is a reference to a dosing schedule of 10:29:47AM
18	Q Example 5. 10:26:29AM	18	"VEGF 2 milligrams (0.5 ml) administered by 10:29:49AM
19	A Okay. And so repeat the question, 10:26:30AM	19	intravitreal injection once every 4 weeks for 10:29:55AM
20	please, in Example 5 trial? 10:26:33AM	20	the first 20 weeks, followed by 2 milligrams 10:29:59AM
21	Q Sure. When the Example 5 DAVINCI 10:26:37AM	21	(0.05 ml) by intravitreal injection once every 10:30:03AM
22	trial data came out, the monthly dosing arm of 10:26:42AM	22	8 weeks." Do you see that? 10:30:09AM
23	2 milligrams of aflibercept performed better 10:26:48AM	23	A Yes, I do. 10:30:11AM
24	than the -- in terms of letters gave with 10:26:52AM	24	Q Was that one of the arms in the 10:30:12AM
25	visual acuity as compared to the arm that dosed 10:26:56AM	25	Phase III DME trial? 10:30:14AM

Page 42			Page 44		
1	A. Yes.	10:30:21AM	1	to review them.	10:34:09AM
2	Q. Is there anywhere in the '601 patent	10:30:24AM	2	Q. Well, when you are talking about	10:34:10AM
3	that you can identify for me that justifies	10:30:29AM	3	primary papers, are they primary papers cited	10:34:12AM
4	following that particular dosing regimen for	10:30:35AM	4	here that you referenced within your	10:34:15AM
5	DME therapy?	10:30:42AM	5	specification or are they just elsewhere in the	10:34:16AM
6	MR. BERL: Objection. Vague.	10:30:44AM	6	general literature?	10:34:19AM
7	Q. As opposed to the other various	10:30:53AM	7	A. I was referring to references that	10:34:28AM
8	doses, dosing regimens you have set forth here	10:30:55AM	8	would be cited herein.	10:34:30AM
9	in Example 7?	10:30:58AM	9	Q. Which section of the specification	10:34:32AM
10	A. Well, part of the data that was	10:31:18AM	10	are you looking at?	10:34:34AM
11	integrated to come up with this dosing regimen	10:31:21AM	11	A. The reference cited section.	10:34:35AM
12	was the very data that you just referred to	10:31:26AM	12	Q. Oh, is it -- is it your	10:34:42AM
13	that showed that a smaller number of monthly	10:31:30AM	13	understanding that this reference -- well, do	10:34:45AM
14	doses followed by an eight week regimen may not	10:31:43AM	14	you have an understanding as to what this	10:34:47AM
15	have done as well.	10:31:49AM	15	references cited section at the front of the	10:34:49AM
16	This was a very small study and one	10:31:51AM	16	patent is referring to?	10:34:52AM
17	cannot count on numerical differences in these	10:31:55AM	17	MR. BERL: Objection.	10:34:54AM
18	small studies, but that was part, a small part	10:31:59AM	18	A. It could also be referring to the	10:35:08AM
19	of all of the data that was integrated to come	10:32:02AM	19	references cited there.	10:35:10AM
20	up with the decision of which regimens to use	10:32:06AM	20	Q. Maybe we can get it this way. Is it	10:35:21AM
21	in Phase III.	10:32:11AM	21	fair to say that we can't look at the text of	10:35:23AM
22	Q. Let me see if I can rephrase it.	10:32:12AM	22	your specification today to find any other data	10:35:25AM
23	What data have you set forth in this '601	10:32:16AM	23	or instruction or rationale that would guide	10:35:33AM
24	patent that would allow someone to conclude	10:32:19AM	24	towards selecting five loading doses as opposed	10:35:36AM
25	that this particular regimen in column 16,	10:32:24AM	25	to three or four or six monthly loading doses	10:35:41AM
Page 43			Page 45		
1	lines 23 to 26, with five loading doses	10:32:29AM	1	with the PRN -- I'm sorry, with the eight week	10:35:45AM
2	followed by eight week dosing -- five monthly	10:32:34AM	2	dosing regimen for DME besides Example 5?	10:35:50AM
3	loading doses followed by eight week dosing,	10:32:37AM	3	MR. BERL: Objection. Vague.	10:35:55AM
4	would be the correct regimen to use for DME as	10:32:40AM	4	A. I would have to reread the whole	10:36:05AM
5	opposed to the various other regimens that are	10:32:47AM	5	patent right now to determine exactly what data	10:36:07AM
6	set forth here?	10:32:50AM	6	is therein and/or what data would be in any of	10:36:11AM
7	MR. BERL: Objection. Vague.	10:32:51AM	7	these many, many references that are cited	10:36:18AM
8	A. Part of the data that was used in	10:33:04AM	8	here.	10:36:20AM
9	coming up with the dosing regimen protocol that	10:33:10AM	9	Q. Well, let's try to cut to the chase	10:36:22AM
10	you referred to is reflected in Table 2 and if	10:33:15AM	10	here. Is there anything in your '601 patent	10:36:28AM
11	I can go through the references, probably	10:33:24AM	11	specifications in columns 1 through 18 that you	10:36:30AM
12	additional data is referred to therein as well.	10:33:28AM	12	believe guides someone specifically for the DME	10:36:40AM
13	Q. And which references are you talking	10:33:32AM	13	indication towards five monthly loading doses	10:36:44AM
14	about?	10:33:33AM	14	before starting the eight week dosing regimen	10:36:48AM
15	A. I would have to review the	10:33:34AM	15	as opposed to any other number of loading	10:36:51AM
16	references and have access to the papers in	10:33:35AM	16	doses?	10:36:56AM
17	order to do that.	10:33:42AM	17	MR. BERL: Objection.	10:36:57AM
18	Q. Within your specification, which	10:33:43AM	18	A. I would have to read.	10:37:02AM
19	references within the specification are you	10:33:44AM	19	Q. Go ahead.	10:37:03AM
20	talking about you need to additionally review?	10:33:47AM	20	A. One through 18?	10:37:04AM
21	MR. BERL: Objection.	10:33:51AM	21	Q. Yes.	10:37:06AM
22	A. These many years later, I can't	10:33:58AM	22	A. (Witness reading document). To	10:37:08AM
23	recall what is in any of the particular	10:34:02AM	23	summarize what I read across these 18 columns	10:45:33AM
24	individual references. I would have to	10:34:04AM	24	or so, it is that what you refer to loading we	10:45:40AM
25	actually have the primary papers in front of me	10:34:06AM	25	refer to as secondary doses in the patent that	10:45:48AM

Page 46		
1	are the number of initial doses after, initial	10:45:51AM
2	secondary doses on a monthly schedule after the	10:45:56AM
3	first dose and we state that this can vary and	10:45:59AM
4	clearly as shown in the section on the Phase	10:46:08AM
5	III trial of the AMD, the results show that for	10:46:13AM
6	AMD one needed or one could get similar results	10:46:18AM
7	with three loading doses.	10:46:30AM
8	We also see that in CRVO. We notice	10:46:33AM
9	that we say that it looks like you need six	10:46:39AM
10	monthly doses and the data in Table 2 indicated	10:46:43AM
11	that the three monthly doses that were	10:46:49AM
12	sufficient in AMD but not sufficient in CRVO	10:46:53AM
13	may not be sufficient in DME based on the data	10:46:58AM
14	that we just reviewed and that was an example	10:47:04AM
15	or examples of, as I mentioned, the integration	10:47:10AM
16	of large amounts of data, probably including a	10:47:14AM
17	lot of data that was in many of the references	10:47:20AM
18	that led us to the design in the point that you	10:47:22AM
19	just -- that you had mentioned a few minutes	10:47:27AM
20	ago in approximately line 23 in column 16.	10:47:30AM
21	Q. Right. I understand that Bayer and	10:47:34AM
22	Regeneron had a whole host of internal data.	10:47:37AM
23	I'm just focused on the data that is actually	10:47:40AM
24	disclosed within these columns 1 to 18 of your	10:47:43AM
25	'601 patent.	10:47:52AM
Page 47		
1	Can you point to me anywhere, based	10:47:55AM
2	on what you just read, that suggested that to	10:47:58AM
3	pick the timing or the number of secondary	10:48:00AM
4	doses you have to first hit a plateau before	10:48:05AM
5	you then switch to the eight week or tertiary	10:48:09AM
6	dosing regimens?	10:48:16AM
7	MR. BERL: Objection.	10:48:19AM
8	Q. When it comes to DME therapy?	10:48:19AM
9	MR. BERL: Objection.	10:48:22AM
10	Q. Did you offer that rationale in your	10:48:25AM
11	specification?	10:48:26AM
12	MR. BERL: Objection.	10:48:27AM
13	A. I can restate what I just said which	10:48:34AM
14	is that we were exploring as we specifically	10:48:37AM
15	said that there could be a different number of	10:48:41AM
16	the so-called secondary doses and in AMD it	10:48:45AM
17	looks like our regimen was very successful	10:48:52AM
18	incorporating an eight month interval after a	10:48:58AM
19	total of three so-called loading doses.	10:49:03AM
20	In Table 2 it appears that at least	10:49:09AM
21	for allowing subsequent eight week interval	10:49:13AM
22	dosing, three doses are not enough. It appears	10:49:18AM
23	that for CRVO we show data that six loading	10:49:22AM
24	doses lead to very good data and so that	10:49:29AM
25	together, with what was available in the public	10:49:36AM

Page 48		
1	literature that is cited in the reference,	10:49:40AM
2	allowed us to integrate the data to come up	10:49:42AM
3	with a proposal in line 23 of column 16.	10:49:48AM
4	MR. BERL: Counsel --	10:49:58AM
5	MS. MAZZOCHI: I want to finish this	10:49:59AM
6	out before we take a break.	10:50:00AM
7	MR. BERL: It's been more than an	10:50:02AM
8	hour and a half. It's abusive.	10:50:03AM
9	MS. MAZZOCHI: It's not responsive	10:50:06AM
10	to my question.	10:50:07AM
11	MR. BERL: I disagree.	10:50:08AM
12	Q. Listen to my question, Dr.	10:50:09AM
13	Yancopoulos so we can make sure we get this	10:50:10AM
14	correct.	10:50:13AM
15	I'm focusing on just the DME	10:50:14AM
16	clinical indication. Can you point to me	10:50:16AM
17	somewhere that says in your specification, so	10:50:24AM
18	columns 1 to 18, that says for DME you need to	10:50:28AM
19	hit a plateau with monthly dosing before you	10:50:37AM
20	can switch to dosing every eight weeks?	10:50:43AM
21	MR. BERL: Objection. Asked and	10:50:48AM
22	answered.	10:50:49AM
23	Q. I'm looking for where you gave that	10:50:50AM
24	rationale specifically in your specification.	10:50:52AM
25	MR. BERL: You don't like the answer	10:50:54AM

Page 49		
1	it doesn't mean he hasn't answered it.	10:50:56AM
2	MS. MAZZOCHI: No, for DME	10:50:58AM
3	specifically.	10:51:00AM
4	MR. BERL: You can answer.	10:51:00AM
5	A. I can give the same answer that I	10:51:01AM
6	have given already. One has to try to	10:51:04AM
7	integrate the collection of all the data. That	10:51:07AM
8	is how one tries to come up with designs for	10:51:11AM
9	clinical trials and with regimens that you, you	10:51:14AM
10	know, think your work is based on the data.	10:51:19AM
11	What we saw was that we could	10:51:23AM
12	successfully utilize a dosing regimen that	10:51:26AM
13	includes an eight week dosing interval in AMD	10:51:32AM
14	when you utilize a three dose loading schedule.	10:51:40AM
15	In Table 2 though it's preliminary Phase II	10:51:47AM
16	data suggests that you don't numerically	10:51:52AM
17	achieve as good vision. You don't get to that	10:51:56AM
18	plateau when you only utilize three loading	10:52:00AM
19	doses then followed by the eight week dosing	10:52:04AM
20	interval.	10:52:09AM
21	For a related disease, it appears	10:52:10AM
22	that you get in Example 6 very good data with	10:52:13AM
23	six loading doses. This led us to propose the	10:52:18AM
24	basics of the regimen that you referred to in	10:52:28AM
25	column 16 together with all the publicly domain	10:52:32AM

Page 50		Page 52	
1	available information in the entire field. 10:52:37AM	1	the document. 11:08:55AM
2	Q. Why select five monthly loading 10:52:41AM	2	A. (Witness reviewing document). 11:09:04AM
3	doses instead of four? 10:52:44AM	3	Q. Do you have page 30? 11:10:14AM
4	MR. BERL: Objection. 10:52:46AM	4	A. Yes. 11:10:16AM
5	Q. What in this patent tells you that 10:52:46AM	5	Q. Do you see the table with your name 11:10:16AM
6	for DME you should use five loading doses and 10:52:48AM	6	at the top? 11:10:19AM
7	not four? 10:52:52AM	7	A. Yes. 11:10:35AM
8	MR. BERL: Objection. This is 10:52:53AM	8	Q. Regeneron has identified the 11:10:37AM
9	becoming abusive. We've asked for a break 10:52:59AM	9	following fact witnesses that Regeneron may 11:10:38AM
10	three times now. It's rare to go an hour 10:53:01AM	10	call at trial, one of them being you. Do you 11:10:41AM
11	40 in a deposition. This will be the last 10:53:04AM	11	see that? 11:10:44AM
12	question and answer and then we will take 10:53:07AM	12	A. Yes. 11:10:46AM
13	a break. 10:53:09AM	13	Q. And one of the topics that Regeneron 11:10:46AM
14	A. Once again, it's the integration of 10:53:09AM	14	says you have information on is "irreparable 11:10:50AM
15	all the data that I refer to that led to that 10:53:12AM	15	harm to Regeneron and damages that would result 11:10:53AM
16	proposal. 10:53:17AM	16	from Mylan's infringement of Regeneron's 11:10:56AM
17	Q. Move to strike as nonresponsive. We 10:53:21AM	17	patents." Do you see that? 11:10:59AM
18	can take our break. 10:53:23AM	18	A. Yes. 11:11:20AM
19	THE VIDEOGRAPHER: We are going off 10:53:25AM	19	Q. What damages do you contend 11:11:21AM
20	the record at 10:53 a.m. 10:53:26AM	20	Regeneron will experience if Mylan is found to 11:11:22AM
21	(Brief recess taken.) 10:53:29AM	21	infringe Regeneron's patents in whole or in 11:11:26AM
22	THE VIDEOGRAPHER: We are back on 11:07:41AM	22	part? 11:11:30AM
23	the record at 11:07 a.m. 11:07:42AM	23	MR. BERL: Objection. Calls for a 11:11:31AM
24	BY MS. MAZZOCHI: 11:07:42AM	24	legal conclusion. 11:11:33AM
25	Q. Dr. Yancopoulos, did you discuss 11:07:44AM	25	A. I haven't specifically thought about 11:12:53AM
Page 51		Page 53	
1	your testimony with counsel over the break? 11:07:45AM	1	the specifics of what these damages would be. 11:13:00AM
2	A. No. 11:07:48AM	2	Q. How about generally? 11:13:04AM
3	Q. I put before you a document that I 11:07:49AM	3	A. As the head of research and 11:13:18AM
4	have marked as Defendant's Exhibit 900 titled 11:07:51AM	4	development, I would think that I would be 11:13:21AM
5	"Regeneron Pharmaceuticals, Inc.'s Objections 11:07:54AM	5	testifying to the impact or damages to our 11:13:26AM
6	and Responses to Defendant's First Set of 11:07:57AM	6	ability to carry out or decrease our efforts in 11:13:32AM
7	Interrogatories (NOS. 1-17)." 11:08:01AM	7	carrying out research and development for new 11:13:39AM
8	(Whereupon document was marked 11:08:03AM	8	medicines. 11:13:42AM
9	Exhibit 900 for identification as of this 11:08:03AM	9	Q. Has Regeneron prepared any documents 11:13:44AM
10	date.) 11:08:03AM	10	that you've seen suggesting that it's going to 11:13:47AM
11	Q. Can you confirm you have that in 11:08:05AM	11	cut back on its R&D expenditures in any 11:13:51AM
12	front of you? 11:08:07AM	12	category if Mylan gets on the market? 11:13:54AM
13	A. Yes. 11:08:07AM	13	MR. BERL: Objection. 11:13:59AM
14	Q. Can you turn to page 30 within the 11:08:09AM	14	A. Can you repeat the question? 11:14:04AM
15	document, page 30? 11:08:11AM	15	Q. Sure. Have you seen any documents 11:14:05AM
16	A. I was just looking at the document. 11:08:17AM	16	prepared at Regeneron suggesting that it's 11:14:07AM
17	Q. Dr. Yancopoulos, can you please turn 11:08:40AM	17	going to cut back on its R&D expenditures in 11:14:10AM
18	to page 30 of the document? 11:08:42AM	18	any category if Mylan gets on the market? 11:14:14AM
19	A. I'm just familiarizing myself with 11:08:43AM	19	A. I have not seen any such documents. 11:14:17AM
20	the document. 11:08:45AM	20	Q. Have you personally had any 11:14:23AM
21	Q. I don't need you to familiarize 11:08:46AM	21	conversations with your CEO about your research 11:14:24AM
22	yourself with the entire document. I just want 11:08:47AM	22	budget is going to get cut if Mylan enters the 11:14:28AM
23	to direct your attention to some text that 11:08:50AM	23	market? 11:14:32AM
24	appears on page 30. 11:08:52AM	24	A. No, I have not. 11:14:35AM
25	MR. BERL: Counsel, he can look at 11:08:53AM	25	Q. I'm going to put before you a 11:14:39AM

Page 54		Page 56	
1	document that I've marked as Defendant's 11:14:40AM	1	A. I'm turning to a specific page? 11:17:35AM
2	Exhibit 901, which has production numbers 11:14:44AM	2	Q. Yes, 487480. Do you have 487480? 11:17:37AM
3	RGN-EYLEA-MYLAN-00487461 through 487503. 11:14:47AM	3	A. I'm just familiarizing myself with 11:18:07AM
4	MR. BERL: I thought the last one 11:14:59AM	4	this to see if I -- (Witness reviewing 11:18:09AM
5	was 901. 11:15:00AM	5	document.) 11:18:10AM
6	Q. Just to be clear, the 11:15:07AM	6	Q. There you go. Do you see on this 11:18:52AM
7	interrogatories are 900. This one is 901. 11:15:08AM	7	page, it's titled "EYLEA Competitive Landscape 11:18:53AM
8	MR. BERL: You identified them as 11:15:12AM	8	Review: Emerging Near-Term Competitors?" 11:18:57AM
9	901 on the record. 11:15:13AM	9	A. Yes. 11:19:01AM
10	MS. MAZZOCHI: I apologize. The 11:15:14AM	10	MR. BERL: Objection. 11:19:01AM
11	interrogatories was 900. 11:15:16AM	11	Q. The individual listed here is Omar 11:19:02AM
12	(Whereupon document was marked 11:15:18AM	12	Gaya. Do you know who he is? 11:19:03AM
13	Exhibit 901 for identification as of this 11:15:18AM	13	A. Yes, I know Omar Gaya. 11:19:07AM
14	date.) 11:15:18AM	14	Q. What has been your interactions with 11:19:11AM
15	Q. In the interrogatories one of the 11:15:23AM	15	him at Regeneron? 11:19:13AM
16	other items that you identified as having 11:15:25AM	16	MR. BERL: Objection. 11:19:15AM
17	knowledge of is irreparable harm to Regeneron 11:15:27AM	17	A. I know he is somebody who works at 11:19:25AM
18	that would result from Mylan's infringement of 11:15:31AM	18	Regeneron, but not in my line of reporting. 11:19:28AM
19	Regeneron's patents. 11:15:34AM	19	Q. Well, in connection with providing 11:19:32AM
20	Are you aware that Regeneron's 11:15:39AM	20	any testimony regarding damages or irreparable 11:19:33AM
21	commercial group has looked at this question of 11:15:42AM	21	harm, do you have any information about what 11:19:38AM
22	what might happen if some biosimilars come into 11:15:47AM	22	Regeneron has done to assess how its business 11:19:41AM
23	the market? 11:15:50AM	23	operations might be impacted by any emerging 11:19:45AM
24	A. I don't recollect being aware of 11:16:06AM	24	near-term competitors? 11:19:49AM
25	these things, but it would not surprise me that 11:16:08AM	25	MR. BERL: Objection. 11:19:51AM
Page 55		Page 57	
1	they had done this work. 11:16:10AM	1	A. Can you repeat the question? 11:20:01AM
2	Q. If you take a look at DX901, can you 11:16:12AM	2	MS. MAZZOCHI: Can you read it back? 11:20:04AM
3	confirm that it's an e-mail dated June 12, 2018 11:16:15AM	3	(Whereupon the record was read back 11:20:25AM
4	from John Magliocchetti to Karen Chu and 11:16:19AM	4	by the reporter.) 11:20:25AM
5	others? 11:16:23AM	5	MR. BERL: Objection. 11:20:26AM
6	A. I can confirm that is what it says 11:16:27AM	6	A. I'm sorry, could you read that 11:20:29AM
7	on the document. 11:16:29AM	7	again? 11:20:30AM
8	Q. There is a reference to the 11:16:31AM	8	(Whereupon the record was read back 11:20:30AM
9	"Regeneron LCM Commercial Perspective." Do you 11:16:32AM	9	by the reporter.) 11:20:57AM
10	know what LCM refers to? 11:16:37AM	10	A. Do I have what? 11:20:58AM
11	MR. BERL: Objection. Lack of 11:16:41AM	11	Q. Any information about what Regeneron 11:20:59AM
12	foundation. 11:16:42AM	12	has done to assess the impact that any emerging 11:21:02AM
13	A. No, I don't know what LCM stands 11:16:55AM	13	near-term competitors might have on its 11:21:05AM
14	for. 11:16:59AM	14	business operations? 11:21:08AM
15	Q. Do you know who John Magliocchetti 11:16:59AM	15	MR. BERL: Objection. That's a 11:21:09AM
16	is? 11:17:00AM	16	different question. Not even a complete 11:21:10AM
17	A. Yes, I know who John Magliocchetti 11:17:01AM	17	one. 11:21:17AM
18	is. 11:17:02AM	18	A. I am sure that Regeneron has done 11:21:22AM
19	Q. Who is he? 11:17:04AM	19	some sort of analyses. I'm not familiar with 11:21:24AM
20	A. He is somebody who worked or 11:17:07AM	20	information about it. 11:21:29AM
21	works -- I don't know if he is still working at 11:17:10AM	21	Q. If you can take a look at the next 11:21:31AM
22	Regeneron. I don't know his specific capacity. 11:17:13AM	22	page of Exhibit 901, which is 487481, one of 11:21:33AM
23	Q. If you could take a look at page 11:17:21AM	23	the emerging near-term competitors identified 11:21:42AM
24	within this document, page RGN-ELYEA-MYLAN 11:17:24AM	24	is "Biosimilar Lucentis & EYLEA." Do you see 11:21:46AM
25	487480. 11:17:28AM	25	that? 11:21:50AM

Page 58

1 MR. BERL: Objection. Lack of 11:21:50AM
2 foundation. 11:21:51AM
3 A. I see it. 11:21:52AM
4 Q. Has a biosimilar Lucentis come on 11:21:52AM
5 the market to your knowledge? 11:21:56AM
6 A. Following biosimilar launches is not 11:21:59AM
7 within my area of expertise, but I believe that 11:22:14AM
8 I have heard that a Lucentis biosimilar has. 11:22:17AM
9 Q. Did your R&D budget change at all as 11:22:21AM
10 a consequence of a biosimilar Lucentis coming 11:22:23AM
11 on the market? 11:22:32AM
12 MR. BERL: Objection. Lack of 11:22:33AM
13 foundation. 11:22:34AM
14 A. No. 11:22:35AM
15 Q. Did you change any of your R&D 11:22:38AM
16 strategies as a consequence of a Lucentis 11:22:41AM
17 biosimilar coming on the market? 11:22:44AM
18 MR. BERL: Objection. Lack of 11:22:47AM
19 foundation. 11:22:48AM
20 A. No. 11:22:55AM
21 Q. Do you plan to change any of your 11:22:56AM
22 existing R&D strategies if an EYLEA biosimilar 11:22:58AM
23 comes on the market? 11:23:04AM
24 MR. BERL: Objection. Vague. 11:23:06AM
25 A. It would depend on other people in 11:23:48AM

Page 59

1 the company's assessment of how that might 11:23:52AM
2 impact our ability to have or support our R&D 11:23:55AM
3 budget. 11:24:04AM
4 Q. Who are those other people that you 11:24:05AM
5 are referring to? 11:24:07AM
6 A. Most notably our chief financial 11:24:19AM
7 officer, Bob Landry, in association with our 11:24:22AM
8 CEO, Len Schleifer, integrating presumably 11:24:26AM
9 information that they get from others. 11:24:31AM
10 Q. If you can take a look at page 11:24:33AM
11 487482 in Defendant's Exhibit 901? 11:24:35AM
12 A. Yes. 11:24:41AM
13 Q. This is back in 2018 there were 11:24:44AM
14 several competitive launches expected in the 11:24:47AM
15 next five years and it goes out through 2023. 11:24:50AM
16 Did any of these competitive launches listed 11:24:54AM
17 here change your R&D budget or strategies? 11:24:58AM
18 MR. BERL: Objection. Lack of 11:25:07AM
19 foundation. 11:25:08AM
20 A. I can't say whether they changed our 11:26:07AM
21 R&D strategy, but the constant threat of other 11:26:12AM
22 medicines for treating the same diseases as 11:26:21AM
23 EYLEA was treating, which always exists in our 11:26:28AM
24 world, is part of our constant drive to try to 11:26:36AM
25 come up and improve on the medicines that we 11:26:45AM

Page 60

1 can offer patients. 11:26:50AM
2 Q. Are there any clinical trials in the 11:26:53AM
3 eye disease field involving VEGF inhibitors 11:27:02AM
4 that you plan on calling off if Mylan enters 11:27:08AM
5 the market? 11:27:13AM
6 MR. BERL: Objection. Vague. 11:27:14AM
7 A. That would depend how -- on how 11:27:44AM
8 Mylan entering the market would be impacting 11:27:49AM
9 our overall budget. 11:27:53AM
10 Q. How do you anticipate Mylan entering 11:28:00AM
11 the market might impact your overall budget? 11:28:03AM
12 MR. BERL: Objection. 11:28:07AM
13 A. As head of research and development, 11:28:20AM
14 I don't generally concern myself with those 11:28:22AM
15 things though if the company had decreased 11:28:26AM
16 revenues, then we would have in my world less 11:28:37AM
17 of a budget to be able to spend on doing our 11:28:44AM
18 research and development overall in our 11:28:47AM
19 attempts to discover and develop new medicines 11:28:51AM
20 for all sorts of diseases. 11:28:58AM
21 Q. But that would be true as well if, 11:29:00AM
22 for example, Novartis or Roche came into the 11:29:02AM
23 market with a competitor product to EYLEA, 11:29:07AM
24 right? 11:29:11AM
25 MR. BERL: Objection. 11:29:12AM

Page 61

1 Q. And took some of your revenues? 11:29:13AM
2 MR. BERL: Vague. 11:29:16AM
3 A. Well, history shows the difficulty 11:29:53AM
4 in general in our industry and in this field in 11:29:56AM
5 particular, is coming up with something new 11:30:02AM
6 that can replace the existing standard is very 11:30:07AM
7 rare. 11:30:16AM
8 Most of these new medicines that are 11:30:20AM
9 listed on this slide in various ways failed and 11:30:22AM
10 actually the rate of success of a biosimilar, 11:30:37AM
11 since it's just a copy or a me too to achieve 11:30:41AM
12 its objective makes it a very different kind of 11:30:49AM
13 concern than an entirely new medicine that is 11:30:59AM
14 trying to improve on the state of the art of 11:31:03AM
15 treating patients. 11:31:07AM

Regeneron Protected Material

Page 62 Regeneron Protected Material	Page 64 Regeneron Protected Material 14 Q. Is it fair to say that the main 11:36:52AM 15 concern that Regeneron has with a Mylan 11:36:56AM 16 biosimilar coming on the market is that the 11:36:59AM 17 Mylan aflibercept biosimilar would be cheaper 11:37:02AM 18 than EYLEA? 11:37:07AM 19 MR. BERL: Objection. Lack of 11:37:09AM 20 foundation. 11:37:11AM 21 A. I don't know if that would be my 11:37:37AM 22 major concern. 11:37:38AM 23 Q. Do you understand if that is 11:37:40AM 24 Regeneron's major concern? 11:37:42AM 25 MR. BERL: Objection. Lack of 11:37:44AM
Regeneron Protected Material	Page 65 1 foundation. 11:37:45AM 2 A. I don't know if that's the major 11:37:49AM 3 concern of any particular individual at 11:37:52AM 4 Regeneron. 11:37:54AM 5 Q. If a Mylan biosimilar comes on the 11:37:58AM 6 market, do you plan on firing any of your 11:38:00AM 7 scientists who work in your R&D division? 11:38:02AM 8 MR. BERL: Objection. Lack of 11:38:06AM 9 foundation. 11:38:07AM 10 A. I don't plan on firing anyone, but I 11:38:13AM 11 could imagine if there was substantial losses 11:38:16AM 12 in revenue from EYLEA, that could have 11:38:19AM 13 budgetary impacts on our organization. 11:38:25AM 14 Q. But those would be monetary impacts, 11:38:32AM 15 right? 11:38:34AM 16 MR. BERL: Objection. Vague. 11:38:35AM 17 A. Budgetary impacts could have many 11:38:51AM 18 implications beyond just the money. 11:38:57AM 19 Q. Maybe I can get at it this way. The 11:39:07AM 20 fundamental concern that Regeneron has is that 11:39:09AM 21 if a Mylan biosimilar comes on the market, it 11:39:12AM 22 is going to lose revenue, right? 11:39:15AM 23 MR. BERL: Objection. Lack of 11:39:19AM 24 foundation. 11:39:20AM 25 A. Can you repeat that question? 11:39:20AM

17 (Pages 62 - 65)

Page 66			Page 68		
1	Q. Yes, the major concern that	11:39:22AM	1	A. As head of R&D, that is not	11:42:35AM
2	Regeneron has about a Mylan biosimilar coming	11:39:24AM	2	something that is really in my purview or	11:42:37AM
3	on the market is that it will lose sales	11:39:27AM	3	thinking.	11:42:40AM
4	revenue?	11:39:29AM	4	Q. Are you aware of any conversations	11:42:41AM
5	MR. BERL: Objection. Lack of	11:39:30AM	5	that have been had that payers might decide to	11:42:43AM
6	foundation.	11:39:32AM	6	change their reimbursement strategies with	11:42:46AM
7	A. Well, I think that there is many	11:39:37AM	7	Regeneron if a Mylan biosimilar comes on the	11:42:49AM
8	individuals at Regeneron and we share many	11:39:39AM	8	market?	11:42:52AM
9	concerns. From my perspective, as I'm most	11:39:41AM	9	MR. BERL: Lack of foundation.	11:42:53AM
10	focused on the research, the scientists and	11:39:47AM	10	A. Once again, not my area of	11:42:59AM
11	patient treatment, having seen the great	11:39:51AM	11	expertise.	11:43:00AM
12	challenges in the field with safely delivering	11:39:59AM	12	Q. I'm going to mark as Defendant's	11:43:04AM
13	medicines to the eye, one major concern that I	11:40:06AM	13	Exhibit 902 a document with production numbers	11:43:06AM
14	would have is whether biosimilars in this field	11:40:10AM	14	RGN-ELYEA-MYLAN-54862 to 63.	11:43:11AM
15	could really be produced safely and not result	11:40:21AM	15	(Whereupon document was marked	11:43:18AM
16	in some of the horrific tragedies that we've	11:40:25AM	16	Exhibit 902 for identification as of this	11:43:18AM
17	seen with some of the agents listed on this	11:40:30AM	17	date.)	11:43:18AM
18	page that have resulted in patients needlessly	11:40:33AM	18	Q. Can you confirm that this is an	11:43:25AM
19	going blind and losing their vision.	11:40:37AM	19	e-mail sent to you and others from Benjamin	11:43:29AM
20	So that would be one major concern	11:40:40AM	20	Drosman on May 19, 2016?	11:43:32AM
21	that I and many others at Regeneron would have.	11:40:42AM	21	A. On this page it says that it's from	11:43:39AM
22	I would believe that others would have other	11:40:47AM	22	Benjamin Drosman to a number of individuals and	11:43:42AM
23	concerns.	11:40:49AM	23	I'm included on the e-mail, yes.	11:43:46AM
24	Q. If a biosimilar or other branded	11:40:51AM	24	Q. Do you know who Benjamin Drosman	11:43:49AM
25	product comes on the market and it can't be	11:40:54AM	25	was?	11:43:52AM
Page 67			Page 69		
1	produced safely that's not going to harm	11:40:58AM	1	A. Yes.	11:43:53AM
2	Regeneron, frankly that would probably benefit	11:41:02AM	2	Q. Who is he?	11:43:53AM
3	Regeneron, wouldn't it?	11:41:04AM	3	A. He is in our regulatory department	11:43:54AM
4	MR. BERL: Objection.	11:41:06AM	4	and is majorly involved in our regulatory	11:43:57AM
5	A. Regeneron's mission has been from	11:41:18AM	5	interactions with the FDA and other agencies.	11:44:03AM
6	the beginning to use science to bring medicines	11:41:20AM	6	Q. Other individuals who are cc'd on	11:44:06AM
7	and help patients and I think any disaster, no	11:41:22AM	7	this e-mail includes Len Schleifer, your CEO?	11:44:08AM
8	matter how indirectly linked to what we do	11:41:31AM	8	A. Yes.	11:44:13AM
9	would be tragic and a disaster and horrible for	11:41:36AM	9	Q. Another one is Murray Goldberg. Was	11:44:13AM
10	the patients that we devote our lives to.	11:41:43AM	10	he the CFO at the time?	11:44:15AM
11	So I would certainly not say that	11:41:46AM	11	A. I don't remember exactly when he	11:44:21AM
12	the only problems would be, you know, those you	11:41:50AM	12	retired, but if he's on the e-mail, I assume he	11:44:22AM
13	describe.	11:41:54AM	13	was still our CFO.	11:44:25AM
14	Q. Has Regeneron suggested they will	11:41:55AM	14	Q. And Neil Stahl. What was his role	11:44:27AM
15	end their EYLEA-4U program if the Mylan	11:41:57AM	15	at the time?	11:44:34AM
16	biosimilar enters the market?	11:42:03AM	16	A. He was head of what we call	11:44:37AM
17	MR. BERL: Objection. Lack of	11:42:06AM	17	preclinical development.	11:44:39AM
18	foundation.	11:42:07AM	18	Q. What was Peter Powchik's role at the	11:44:41AM
19	A. I know nothing about that.	11:42:08AM	19	time?	11:44:43AM
20	Q. Has Regeneron suggested that they	11:42:10AM	20	A. He would have been head of our	11:44:56AM
21	will reduce donations to any funds that support	11:42:11AM	21	clinical development.	11:44:57AM
22	patient access to drug products if a Mylan	11:42:18AM	22	Q. And what was Robert Terifay's role	11:45:00AM
23	biosimilar comes on the market?	11:42:25AM	23	at the time?	11:45:02AM
24	MR. BERL: Objection. Lack of	11:42:27AM	24	A. I can't remember when various people	11:45:20AM
25	foundation.	11:42:28AM	25	left Regeneron or not, but if he's listed here,	11:45:23AM

Page 70		Page 72	
1	he would have been head of commercial. 11:45:25AM	1	their patients needed monthly EYLEA doses 11:52:09AM
2	Q. So there were some pretty heavy 11:45:29AM	2	beyond the three monthly loading doses had 11:52:12AM
3	players within the corporate structure on this 11:45:30AM	3	merit? 11:52:15AM
4	e-mail that Mr. Drosman was communicating with; 11:45:33AM	4	MR. BERL: Objection. 11:52:16AM
5	is that fair? 11:45:36AM	5	A. It was very difficult in prospective 11:52:36AM
6	A. A number of senior individuals at 11:45:41AM	6	studies to definitively demonstrate in the 11:53:08AM
7	the company, yes. 11:45:43AM	7	general population that four week dosing was 11:53:13AM
8	Q. Now, according to what Mr. Drosman 11:45:48AM	8	better than eight week dosing though I could 11:53:23AM
9	indicated here in the e-mail, payers were 11:45:50AM	9	believe that physicians thought that they could 11:53:26AM
10	denying patients reimbursement for EYLEA Q4 11:45:54AM	10	identify some patients who would benefit from 11:53:31AM
11	treatment when needed, right? 11:45:59AM	11	monthly dosing. 11:53:35AM
12	A. Can I have a moment to just read 11:46:06AM	12	Q. Well, did you ever investigate why 11:53:37AM
13	this? 11:46:07AM	13	your three monthly loading doses followed by Q8 11:53:40AM
14	Q. Sure. 11:46:08AM	14	dosing didn't work for these patients? 11:53:45AM
15	A. (Witness reading document). Okay. 11:46:10AM	15	MR. BERL: Objection, lack of 11:53:49AM
16	Q. So do you recall the situation where 11:48:46AM	16	foundation. 11:53:50AM
17	patients were being denied EYLEA monthly 11:48:48AM	17	A. We did some retrospective analyses 11:54:05AM
18	treatments when needed and prescribers were 11:48:51AM	18	to try to identify the types of patients who 11:54:08AM
19	being denied payments for monthly 11:48:54AM	19	perhaps might need more frequent dosing. 11:54:14AM
20	administration of EYLEA? 11:48:56AM	20	Q. What did you discover? 11:54:18AM
21	A. Yes, I recall this issue. 11:48:59AM	21	A. We came up with some retrospective 11:54:28AM
22	Q. One of the things that Regeneron did 11:49:02AM	22	evidence that suggested that maybe there were 11:54:33AM
23	in response to this was to change its FDA 11:49:05AM	23	some patients, but we never definitively proved 11:54:36AM
24	approved labeling for wet AMD. Do you recall 11:49:09AM	24	it in a prospective fashion in clinical trials. 11:54:43AM
25	that? 11:49:15AM	25	Q. So can a doctor say in advance 11:54:50AM
Page 71		Page 73	
1	A. I recall, as indicated on this 11:49:55AM	1	whether this three month loading dose followed 11:54:53AM
2	document, that we prepared a labeling 11:49:59AM	2	by every eight week dosing is or isn't going to 11:54:56AM
3	submission to be submitted to the FDA for the 11:50:03AM	3	work for a particular patient? 11:54:59AM
4	FDA to allow a change in the label. 11:50:09AM	4	MR. BERL: Objection. 11:55:03AM
5	Q. Is that something you were 11:50:13AM	5	Q. With aflibercept? 11:55:09AM
6	substantively involved in or you were just 11:50:14AM	6	MR. BERL: Objection. Lack of 11:55:16AM
7	being kept in the loop as a courtesy? 11:50:17AM	7	foundation. 11:55:27AM
8	A. It's hard to define the word 11:50:42AM	8	A. I think the clinical trial results 11:55:49AM
9	substantively in a very clear way. 11:50:46AM	9	show the definitive data for the overall 11:55:51AM
10	Q. Well, did you have any actual input 11:50:56AM	10	population and the average patient, but we all 11:55:55AM
11	into the initiation of a dosing indication 11:51:00AM	11	know that individual results for almost any 11:56:00AM
12	change with the FDA or was that something being 11:51:08AM	12	drug for any disease vary for each individual. 11:56:05AM
13	driven by commercial and regulatory? 11:51:12AM	13	Q. Why was it important to Regeneron to 11:56:13AM
14	MR. BERL: Objection. 11:51:15AM	14	change its package insert to add instructions 11:56:16AM
15	A. I was aware that some physicians 11:51:28AM	15	for monthly dosing? 11:56:22AM
16	felt that some of their patients needed monthly 11:51:31AM	16	MR. BERL: Objection. 11:56:30AM
17	dosing after the first twelve weeks and they 11:51:34AM	17	Q. So that doctors could get 11:56:31AM
18	were being denied coverage for it and that we 11:51:38AM	18	reimbursed? 11:56:33AM
19	needed to try to come up with a solution so we 11:51:42AM	19	MR. BERL: Objection. 11:56:35AM
20	could get these patients who needed monthly 11:51:47AM	20	A. I think as described in this 11:56:51AM
21	dosing insurance coverage so that they would 11:51:52AM	21	document, patients were being denied monthly 11:56:53AM
22	not be denied treatment that their physicians 11:51:57AM	22	treatment when their physicians believe that 11:56:57AM
23	thought that they needed. 11:52:00AM	23	they needed monthly treatment and this was 11:57:02AM
24	Q. Well, scientifically did you think 11:52:01AM	24	being denied by insurance companies and they 11:57:08AM
25	that what these physicians are saying is that 11:52:06AM	25	were pointing to the language in the 11:57:12AM

Page 74		Page 76	
1	prescribing label to justify why they were	11:57:16AM	1 of this date.) 12:02:05PM
2	denying insurance coverage for these patients	11:57:20AM	2 Q. If you take a look at the dosage in 12:02:33PM
3	despite their physicians' recommendations and	11:57:24AM	3 administration section on the front page of 12:02:38PM
4	we were trying to be responsive to this need	11:57:27AM	4 Defendant's Exhibit 904, which is stated as 12:02:40PM
5	that physicians felt that they needed to do	11:57:31AM	5 having been revised in May of 2016, can you 12:02:46PM
6	this for some of their patients and their	11:57:35AM	6 confirm that the new language added for the AMD 12:02:50PM
7	patients were not being covered by insurance.	11:57:37AM	7 designation is "Some patients may need every 4 12:02:57PM
8	They were being denied.	11:57:44AM	8 week (monthly) dosing after the first 12 weeks 12:03:02PM
9	Q. So the insurance companies were	11:57:45AM	9 (3 months)?" 12:03:09PM
10	construing monthly dosing with EYLEA as an off	11:57:47AM	10 MR. BERL: Objection. 12:03:17PM
11	label use for AMD and DME?	11:57:50AM	11 A. (Witness reviewing document). What 12:03:44PM
12	MR. BERL: Objection. Lack of	11:57:53AM	12 was the question again? 12:03:54PM
13	foundation.	11:57:55AM	13 Q. Can you confirm that the new 12:03:56PM
14	A. Insurance companies are frequently	11:58:55AM	14 language added to the AMD Dosage and 12:03:59PM
15	looking for reasons to deny insurance coverage	11:59:00AM	15 Administration section of the labeled revised 12:04:04PM
16	for patients and they based their decisions to	11:59:05AM	16 May of 2016 was the instruction "Some patients 12:04:07PM
17	deny insurance coverage for some patients based	11:59:17AM	17 may need every 4 week (monthly) dosing after 12:04:13PM
18	on the language in the label and that motivated	11:59:20AM	18 the first 12 weeks (3 months)?" 12:04:18PM
19	us to try to change the language so that	11:59:27AM	19 A. No, that was not the only changes in 12:04:24PM
20	insurers could not deny insurance coverage to	11:59:31AM	20 this section. 12:04:26PM
21	their patients whose doctors felt might go	11:59:36AM	21 Q. Was that language added? 12:04:28PM
22	blind if they weren't given this treatment.	11:59:42AM	22 A. Well, let me read the section that 12:04:34PM
23	Q. On a monthly basis?	11:59:45AM	23 was altered. It says "Although EYLEA may be 12:04:37PM
24	A. On the basis that the doctor was	11:59:49AM	24 dosed as frequently as 2 milligrams every 4 12:04:41PM
25	recommending.	11:59:51AM	25 weeks (monthly), additional efficacy was not 12:04:45PM
Page 75		Page 77	
1	Q. So Regeneron added to their dosing	11:59:53AM	1 demonstrated in most patients when EYLEA was 12:04:48PM
2	and indication labeling quote, "Some patients	11:59:58AM	2 dosed every 4 weeks compared to every 8 weeks. 12:04:51PM
3	may need monthly dosing after the first twelve	12:00:02PM	3 Some patients may need every 4 week (monthly) 12:04:55PM
4	weeks," right?	12:00:06PM	4 dosing after the first 12 weeks (3 months)." 12:04:58PM
5	A. What the last two sentences in this	12:00:37PM	5 Q. And this added language in the 12:05:04PM
6	consensus wording based on language proposed by	12:00:39PM	6 May 2016 label for AMD that we see in DX904 12:05:07PM
7	the FDA was "Although EYLEA may be dosed as	12:00:41PM	7 gave prescribers more flexibility to prescribe 12:05:12PM
8	frequently as 2 milligrams every 4 weeks	12:00:45PM	8 EYLEA monthly for their patients and get 12:05:18PM
9	(monthly), additional efficacy was not	12:00:49PM	9 reimbursed; is that fair? 12:05:22PM
10	demonstrated in most patients when EYLEA was	12:00:53PM	10 MR. BERL: Objection. Lack of 12:05:25PM
11	dosed every 4 weeks as compared to every 8	12:00:57PM	11 foundation. 12:05:29PM
12	weeks. [See Clinical Studies (14.1)]. Some	12:01:00PM	12 A. Well, summarized in this document 12:05:43PM
13	patients may need monthly dosing after the	12:01:04PM	13 that you gave me, the reason for the change in 12:05:46PM
14	first twelve weeks."	12:01:07PM	14 language was because patients were being denied 12:05:51PM
15	I don't know if this is the final	12:01:11PM	15 by their insurance companies coverage for their 12:05:56PM
16	wording in the label, but that was the wording	12:01:12PM	16 physician recommended treatment and in order to 12:06:01PM
17	based on language proposed by the FDA according	12:01:15PM	17 not have a reason in the label that the 12:06:14PM
18	to this document.	12:01:18PM	18 insurance companies could use to deny paying 12:06:20PM
19	Q. Well, let me give you — just so you	12:01:19PM	19 for the medicine for the patients, this 12:06:25PM
20	can confirm it, what I will mark as	12:01:21PM	20 language, which according to this document was 12:06:33PM
21	Exhibit 903, which has production numbers	12:01:24PM	21 proposed by the FDA, was utilized to change the 12:06:38PM
22	MYL-AFL5190 through 5215, and 904 which has	12:01:31PM	22 label. 12:06:44PM
23	production numbers MYL-AFL5216 through 5241.	12:01:39PM	23 Q. Right, and if physicians knew that 12:06:46PM
24	(Whereupon documents were marked	12:02:05PM	24 they could not get reimbursed for dosing EYLEA 12:06:49PM
25	Exhibits 903 and 904 for identification as	12:02:05PM	25 monthly in those patients, that increased the 12:06:55PM

Page 78	Page 80
1 risk they might switch to some other product 12:06:58PM 2 where they could get reimbursement for their 12:07:01PM 3 patients, right? 12:07:04PM 4 MR. BERL: Objection. Lack of 12:07:05PM 5 foundation. 12:07:06PM 6 A. That question is so hypothetical and 12:07:19PM 7 outside the bounds of what we have been 12:07:22PM 8 discussing that I don't even know how to answer 12:07:24PM 9 that. 12:07:25PM 10 Q. Well, didn't this change to the 12:07:27PM 11 label that we see in DX904 for AMD and a 12:07:29PM 12 similar one that is made for DME make it easier 12:07:35PM 13 for doctors to get reimbursed for prescribing 12:07:39PM 14 EYLEA on a monthly dosing basis after the three 12:07:44PM 15 and five month loading dose periods for AMD and 12:07:52PM 16 DME? 12:07:56PM 17 A. It specifically was designed and 12:08:01PM 18 seemed to allow for patients who were being 12:08:03PM 19 denied their physician recommended treatment to 12:08:07PM 20 actually get insurance coverage for these 12:08:13PM 21 treatments that they were being denied. 12:08:18PM 22 Q. And the treatment they were being 12:08:20PM 23 denied was monthly dosing? 12:08:21PM 24 MR. BERL: Objection. 12:08:25PM 25 Q. So this change to the label made it 12:08:27PM	1 this language from the FDA that would allow for 12:09:46PM 2 monthly dosing in wet AMD and DME beyond the 12:09:51PM 3 loading dose period? 12:09:59PM 4 MR. BERL: Objection. Lack of 12:10:02PM 5 foundation. Vague. 12:10:03PM 6 A. I think I have answered this. It's 12:10:05PM 7 because patients were being denied insurance 12:10:07PM 8 coverage for their physician recommended 12:10:13PM 9 treatment and so we had a discussion in the FDA 12:10:15PM 10 proposed language that would not allow the 12:10:22PM 11 insurance companies to deny coverage to the 12:10:25PM 12 patients for their physician recommended 12:10:30PM 13 treatments. 12:10:33PM 14 Q. Which was monthly dosing? 12:10:34PM 15 MR. BERL: Objection. 12:10:38PM 16 A. I can read this again. "This 12:10:41PM 17 communication is in follow-up to the pair issue 12:10:45PM 18 whereby patients are being denied EYLEA Q4 12:10:48PM 19 treatment when needed. For Q4 administrations, 12:10:51PM 20 the ophthalmology team was tasked with 12:10:55PM 21 discussing a proposal with the FDA to clarify 12:11:01PM 22 wording in the EYLEA Dosing Administration 12:11:02PM 23 section of the US package insert." 12:11:06PM 24 Q. Do you agree that the language added 12:11:10PM 25 in DX904 to the AMD and DME indications allows 12:11:13PM
Page 79	Page 81
1 easier for patients to get insurance coverage 12:08:29PM 2 for doctors dosing EYLEA monthly for AMD and 12:08:32PM 3 DME, right? 12:08:36PM 4 MR. BERL: Objection. Lack of 12:08:38PM 5 foundation. 12:08:40PM 6 A. Well, you're restating it in other 12:08:41PM 7 words, which I don't know why there is a need 12:08:44PM 8 to do it because it specifically is in this 12:08:46PM 9 document. It was a FDA proposed language to 12:08:48PM 10 address the issues that patients were being 12:08:53PM 11 denied insurance coverage for their physician 12:08:57PM 12 recommended treatment. So that is exactly what 12:09:02PM 13 it was and I don't see the need for trying to 12:09:06PM 14 say it in other words. 12:09:09PM 15 Q. Well, because to be clear, the 12:09:11PM 16 physician recommended treatment that the 12:09:13PM 17 patients wanted reimbursement for was dosing 12:09:15PM 18 them with EYLEA monthly beyond the loading dose 12:09:18PM 19 phases, right? 12:09:22PM 20 A. I think the language that I read 12:09:25PM 21 directly from this document is clearer than how 12:09:27PM 22 you are rephrasing it. So I rather just stick 12:09:30PM 23 to the language that is clear cut and in the 12:09:33PM 24 document. 12:09:37PM 25 Q. Well, why did Regeneron agree to 12:09:40PM	1 doctors to treat their patients monthly beyond 12:11:25PM 2 the loading dose period? 12:11:30PM 3 MR. BERL: Objection. Vague. Lack 12:11:33PM 4 of foundation. 12:11:36PM 5 A. I don't understand why you want to 12:11:38PM 6 reword exactly what was written and what I read 12:11:40PM 7 which describes things very clearly as to why 12:11:45PM 8 this change was made. So I stick with the 12:11:49PM 9 wording that I'm reading off the page which is 12:11:53PM 10 clear cut. 12:11:55PM 11 Q. Because what I'm trying to do is 12:11:57PM 12 explain in lay language for our judge that the 12:11:59PM 13 practical result of this is that this label 12:12:03PM 14 language addition made it easier for doctors to 12:12:08PM 15 be able to prescribe EYLEA monthly for AMD and 12:12:13PM 16 DME and get reimbursed, right? 12:12:20PM 17 MR. BERL: Objection. Vague. Lack 12:12:23PM 18 of foundation. 12:12:24PM 19 A. I think the judge can understand 12:12:26PM 20 that patients were being denied insurance 12:12:29PM 21 coverage for their physician recommended 12:12:32PM 22 treatment and the language was changed so that 12:12:35PM 23 the insurance companies could not use the 12:12:40PM 24 language to deny coverage to their patients. 12:12:44PM 25 Q. Wasn't Regeneron concerned that 12:12:46PM

Page 82		Page 84		
1	doctors were prescribing EYLEA for monthly	12:12:50PM	1 Q. Well, according to Defendant's	12:16:33PM
2	dosing regimens when the clinical trial data	12:12:58PM	2 Exhibit 902, second to last paragraph on the	12:16:35PM
3	was directed to three monthly doses only	12:13:04PM	3 first page, it says, "Dr. Chambers understood	12:16:39PM
4	followed by every eight week dosing?	12:13:09PM	4 the point that this issue is arising on a daily	12:16:43PM
5	MR. BERL: Objection. Lack of	12:13:11PM	5 basis and indicated that the division would	12:16:46PM
6	foundation.	12:13:12PM	6 review the supplement as soon as possible."	12:16:49PM
7	A. The question was, wasn't Regeneron	12:13:23PM	7 Does that sound like a tiny minority to you?	12:16:52PM
8	concerned?	12:13:26PM	8 MR. BERL: Objection.	12:16:56PM
9	Q. Right.	12:13:27PM	9 A. Well, EYLEA has saved the vision of	12:17:07PM
10	MR. BERL: Objection. Lack of	12:13:34PM	10 millions of individuals and is being given to	12:17:11PM
11	foundation.	12:13:41PM	11 many, many individuals, millions of doses a	12:17:17PM
12	A. What is in the label and what tends	12:13:42PM	12 year so if .01 percent of individuals were	12:17:22PM
13	to be standard use by physicians is the data	12:13:51PM	13 being treated monthly, the issue would be	12:17:32PM
14	that describes the clinical results	12:13:56PM	14 arising on a daily basis in substantial numbers	12:17:35PM
15	specifically with the regimen that is used on	12:13:59PM	15 of people. So because so many people are going	12:17:41PM
16	the average patient population based on all the	12:14:01PM	16 blind because of these diseases, even a small	12:17:45PM
17	criteria that is used to select and treat the	12:14:05PM	17 percentage being treated more frequently would	12:17:49PM
18	patients.	12:14:12PM	18 result in issues coming up on a daily basis.	12:17:54PM
19	The results are very specific for	12:14:13PM	19 Q. Right, and if a large percentage	12:17:58PM
20	the dosing regimen and for the very specific	12:14:16PM	20 were being treated more frequently, they would	12:17:59PM
21	patients who were included in that population.	12:14:20PM	21 also be coming up on a daily basis, right?	12:18:02PM
22	The FDA and current practice allows physicians	12:14:31PM	22 MR. BERL: Objection. Lack of	12:18:07PM
23	the individual freedom to sometimes treat	12:14:36PM	23 foundation.	12:18:09PM
24	different individuals differently for various	12:14:44PM	24 A. But I don't think that there is any	12:18:19PM
25	reasons that they would then have to defend if,	12:14:48PM	25 evidence for that and the line you quoted from,	12:18:20PM

Page 83		Page 85		
1	God forbid, something goes wrong, if it is not	12:14:51PM	1 Wiley Chambers does not in any way, shape or	12:18:24PM
2	used specifically as per the label, but they do	12:14:56PM	2 form imply that it was large numbers of	12:18:28PM
3	have the freedom to use their medical judgments	12:14:59PM	3 patients.	12:18:30PM
4	to sometimes use medicines in other ways.	12:15:02PM	4 Q. Has Regeneron done any surveys of	12:18:31PM
5	If, God forbid, something goes	12:15:05PM	5 doctors to find out how many of them are	12:18:33PM
6	wrong, then they have to defend their decision,	12:15:08PM	6 treating -- are using EYLEA to treat less	12:18:35PM
7	but they do have that freedom.	12:15:10PM	7 frequently than every two weeks with their	12:18:39PM
8	MR. BERL: We have been going for	12:15:14PM	8 patients?	12:18:41PM
9	more than an hour. When you get to a	12:15:15PM	9 MR. BERL: Objection.	12:18:42PM
10	breaking point.	12:15:17PM	10 A. I think you misspoke.	12:18:45PM
11	Q. Has Regeneron studied how many	12:15:18PM	11 Q. Sorry, every eight weeks with their	12:18:46PM
12	doctors are actually using EYLEA for monthly	12:15:20PM	12 patients?	12:18:48PM
13	dosing beyond the three months of loading doses	12:15:23PM	13 MR. BERL: Objection. Lack of	12:18:50PM
14	for AMD?	12:15:26PM	14 foundation.	12:18:50PM
15	MR. BERL: Objection. Lack of	12:15:27PM	15 A. I am sure we have done work to	12:18:52PM
16	foundation.	12:15:29PM	16 estimate the relative usage in different	12:18:59PM
17	A. I don't know if we studied that. I	12:15:38PM	17 patients of EYLEA.	12:19:05PM
18	believe that we know roughly what percentage of	12:15:43PM	18 Q. To your knowledge, are clinicians	12:19:10PM
19	patients might be treated monthly.	12:15:49PM	19 still using EYLEA in a loading dose followed by	12:19:13PM
20	Q. What is Regeneron's understanding or	12:15:57PM	20 a PRN regimen?	12:19:16PM
21	estimation of how many patients are being	12:15:59PM	21 MR. BERL: Objection. Vague.	12:19:18PM
22	treated monthly?	12:16:01PM	22 A. I don't know the specifics, but to	12:19:30PM
23	MR. BERL: Objection.	12:16:02PM	23 my knowledge I believe that PRN has fallen out	12:19:31PM
24	A. I don't think that I know that	12:16:26PM	24 of favor.	12:19:34PM
25	number though I believe it's a small minority.	12:16:28PM	25 Q. Well, you never liked PRN dosing	12:19:36PM

Page 86		Page 88	
1	regimen as a concept, right? 12:19:38PM	1	application? 12:34:34PM
2	MR. BERL: Objection. Vague. Are 12:19:40PM	2	A. Let me take a minute to familiarize 12:34:38PM
3	we moving on to something else? 12:19:45PM	3	myself with this. (Witness reviewing 12:34:40PM
4	MS. MAZZOCHI: No. 12:19:46PM	4	document). 12:34:43PM
5	MR. BERL: How many times do I have 12:19:47PM	5	Okay, I familiarized myself with the 12:47:54PM
6	to ask for a break to get a break? I 12:19:48PM	6	document. 12:47:57PM
7	never experienced it. Again, it is 12:19:51PM	7	Q. Can you confirm that there is no 12:47:57PM
8	substantially more than an hour. Let's 12:19:53PM	8	Example 6 and Example 7 in your original 12:47:58PM
9	take a break after this question. 12:19:56PM	9	provisional application filed DX905? 12:48:03PM
10	Q. You can answer. 12:19:58PM	10	A. Yes, I see there are five examples 12:48:17PM
11	MR. BERL: Do you remember the 12:20:01PM	11	filed. 12:48:19PM
12	question? 12:20:01PM	12	Q. So Examples 6 and 7 are missing, 12:48:20PM
13	A. Could you repeat the question? 12:20:02PM	13	right? 12:48:23PM
14	Q. Sure. 12:20:03PM	14	MR. BERL: Objection. 12:48:25PM
15	MS. MAZZOCHI: Go ahead and read it 12:20:03PM	15	A. I see five examples. I don't see an 12:48:27PM
16	back. 12:20:05PM	16	Example 6 or 7. 12:48:30PM
17	(Whereupon the record was read back 12:20:16PM	17	Q. Now, can you explain how a person 12:48:33PM
18	by the reporter.) 12:20:17PM	18	could get to the specific method of using five 12:48:37PM
19	A. I don't like is the right term. PRN 12:20:19PM	19	monthly loading doses followed by an eight week 12:48:42PM
20	dosing depends on a patient losing vision 12:20:24PM	20	dosing regimen for DME based on the information 12:48:45PM
21	before they are treated again and my view that 12:20:36PM	21	provided in just this provisional application 12:48:50PM
22	I did publicly often state was that that was a 12:20:41PM	22	DX905? 12:48:54PM
23	way to substantially -- to lead to substantial 12:20:52PM	23	MR. BERL: Objection. Calls for 12:48:56PM
24	under treatment of patients and cause average 12:20:57PM	24	expert testimony. This here is a fact 12:48:58PM
25	loss of vision in the many patients as opposed 12:21:02PM	25	witness. 12:49:08PM
Page 87		Page 89	
1	to define treatment regimens that would not 12:21:06PM	1	A. Well, on page four it specifically 12:50:28PM
2	depend on people losing vision before they're 12:21:11PM	2	says that, "The methods of the invention may 12:50:30PM
3	retreated and I believe the evidence has backed 12:21:15PM	3	comprise administering to a patient any number 12:50:34PM
4	up that perspective over time. 12:21:19PM	4	of secondary" or so called, you refer to them 12:50:37PM
5	MS. MAZZOCHI: We can take a break. 12:21:22PM	5	as loading doses. "For example, in certain 12:50:39PM
6	THE VIDEOGRAPHER: We are going off 12:21:24PM	6	embodiments only a single secondary," you refer 12:50:41PM
7	the record at 12:21 p.m. 12:21:25PM	7	to as loading doses, "administered" and in 12:50:45PM
8	(Brief recess taken.) 12:21:29PM	8	other embodiments, 2, 3, 4 or 5 or 6 "secondary 12:50:47PM
9	THE VIDEOGRAPHER: We are back on 12:33:42PM	9	doses can be administered to the patients." 12:50:53PM
10	the record at 12:33 p.m. 12:33:43PM	10	So then we -- it reflects back to, I 12:50:56PM
11	BY MS. MAZZOCHI: 12:33:45PM	11	guess, some of the reasoning we discussed when 12:51:03PM
12	Q. Doctor, I would like to put before 12:33:46PM	12	we were looking at the other document that in 12:51:05PM
13	you a document that I have marked as 12:33:47PM	13	the AMD example showing the two Phase III 12:51:12PM
14	Defendant's Exhibit 905, US Provisional Patent 12:33:49PM	14	studies. It seemed as if two secondary, three 12:51:19PM
15	Application 61/432245 filed January 13, 2011. 12:33:55PM	15	loading total, injections before going on to 12:51:27PM
16	(Whereupon document was marked 12:34:08PM	16	every eight week dosing resulted in very 12:51:32PM
17	Exhibit 905 for identification as of this 12:34:08PM	17	similar efficacy to continued monthly dosing 12:51:37PM
18	date.) 12:34:08PM	18	with either VEGF-Trap or the existing standard 12:51:42PM
19	Q. Do you know whether you've seen any 12:34:10PM	19	of care. 12:51:47PM
20	of the provisional applications for your patent 12:34:12PM	20	In Table 2, where we look at Phase 12:51:50PM
21	before? 12:34:15PM	21	II clinical data in diabetic macular edema, it 12:51:55PM
22	A. I don't remember. 12:34:22PM	22	suggests that the so-called number of secondary 12:52:02PM
23	Q. If you can take a look through it, 12:34:22PM	23	doses or loading regimens might not have been 12:52:05PM
24	can you confirm that there is no Example 6 and 12:34:25PM	24	enough to match the efficacy of continued 12:52:11PM
25	no Example 7 in this provisional patent 12:34:29PM	25	monthly dosing which suggested that we would 12:52:17PM

Page 90		Page 92	
1	have to do more secondary or so-called loading doses.	12:52:23PM	12:52:31PM
2			
3	Q. Right, but what would cause -- what	12:52:32PM	
4	would justify selecting five, what I would call	12:52:38PM	
5	loading doses, in the language you pointed to	12:52:43PM	
6	in paragraph 18 would be four secondary doses	12:52:45PM	
7	as opposed to five, six, seven, eight or more?	12:52:50PM	
8	MR. BERL: Objection. Calls for	12:52:54PM	
9	expert testimony.	12:52:55PM	
10	A. I don't think that my answer has	12:53:01PM	
11	changed from when I tried to answer the same	12:53:03PM	
12	question previously.	12:53:09PM	
13	It was the collection of all the	12:53:12PM	
14	data available to us at the time that chose us	12:53:14PM	
15	to test that regimen and until we actually	12:53:21PM	
16	tested it and saw the results, you could not be	12:53:25PM	
17	certain, but the collection of data obviously	12:53:39PM	
18	allowed us to predict the dosing regimen which	12:53:44PM	
19	did work and which was confirmed with the Phase	12:53:48PM	
20	III clinical trial results.	12:53:54PM	
21	Q. Now, but in paragraph 18 that you	12:53:57PM	
22	were looking at in DX905, again I just want to	12:54:00PM	
23	be clear, you list here two or more e.g. two,	12:54:09PM	
24	three, four, five, six, seven, eight or more	12:54:17PM	
25	secondary doses are administered to the patient	12:54:21PM	
Page 91		Page 93	
1	for DME. Why pick just four and not five, six,	12:54:26PM	12:54:32PM
2	seven, eight or more?	12:54:32PM	
3	MR. BERL: Objection.	12:54:37PM	
4	Q. What lets you single out four as	12:54:50PM	
5	compared to any of the other options you list	12:54:52PM	
6	here?	12:54:55PM	
7	MR. BERL: Objection.	12:54:55PM	
8	A. Well, as I said, Table 2 pointed out	12:55:06PM	
9	to what was too few and we had an assortment of	12:55:09PM	
10	additional data which we incorporated into the	12:55:22PM	
11	thinking. As I said, that was in the public	12:55:28PM	
12	domain, that was also described in the other	12:55:32PM	
13	document that we looked at that suggested that	12:55:36PM	
14	it would be possible that those amount of doses	12:55:39PM	
15	would be sufficient and may be optimal and our	12:55:46PM	
16	thinking that led us to that ultimately was	12:55:51PM	
17	confirmed by the results of the Phase III	12:55:56PM	
18	clinical trials.	12:56:01PM	
19	Q. So you believe that simply picking	12:56:02PM	
20	the number of secondary doses as four was just	12:56:04PM	
21	a matter of optimizing?	12:56:09PM	
22	MR. BERL: Objection. Misstates	12:56:11PM	
23	testimony.	12:56:12PM	
24	A. Is just a matter of optimizing?	12:56:23PM	
25	Q. Optimizing the method for DME?	12:56:26PM	
1	A. Can you restate that question again?	12:56:29PM	
2	Q. So, sure. If I understand you, the	12:56:30PM	
3	selection, if we are using the paragraph 18	12:56:33PM	
4	language, the selection of four secondary	12:56:36PM	
5	monthly doses for the DME regimen, that was	12:56:38PM	
6	just you optimizing the final dosing method?	12:56:41PM	
7	MR. BERL: Objection. Misstates	12:56:48PM	
8	testimony.	12:56:49PM	
9	A. I'm not sure what it really means to	12:57:09PM	
10	say just optimizing the treatment regimen.	12:57:12PM	
11	What we were trying to do, and as I said,	12:57:16PM	
12	integrating many bits of information and data	12:57:19PM	
13	that we had was to design a dosing regimen that	12:57:27PM	
14	had many components, not only the numbers of	12:57:37PM	
15	secondary doses, but to design an overall	12:57:41PM	
16	dosing regimen that we thought could be shown	12:57:45PM	
17	when used according to the overall dosing	12:57:49PM	
18	regimen to deliver as much benefit to patients	12:57:51PM	
19	in terms of saving or improving their vision	12:58:01PM	
20	while reducing significantly the treatment	12:58:10PM	
21	burden for those patients in terms of the	12:58:15PM	
22	number of injections in their eye and if we	12:58:18PM	
23	didn't get it just right, we could have failed	12:58:22PM	
24	to show that and the clinical trials could have	12:58:31PM	
25	failed, which is frankly more the rule than the	12:58:36PM	
1	exception for clinical trials.	12:58:39PM	
2	As you know, the vast majority of	12:58:42PM	
3	clinical trials in our business fail, including	12:58:44PM	
4	the ones that you are showing me from all the	12:58:47PM	
5	competitors on the previous slides. So just	12:58:49PM	
6	optimizing seems to minimize or belittle the	12:58:56PM	
7	amount of integration of so much data to	12:59:03PM	
8	correctly design a clinical trial that would	12:59:09PM	
9	show what it's intended to do using a complex	12:59:14PM	
10	overall regimen in a very defined and selected	12:59:18PM	
11	population of patients.	12:59:23PM	
12	So that that is sort of, you know,	12:59:27PM	
13	the rare art and the science which	12:59:33PM	
14	differentiates the rare trials which are	12:59:36PM	
15	successful in showing not only a benefit to	12:59:41PM	
16	patients, but an improvement over the standard	12:59:48PM	
17	of care. These are very rare successes and it	12:59:51PM	
18	takes a lot of art and science to figure out	12:59:54PM	
19	how to figure everything out correctly in order	12:59:57PM	
20	to get that success.	1:00:05PM	
21	Q. When you --	1:00:08PM	
22	A. So I'm not sure I understand what	1:00:10PM	
23	just optimizing means.	1:00:12PM	
24	Q. When you were talking about the	1:00:13PM	
25	focus on what I'm calling five loading doses,	1:00:16PM	

Page 94		
1	what would be four secondary doses using the	1:00:19PM
2	language of paragraph 18 in DX905, you actually	1:00:22PM
3	had the CRVO clinical data. That CRVO clinical	1:00:27PM
4	data is not in Exhibit 905, so how can someone	1:00:32PM
5	reach the conclusion of using four monthly	1:00:37PM
6	secondary doses from the information found just	1:00:39PM
7	in DX905?	1:00:44PM
8	MR. BERL: Vague as to someone.	1:00:49PM
9	Calls for expert testimony.	1:00:51PM
10	A. As I said before, trying to	1:01:18PM
11	precisely to recollect sequence of events and	1:01:22PM
12	every single piece of information as I said, I	1:01:27PM
13	or we were integrating many pieces of	1:01:33PM
14	information during our thinking at any given	1:01:35PM
15	time. It's hard for me to know at any given	1:01:38PM
16	point in time more than ten years later what	1:01:42PM
17	information I had at which time that led me to	1:01:46PM
18	get to certain conclusions.	1:01:49PM
19	Q. You see this is why I think you and	1:01:51PM
20	I have been having a disconnect.	1:01:53PM
21	MR. BERL: Sorry, were you done, Dr.	1:01:55PM
22	Yancopoulos? You can't interrupt his	1:01:57PM
23	answers.	1:02:03PM
24	Q. Dr. Yancopoulos, I'm not asking you	1:02:04PM
25	what was your thinking sitting at Regeneron.	1:02:06PM

Page 95		
1	I'm asking you, from the information contained	1:02:08PM
2	in your patent application that we are looking	1:02:10PM
3	at, DX905, what guidance or instruction is in	1:02:14PM
4	your patent application that allows the	1:02:19PM
5	selection of a four secondary monthly dosing	1:02:26PM
6	regimen for DME? What is in this document, not	1:02:33PM
7	what you were thinking about at Regeneron with	1:02:37PM
8	all the clinical data you had available to you?	1:02:38PM
9	MR. BERL: Objection. Calls for	1:02:42PM
10	expert testimony. He is here to talk	1:02:43PM
11	about what he did. You want to take an	1:02:44PM
12	expert deposition --	1:02:47PM
13	MS. MAZZOCHI: It's okay.	1:02:48PM
14	MR. BERL: You're asking him expert	1:02:48PM
15	testimony questions about what someone	1:02:51PM
16	else would do. Of course you are. That	1:02:52PM
17	is why you don't want him talking about	1:02:52PM
18	what he did.	1:02:52PM
19	MS. MAZZOCHI: I'm asking him about	1:02:54PM
20	what is in his own patent.	1:02:55PM
21	MR. BERL: He's a precipitant	1:02:58PM
22	witness. This is totally inappropriate	1:03:00PM
23	and you interrupted his last answer	1:03:02PM
24	improperly. Just because you don't like	1:03:05PM
25	the answer doesn't mean you can interrupt	1:03:08PM

Page 96		
1	what you don't like and start asking other	1:03:08PM
2	questions.	1:03:08PM
3	Objection. You can answer if you	1:03:09PM
4	can, if you happen to remember the	1:03:10PM
5	question and understand it.	1:03:13PM
6	A. Can you repeat the question?	1:03:16PM
7	Q. Sure. What information is in this	1:03:17PM
8	document, your DX905, your provisional patent	1:03:20PM
9	application that justifies a dosing regimen	1:03:25PM
10	with only four monthly secondary doses followed	1:03:32PM
11	by an eight week dosing regimen to treat DME?	1:03:38PM
12	MR. BERL: Objection. Vague. Calls	1:03:44PM
13	for expert testimony.	1:03:46PM
14	A. Well, all I can do is restate my	1:03:51PM
15	recollection of my state of the thinking as I	1:03:57PM
16	was coming up with and designing the various	1:04:04PM
17	overall regimens that were used for the	1:04:09PM
18	different indications, whether it be macular	1:04:14PM
19	degeneration, diabetic eye disease, CRVO and so	1:04:18PM
20	forth and as I described, I was integrating	1:04:24PM
21	many disparate pieces of information from our	1:04:28PM
22	own clinical trials which I pointed to, various	1:04:32PM
23	tables and so forth that are in these various	1:04:36PM
24	documents you sent me, as well as information	1:04:40PM
25	that was in the public domain and things were	1:04:42PM

Page 97		
1	constantly changing and as I said before, more	1:04:45PM
2	than ten years later, it's hard to remember at	1:04:49PM
3	any particular date what all the information	1:04:52PM
4	was that I had available to me that made me	1:04:55PM
5	make my choices and decisions that I made ten	1:04:59PM
6	or 15 years ago, but the big picture is the art	1:05:02PM
7	and science and why some people are able to	1:05:09PM
8	design trials that can work is because, while	1:05:12PM
9	the vast majority fail, is because you	1:05:16PM
10	correctly integrate many pieces of information	1:05:19PM
11	to come together to make the decisions that you	1:05:24PM
12	make.	1:05:30PM
13	Q. Move to strike as once again	1:05:30PM
14	nonresponsive.	1:05:32PM
15	In paragraph 18 when you state "In	1:05:33PM
16	other embodiments, two or more (e.g., 2, 3, 4,	1:05:36PM
17	5, 6, 7, 8, or more) tertiary doses are	1:05:39PM
18	administered to the patient," what is the upper	1:05:43PM
19	limit on more?	1:05:46PM
20	MR. BERL: Objection.	1:05:47PM
21	A. It says here, "In other embodiments	1:05:58PM
22	two or more (e.g., 2, 3, 4, 5, 6, 7, 8 or more)	1:06:00PM
23	secondary doses are administered to the	1:06:07PM
24	patient."	1:06:11PM
25	Q. Right, what is the upper limit on	1:06:12PM

Page 98		Page 100	
1	more? 1:06:15PM	1	A. I can only speak to my recollection 1:11:52PM
2	MR. BERL: Objection. 1:06:15PM	2	of the intention and why you would have this 1:11:53PM
3	A. As I'm reading the sentence, it says 1:06:16PM	3	loading phase and it's, as I described, the 1:11:59PM
4	simply, in other embodiments two or more, for 1:06:20PM	4	notion is you give more frequent dosing for the 1:12:03PM
5	example, two, three, four, five, six, seven, 1:06:27PM	5	period of time that you would think you would 1:12:08PM
6	eight or more secondary doses are administered 1:06:30PM	6	need to control, get the disease under control, 1:12:10PM
7	to the patients. I don't see a specification 1:06:35PM	7	reach a plateau activity and then you could 1:12:17PM
8	beyond that. 1:06:39PM	8	allow for less burdensome treatment to maintain 1:12:21PM
9	Q. Go up to infinity? 1:06:39PM	9	that benefit. 1:12:27PM
10	MR. BERL: Objection. 1:06:43PM	10	That was the intention of this whole 1:12:28PM
11	Q. The lifetime of a patient? 1:06:43PM	11	approach and, in fact, we saw data from the 1:12:32PM
12	MR. BERL: Objection. 1:06:46PM	12	Phase II trials that said that if you don't do 1:12:39PM
13	A. It says here, "In certain 1:06:51PM	13	some period of loading, you don't get to and 1:12:44PM
14	embodiments" and in other embodiments and I 1:07:35PM	14	maintain with more protracted dosing the 1:12:48PM
15	guess an embodiment refers to a setting or a 1:07:38PM	15	benefit and we saw that in both AMD and DME and 1:12:52PM
16	particular application and in age related 1:07:42PM	16	that validates this notion that you need some 1:12:58PM
17	macular degeneration in that setting there 1:07:48PM	17	and it depends on the disease, a period of more 1:13:03PM
18	are -- in our tested and clinically validated 1:07:55PM	18	intense dosing and then if you have a good 1:13:06PM
19	regimen there were two secondary doses 1:08:02PM	19	enough VEGF antagonist, a good enough drug, you 1:13:09PM
20	administered to the patients. In the ultimate 1:08:08PM	20	can replace the standard of care which is 1:13:15PM
21	DME embodiment there were four and in the 1:08:15PM	21	forever treating intensely and now treat in a 1:13:18PM
22	ultimate CRVO embodiment there were five. 1:08:21PM	22	more protractive fashion that is longer 1:13:24PM
23	Q. But you used the term or more in 1:08:31PM	23	intervals between dosing, substantially 1:13:28PM
24	your patent specification. Did you intend that 1:08:34PM	24	decreasing the treatment burden on these 1:13:31PM
25	phrase or more to have any limit at all? 1:08:37PM	25	elderly patients who have to come in for these 1:13:34PM
Page 99		Page 101	
1	MR. BERL: Objection. 1:08:45PM	1	injections directly into their eye and you can 1:13:38PM
2	A. Well, I think if you're talking 1:09:41PM	2	switch to that. 1:13:41PM
3	about intention, the way I was always thinking 1:09:43PM	3	So that was the dream, the data that 1:13:42PM
4	about it was there would be a period of loading 1:09:46PM	4	we had created a molecule that could succeed 1:13:46PM
5	at which one point one has maximally calmed 1:09:51PM	5	used in this manner and that's ultimately what 1:13:50PM
6	down the disease and at that point you could 1:09:57PM	6	the data showed that dependent on the disease, 1:13:54PM
7	hopefully switch to a less burdensome, a longer 1:10:01PM	7	a treatment of intense dosing followed, as the 1:13:57PM
8	treatment interval, between doses, i.e. 1:10:07PM	8	data said, we had created a better VEGF 1:14:06PM
9	tertiary dose. 1:10:11PM	9	antagonist, instead of having to keep up that 1:14:09PM
10	So the intention was always that 1:10:13PM	10	intense dosing forever, we could then switch to 1:14:13PM
11	there would be a limited period of so-called 1:10:14PM	11	longer interval dosing that could half the 1:14:16PM
12	loading followed by an X-period where less 1:10:20PM	12	treatment burden on the patients, on the 1:14:19PM
13	burdensome treatment paradigm could be 1:10:30PM	13	physicians and on society. 1:14:23PM
14	utilized. 1:10:34PM	14	Q. Can you point me to a page or a line 1:14:24PM
15	Q. Is there anywhere in this 905 1:10:35PM	15	or a paragraph where you take what you just 1:14:27PM
16	exhibit, your provisional patent document, 1:10:40PM	16	described as your intention, your dream, your 1:14:31PM
17	where you set forth that reasoning on when you 1:10:41PM	17	concept of maximizing it? Where did you 1:14:34PM
18	should cut off the secondary dosing period to 1:10:48PM	18	actually commit that concept to writing in the 1:14:39PM
19	then initiate the tertiary dosing period? 1:10:51PM	19	text of this patent specification? 1:14:43PM
20	MR. BERL: Objection. 1:10:58PM	20	MR. BERL: Objection. 1:14:46PM
21	Q. This concept that you hit a plateau 1:10:59PM	21	Q. That you would max out treatment 1:14:50PM
22	or you've gotten the disease under control and 1:11:03PM	22	with the secondary dosing and then you could 1:14:51PM
23	then you can start backing off with the 1:11:05PM	23	back off with the tertiary dosing? 1:14:54PM
24	extended interval? 1:11:07PM	24	A. Okay. Let me read from the "Brief 1:15:10PM
25	MR. BERL: Objection. Vague. 1:11:11PM	25	Summary of the Invention on" page one. "The 1:15:13PM

Page 102			Page 104		
1	present invention provides methods for treating	1:15:20PM	1	here.	1:18:16PM
2	angiogenic eye disorders. The methods of the	1:15:24PM	2	MR. BERL: Objection.	1:18:17PM
3	invention comprise sectionally administering	1:15:27PM	3	Q. I didn't see it, but it's your	1:18:18PM
4	multiple doses of a VEGF agonist to a patient	1:15:31PM	4	patent. That's why I'm asking you to identify	1:18:20PM
5	over time. In particular, the methods of the	1:15:35PM	5	it for me.	1:18:22PM
6	invention comprise sequentially administering	1:15:40PM	6	MR. BERL: Objection. Asked and	1:18:23PM
7	to the patient a single initial dose of a VEGF	1:15:44PM	7	answered repeatedly.	1:18:24PM
8	antagonist, followed by one or more secondary	1:15:47PM	8	A. I think it's all in here.	1:18:30PM
9	doses of the VEGF antagonist," at the intense	1:15:51PM	9	Q. Just in that paragraph -- that's the	1:18:31PM
10	dosing frequency, "followed by one or more	1:15:55PM	10	one you are pointing to? Can you point me to	1:18:34PM
11	tertiary doses of the VEGF antagonists," at the	1:15:59PM	11	any other text that says you should stop the	1:18:36PM
12	less intensive dosing frequency.	1:16:03PM	12	secondary dosing phase and move into the	1:18:39PM
13	"The present inventors have	1:16:05PM	13	tertiary dosing phase when you've hit a maximum	1:18:42PM
14	surprisingly discovered that beneficial	1:16:08PM	14	efficacy or you've met a plateau with the	1:18:47PM
15	therapeutic effects can be achieved in patients	1:16:11PM	15	secondary doses?	1:18:52PM
16	suffering from angiogenic eye disorders by	1:16:14PM	16	MR. BERL: Objection.	1:18:54PM
17	administering a VEGF antagonist to a patient at	1:16:15PM	17	A. Well, paragraph 18 on page four. I	1:18:55PM
18	a frequency of once every 8 or more weeks,	1:16:17PM	18	can read it again. "The methods of the	1:18:58PM
19	especially when such doses are preceded by	1:16:22PM	19	invention may comprise administering to a	1:19:00PM
20	about three doses administered to the patient	1:16:26PM	20	patient any number of secondary and/or tertiary	1:19:03PM
21	at a frequency of about 2 to 4 weeks."	1:16:28PM	21	doses of a VEGF agonist. For example, in	1:19:05PM
22	I think that that in legal jargonese	1:16:34PM	22	certain embodiments," and as we said, it turns	1:19:09PM
23	captures exactly what I was trying to say and	1:16:37PM	23	out in AMD, based on the collection of data at	1:19:11PM
24	what was the intent. A short period of intense	1:16:42PM	24	the time, including our own data, including our	1:19:16PM
25	dosing and instead of -- which was the standard	1:16:48PM	25	own Phase I and Phase II data, it drove us to	1:19:19PM

Page 103			Page 105		
1	of care, was to keep that intense dosing going	1:16:52PM	1	believe and also understanding very importantly	1:19:23PM
2	because the VEGF agents at the time were not	1:16:55PM	2	where, as I said before, we understood where	1:19:27PM
3	potent enough to last a long time, the dream	1:16:58PM	3	the current standard of care would fail.	1:19:30PM
4	and the realization was that we can then shift	1:17:01PM	4	So it led us to propose an overall	1:19:32PM
5	the patients to exactly as I read in the	1:17:05PM	5	dosing regimen that we believed could succeed,	1:19:35PM
6	summary of invention to this less burdensome.	1:17:08PM	6	but was very risky, which we tested in Phase	1:19:38PM
7	We doubled the treatment burden.	1:17:13PM	7	III and turned out to be correct. Two loading	1:19:44PM
8	That means that the poor elderly patients,	1:17:15PM	8	doses, we once again integrated all the	1:19:48PM
9	their health, their healthcare providers who	1:17:18PM	9	available data and came up with four secondary	1:19:51PM
10	are often taking a day off from work to take	1:17:21PM	10	doses or five loading doses in DME, which was	1:19:54PM
11	them to the doctors, the doctors whose offices	1:17:25PM	11	based on all the data, but was risky.	1:20:02PM
12	were overcrowded and so forth, this could half	1:17:28PM	12	We did two large base clinical	1:20:05PM
13	the treatment burden for these poor patients,	1:17:31PM	13	trials and once again, we had multiple arms in	1:20:09PM
14	their family members or other people who are	1:17:34PM	14	the study because we didn't actually know which	1:20:13PM
15	helping them out and their physicians and all	1:17:38PM	15	of the regimens. We were testing -- remember	1:20:15PM
16	of society.	1:17:42PM	16	in every single one of our trials, we tested	1:20:17PM
17	So I think that this summarizes	1:17:44PM	17	multiple regimens. We didn't know which one	1:20:19PM
18	exactly what was the intention and the dream	1:17:47PM	18	might actually produce the benefit for the	1:20:22PM
19	and what we surprisingly ultimately achieved.	1:17:51PM	19	patients and it turns out that in both sets of	1:20:25PM
20	Q. But where does it suggest, as you	1:17:58PM	20	trials, in AMD and in DME, and then	1:20:28PM
21	stated earlier, that you end the secondary	1:17:59PM	21	subsequently in CRVO, that we came up with a	1:20:32PM
22	phase and switch to the tertiary phase because	1:18:03PM	22	regimen, as I said in the AMD case and in the	1:20:35PM
23	you've reached a plateau or you've maxed out	1:18:05PM	23	DME case, one of three regimens that	1:20:40PM
24	the effect of a drug? That's the specific	1:18:09PM	24	convincingly worked and provided better	1:20:43PM
25	point that I'm trying to articulate you got in	1:18:12PM	25	benefit, most dramatically as demonstrated by	1:20:45PM

Page 106		Page 108	
1	having the treatment burden for patients. 1:20:49PM	1	doses, we might have a whole new paradigm that 1:23:28PM
2	So we used all the available data, 1:20:54PM	2	after loading you could get to a good place and 1:23:31PM
3	came up with a clinical trial design that had 1:20:57PM	3	then maintain it by cutting the treatment 1:23:35PM
4	three arms. None of them were guaranteed to 1:21:00PM	4	burden. 1:23:38PM
5	show a benefit. Two out of the three arguably 1:21:05PM	5	That was one out of three arms 1:23:39PM
6	didn't show a benefit compared to the existing 1:21:09PM	6	because it was highly speculative and risky. 1:23:41PM
7	standard of care. One out of the three did and 1:21:11PM	7	That was one of the three arms in the AMD study 1:23:45PM
8	that's the one that became adopted as the new 1:21:14PM	8	and it was one of the three arms in the DME 1:23:49PM
9	gold standard of care for both AMD and DME 1:21:18PM	9	study. I can tell you many people believed 1:23:53PM
10	because it provided such a substantial and 1:21:23PM	10	otherwise and bet against us. 1:23:58PM
11	unexpected benefit to the patients, which was 1:21:26PM	11	In fact, if you look at outside 1:24:01PM
12	that after loading, it halved the burden on 1:21:32PM	12	world indicators, they did not think that this 1:24:04PM
13	them in terms of having this onerous treatment. 1:21:36PM	13	possibility that we were hoping for was going 1:24:09PM
14	MS. MAZZOCHI: Move to strike as 1:21:41PM	14	to turn out. All you have to do is read the 1:24:12PM
15	nonresponsive. 1:21:42PM	15	reports of the financial analysts. We did not 1:24:16PM
16	MR. BERL: Objection. 1:21:44PM	16	think that we were going to actually succeed 1:24:21PM
17	Q. Where in the 905 patent 1:21:44PM	17	nor even know which out of our three arms, if 1:24:23PM
18	specification, your original provisional 1:21:46PM	18	any, would have succeeded and then strikingly 1:24:27PM
19	application? Do you state that the goal of the 1:21:49PM	19	we did succeed and honestly the world 1:24:31PM
20	secondary dosing regimen is to max out or 1:21:51PM	20	recognized it, everybody from the financial 1:24:36PM
21	plateau or get the disease under control 1:21:57PM	21	analysts to the key opinion leaders in the 1:24:38PM
22	MR. BERL: Objection. Asked and 1:22:02PM	22	field that we had done something dramatically 1:24:41PM
23	answered many times. 1:22:03PM	23	different. 1:24:43PM
24	Q. Give me the page and line numbers. 1:22:09PM	24	We had come up with a whole new way 1:24:45PM
25	MR. BERL: Objection. 1:22:12PM	25	to treat this disease, which is exactly as I 1:24:47PM
Page 107		Page 109	
1	A. Maybe I can point out again that in 1:22:13PM	1	have tried to describe and it was -- until we 1:24:50PM
2	our trial -- 1:22:15PM	2	tested it, it was a great idea, I think, and it 1:24:53PM
3	Q. No, I want it in this text, in this 1:22:16PM	3	was a great possibility and it was a dream that 1:24:59PM
4	patent. 1:22:19PM	4	we could help these patients by cutting in half 1:25:01PM
5	MR. BERL: Objection. 1:22:19PM	5	the number of times that these elderly patients 1:25:03PM
6	A. In our trial we actually tested 1:22:20PM	6	and their caretakers would have to go and wait 1:25:07PM
7	multiple regimens because we did, as people do 1:22:22PM	7	in a doctor's office, essentially take a whole 1:25:11PM
8	when they design clinical trials, they 1:22:28PM	8	day, get an injection in the eye with all those 1:25:15PM
9	integrate as much data as they can to make the 1:22:31PM	9	problems and so forth. 1:25:17PM
10	right decisions. The numbers show that most 1:22:34PM	10	So we had this dream that we could 1:25:19PM
11	people fail. They fail to actually come up 1:22:37PM	11	cut that in half. We didn't entirely bet on it 1:25:21PM
12	with something that is as good or better and 1:22:41PM	12	completely because we had multiple other arms 1:25:24PM
13	that succeeds in clinical trials. 1:22:45PM	13	in all of our trials and frankly, as I said, 1:25:27PM
14	We actually had a treatment regimen 1:22:47PM	14	most of the world bet that we were going to be 1:25:30PM
15	where in case we were wrong and you had to 1:22:50PM	15	wrong and miraculously, if you want to thank 1:25:34PM
16	treat forever as you said monthly, if we had to 1:22:54PM	16	God or you want to thank the designers, it all 1:25:43PM
17	do that, we had such a treatment arm, but that 1:22:59PM	17	worked out and the exact regimens overall, very 1:25:47PM
18	arm would not necessarily have shown benefit 1:23:04PM	18	complex regimens, they included many things 1:25:51PM
19	for treatment burden compared to the existing 1:23:07PM	19	beyond just the number of loading doses and the 1:25:56PM
20	standard of care because that's what the 1:23:10PM	20	switch to the eight-week interval, but the 1:26:00PM
21	standard of care was doing, but we weren't 1:23:12PM	21	overall regimens proved dramatically successful 1:26:03PM
22	sure. So we did try that, but we also had -- 1:23:13PM	22	and created an entirely new state of the art 1:26:09PM
23	based on everything that I described, a 1:23:17PM	23	and standard of care for this disease and 1:26:14PM
24	hypothesis that for AMD with three total 1:23:20PM	24	changed the treatment paradigm for patients and 1:26:16PM
25	loading doses and for DME with five loading 1:23:25PM	25	for doctors. 1:26:19PM

Page 110			Page 112		
1	MS. MAZZOCHI: Move to strike as	1:26:20PM	1	and you go to more protracted dosing and you	1:29:11PM
2	again as nonresponsive.	1:26:21PM	2	lose efficacy. You could use the PIER study as	1:29:15PM
3	MR. BERL: What do you think happens	1:26:23PM	3	an exact example of that. They showed you get	1:29:21PM
4	with that? That's what he said.	1:26:23PM	4	to a certain point.	1:29:24PM
5	Q. Dr. Yancopoulos, you have in front	1:26:25PM	5	If you keep intense dosing, you keep	1:29:25PM
6	of you the document DX905, right, Provisional	1:26:27PM	6	that, you back off on the dosing, you lose	1:29:27PM
7	Patent Application? Point to me the text, not	1:26:30PM	7	that. That was the state of the field at the	1:29:30PM
8	what is outside this document, what is in this	1:26:35PM	8	time. That is what everybody new and people	1:29:34PM
9	document that says the purpose or the goal of	1:26:38PM	9	did not think -- people largely didn't believe	1:29:39PM
10	the secondary dosing step is to get you to a	1:26:42PM	10	and I know because everybody was arguing with	1:29:42PM
11	good place, get you to a clinical plateau.	1:26:47PM	11	me, that on average you could not move all	1:29:44PM
12	Where, within this document, in this document	1:26:50PM	12	patients or the vast majority of patients to a	1:29:50PM
13	alone, did you state that was the purpose for	1:26:53PM	13	protracted dosing regimen and on average	1:29:53PM
14	the secondary dosing period?	1:26:56PM	14	maintain the benefit that you got during the	1:29:57PM
15	MR. BERL: Objection. Asked and	1:26:58PM	15	initial intense dosing phase.	1:29:59PM
16	answered.	1:26:59PM	16	It had failed for the current	1:30:04PM
17	A. I believe that I have answered that	1:27:14PM	17	standard of care drug at the time as I	1:30:07PM
18	question many times.	1:27:15PM	18	mentioned in the PIER study and many, if not	1:30:10PM
19	Q. Give me the pages, paragraphs or	1:27:17PM	19	most, if not all physicians were arguing that	1:30:14PM
20	line numbers.	1:27:19PM	20	if you wanted, only some people could maybe be	1:30:17PM
21	MR. BERL: You can't interrupt him.	1:27:20PM	21	extended and they were using PIER end dosing to	1:30:20PM
22	You're repeatedly interrupting him. You	1:27:23PM	22	extend just the rare patients. We had the	1:30:25PM
23	can't do that. Asked and answered.	1:27:28PM	23	theory that because we believed we had a better	1:30:30PM
24	A. I can reread the brief summary of	1:27:32PM	24	drug, a better blocker of VEGF that we could	1:30:34PM
25	the invention, which I think encapsulates our	1:27:36PM	25	actually do what had failed before, what people	1:30:38PM
Page 111			Page 113		
1	strategy and our thinking.	1:27:40PM	1	couldn't do, the state of the field at the	1:30:42PM
2	Q. You're changing my question when you	1:27:44PM	2	time, as I said, people tried and failed.	1:30:44PM
3	say that. I'm asking you where -- okay, if you	1:27:46PM	3	You intensively dose for a while and	1:30:48PM
4	want to focus on paragraph five, where do you	1:27:49PM	4	then you back off. State of the field is you	1:30:51PM
5	specifically say that the point of the	1:27:51PM	5	lose your gains. Our theory was our drug was	1:30:56PM
6	secondary dosing period is to get the patient	1:27:53PM	6	good enough and we could use our insights to	1:31:00PM
7	to a maximum efficacy or good place or get the	1:27:57PM	7	understand what interval, but we could get on	1:31:04PM
8	disease under control? Where do you say that	1:28:03PM	8	average the population all to shift to a	1:31:07PM
9	in paragraph five?	1:28:05PM	9	protracted dosing interval that would cut the	1:31:13PM
10	MR. BERL: Objection. Asked and	1:28:07PM	10	treatment burden in half while maintaining the	1:31:15PM
11	answered.	1:28:08PM	11	same benefit that you see with intense dosing.	1:31:19PM
12	A. I think this brief summary of the	1:28:19PM	12	And so we went up against the	1:31:23PM
13	invention accurately captures the whole purpose	1:28:21PM	13	standard of care using intense dosing	1:31:25PM
14	of this invention in the context of the field.	1:28:27PM	14	throughout the entire year. We went up against	1:31:28PM
15	Let me finish, please.	1:28:32PM	15	our own drug using intense dosing throughout	1:31:31PM
16	In the context of the field people,	1:28:33PM	16	the whole year and we did what had failed for	1:31:34PM
17	as you said before, were continuing intensive	1:28:35PM	17	the standard of care with PIER. We intensely	1:31:38PM
18	dosing, so-called secondary dosing or loading	1:28:40PM	18	dosed for a period of time and then we backed	1:31:42PM
19	dosing forever because when they try to back	1:28:44PM	19	off. Giving our drug, because it was a better	1:31:47PM
20	off on that, they started losing the activity	1:28:49PM	20	VEGF blocker, every eight weeks on average we	1:31:53PM
21	that they had obtained.	1:28:54PM	21	achieved statistically the same results. So	1:31:56PM
22	The state of the field understood	1:28:56PM	22	that was the intention. It was based on the	1:32:02PM
23	this. You can look at multiple clinical trials	1:29:00PM	23	state of the field at the time.	1:32:06PM
24	outside in the public domain where you do the	1:29:05PM	24	I think it's well summarized in the	1:32:07PM
25	intense dosing, you get up to a certain point	1:29:08PM	25	summary of the invention and like I said,	1:32:09PM

Page 114

1 unlike most clinical trials, at least one of 1:32:12PM
2 our three arms worked spectacularly and changed 1:32:17PM
3 the practice of medicine which rarely happens 1:32:21PM
4 in our world. 1:32:24PM
5 Q. If I understand your last answer, 1:32:25PM
6 you believe it was the properties of 1:32:26PM
7 aflibercept itself that allowed this type of 1:32:31PM
8 dosing regimen to work where it had failed with 1:32:34PM
9 other molecules? 1:32:38PM
10 MR. BERL: Objection. Misstates 1:32:40PM
11 testimony. 1:32:43PM
12 A. This dosing regimen worked because 1:32:53PM
13 we had a molecule that was a better molecule. 1:33:04PM
14 Q. Which was aflibercept? 1:33:07PM
15 A. Which was aflibercept. 1:33:12PM
16 Q. Let's take our lunch break. 1:33:13PM
17 THE VIDEOGRAPHER: We are going off 1:33:15PM
18 the record at 1:33 p.m. 1:33:15PM
19 (Lunch recess taken.) 1:33:17PM
20 AFTERNOON SESSION 1:50:01PM
21 THE VIDEOGRAPHER: We are back on 2:12:14PM
22 the record at 2:12 p.m. 2:12:15PM
23 CONTINUED EXAMINATION BY MS. MAZZOCHI: 2:12:16PM
24 Q. Dr. Yancopoulos, in connection with 2:12:18PM
25 filing your patent applications we looked at 2:12:21PM

Page 115

1 earlier, did you ever review your files to 2:12:24PM
2 identify information that you had to disclose 2:12:26PM
3 to the PTO? 2:12:29PM
4 A. At the time of putting together the 2:12:41PM
5 filings? 2:12:43PM
6 Q. At any time. 2:12:45PM
7 A. At any time. Before or since? 2:12:46PM
8 Q. Right. 2:12:50PM
9 A. Did I review what again? 2:12:51PM
10 Q. Did you review your files to 2:12:54PM
11 identify information that you had a duty to 2:12:55PM
12 disclose to the patent office? 2:12:59PM
13 A. I would say yes. 2:13:16PM
14 Q. Can you describe the nature of the 2:13:18PM
15 search or file review that you did? 2:13:20PM
16 A. Like I said before, this is 10, 15 2:13:49PM
17 years ago. It is hard to remember any 2:13:51PM
18 specifics. I'm just saying that at various 2:13:55PM
19 points, I reviewed my files that had to do with 2:14:00PM
20 information that we would be including in, you 2:14:05PM
21 know, patent files. I didn't have any 2:14:09PM
22 customary or systematic approach, but 2:14:15PM
23 obviously, I must have and I must have reviewed 2:14:20PM
24 files having to do with filing of patent 2:14:26PM
25 applications. 2:14:29PM

Page 116

1 Q. But you believe the last time you 2:14:29PM
2 did that was probably 10 or more years ago? 2:14:30PM
3 A. To review files that had to do with 2:14:36PM
4 filing information for the patent office with 2:14:39PM
5 regards to this subject matter, I don't 2:14:42PM
6 remember recently reviewing them for that 2:14:51PM
7 purpose. 2:14:53PM
8 Q. Do you know whether you've taken any 2:14:54PM
9 other affirmative steps to ensure you're 2:14:56PM
10 complying with your duty of candor, good faith, 2:14:59PM
11 and fair dealing with the patent office? 2:15:02PM
12 MR. BERL: Objection. 2:15:04PM
13 A. Could you repeat the question? 2:15:20PM
14 Q. Do you know whether you've taken any 2:15:21PM
15 other affirmative steps to ensure you complied 2:15:23PM
16 with your duty of candor, good faith, and fair 2:15:27PM
17 dealing with the patent office in connection 2:15:30PM
18 with these patent applications? 2:15:32PM
19 MR. BERL: Objection. 2:15:34PM
20 Q. That are the subject of this 2:15:34PM
21 litigation? 2:15:36PM
22 A. I'm not sure of the legal definition 2:15:37PM
23 of good faith, but I try to use good faith in 2:15:50PM
24 all my dealings with everybody including the 2:15:53PM
25 patent office, so I would have — you know, I 2:15:55PM

Page 117

1 always try to be candid, so I would have just 2:16:00PM
2 used my normal way of going about things to be 2:16:04PM
3 candid and deal in good faith and do what's 2:16:09PM
4 right. 2:16:16PM
5 Q. Do you recall whether you've ever 2:16:17PM
6 asked anyone else to review your files to 2:16:20PM
7 identify information that you were aware of in 2:16:24PM
8 order to comply with your duty of disclosure 2:16:27PM
9 with the U.S. Patent and Trademark Office in 2:16:30PM
10 connection with your two patents at issue in 2:16:33PM
11 this litigation or the patent family? 2:16:36PM
12 A. With regard to the litigation or 2:16:40PM
13 with regard to the filings? 2:16:43PM
14 Q. With regard to the PTO filings. 2:16:45PM
15 MR. BERL: Objection. 2:16:48PM
16 A. I don't recall if I ever had anybody 2:16:48PM
17 review my files with regard to the PTO filings. 2:16:50PM
18 Q. In connection with the prosecution 2:16:55PM
19 of your patent applications before the PTO, 2:16:56PM
20 what steps did you take, particularly since you 2:16:59PM
21 were the chief scientific officer at Regeneron, 2:17:02PM
22 to ensure that the scientific representations 2:17:04PM
23 that you and your attorneys made to the PTO 2:17:07PM
24 were truthful and accurate? 2:17:10PM
25 MR. BERL: Objection. 2:17:12PM

Page 118 1 A. During the course of our patent, 2:17:49PM 2 individuals putting together the patents as 2:17:54PM 3 need be, I worked with them and reviewed their 2:18:00PM 4 documents, and in large part, relied on them to 2:18:02PM 5 make sure all the people who are necessarily 2:18:09PM 6 reviewing things were reviewing them, but I 2:18:13PM 7 also reviewed a lot of the documents at various 2:18:16PM 8 points. 2:18:20PM 9 Q. Right. Did you review the patent 2:18:25PM 10 specifications themselves for scientific 2:18:27PM 11 accuracy? 2:18:30PM 12 MR. BERL: Objection. 2:18:32PM 13 A. I would have reviewed parts of the 2:18:42PM 14 documents that were put together. I can't say 2:18:47PM 15 that I know exactly whether I reviewed 2:18:51PM 16 everything or not. 2:18:56PM 17 Q. Did you review the accuracy of the 2:18:59PM 18 scientific representations that your attorneys 2:19:01PM 19 were making to the PTO on your behalf when 2:19:05PM 20 prosecuting your patent applications? 2:19:08PM 21 A. Prosecuting means putting them 2:19:13PM 22 together? 2:19:16PM 23 Q. No. It means the back and forth 2:19:17PM 24 process between the PTO and the patent 2:19:18PM 25 applicant before the patent issues. 2:19:22PM	Page 120 1 Can I have a pen? Am I allowed to make 2:26:53PM 2 notations? 2:27:01PM 3 THE COURT REPORTER: No, not on the 2:27:02PM 4 exhibit. 2:27:02PM 5 Q. My question is simply whether you 2:27:03PM 6 met or spoken with the attorney who is listed 2:27:06PM 7 on the last page? 2:27:08PM 8 A. And I'm just reviewing the document. 2:27:09PM 9 I do have to say it's a great document. It 2:27:11PM 10 makes a lot of -- it has a lot of responses to 2:27:16PM 11 the questions that you were asking before, but 2:27:19PM 12 restates what I was trying to state in all of 2:27:23PM 13 my answers. So what was your question again? 2:27:25PM 14 Q. The last page, Carl Bozicevic, have 2:27:29PM 15 you ever met with or spoken with or interacted 2:27:33PM 16 with him before? 2:27:36PM 17 A. I do not believe that this is an 2:27:37PM 18 employee of Regeneron. I don't believe that I 2:27:46PM 19 have met with him or at least I don't remember 2:27:50PM 20 meeting with him. 2:27:52PM 21 Q. Okay. I would like you to turn to 2:27:53PM 22 page 6 of Defendant's Exhibit 910, and do you 2:27:54PM 23 see that there is a heading that says "Double 2:28:02PM 24 Patenting Rejection"? 2:28:04PM 25 A. Yep. 2:28:06PM
Page 119 1 MR. BERL: Objection, lack of 2:19:27PM 2 foundation. 2:19:30PM 3 A. I did not directly oversee the 2:19:34PM 4 prosecution and I relied on our patent people 2:19:36PM 5 to let me know when they wanted me to review 2:19:41PM 6 something. 2:19:45PM 7 Q. I'm going to mark as Defendant's 2:19:49PM 8 Exhibit 910 a document with production numbers 2:19:50PM 9 RGN-EYLEA-MYLAN-13908 through 971. And for the 2:19:54PM 10 record, this is a document titled "Amendment 2:20:04PM 11 Under 37 C.F.R. Section 1.111" in connection 2:20:06PM 12 with the prosecution of Application Number 2:20:12PM 13 13/940,370, filing date July 12, 2013. "Title: 2:20:14PM 14 Use of VEGF Antagonist to Treat Angiogenic 2:20:23PM 15 Eye Disorders" filed by Carl Bozicevic on 2:20:27PM 16 September 11, 2015. 2:20:32PM 17 Dr. Yancopoulos, if you can take a 2:20:34PM 18 look at the last page of this exhibit, there is 2:20:44PM 19 a reference to an attorney named Carl 2:20:47PM 20 Bozicevic, B-O-Z-I-C-E-V-I-C. Have you ever 2:20:49PM 21 meet with or spoken with that attorney? 2:20:55PM 22 (Whereupon Exhibit 910 was marked 2:20:57PM 23 for identification.) 2:20:57PM 24 A. I'm just familiarizing myself with 2:21:01PM 25 the document (Witness reviewing document.) 2:21:03PM	Page 121 1 Q. I would like to start in the fifth 2:28:10PM 2 paragraph under that heading that reads, "At 2:28:12PM 3 the time of the invention the well accepted 2:28:16PM 4 standard of care for the treatment of the 2:28:19PM 5 neovascular (or wet) form of age-related 2:28:22PM 6 macular degeneration was to administer an 2:28:27PM 7 antibody formulation (ranibizumab) by injection 2:28:30PM 8 to the eye once per month (see the attached 2:28:36PM 9 Heier et al. paper)." Do you see that? 2:28:38PM 10 A. Yes, I do. 2:28:44PM 11 Q. Just so you have it, let me give you 2:28:46PM 12 as Exhibit 911, the referenced paper which is 2:28:50PM 13 RGN-EYLEA-MYLAN 13628 through 29. "RhuFab V2 2:28:56PM 14 in Wet AMD - 6 Month Continued Improvement 2:29:06PM 15 Following Multiple Intravitreal Injections" 2:29:13PM 16 Invest Ophthalmol Science 2003." Do you have 2:29:18PM 17 that before you? 2:29:25PM 18 (Whereupon Exhibit 911 was marked 2:29:26PM 19 for identification.) 2:29:26PM 20 A. (Witness reviewing document.) Yes, 2:30:40PM 21 I see this document. 2:31:03PM 22 Q. Now, with regard to the standard of 2:31:04PM 23 care, do you know what time period was being 2:31:10PM 24 referred to? 2:31:15PM 25 MR. BERL: Objection, lack of 2:31:17PM

Page 122		Page 124	
1	foundation. 2:31:18PM	1	is that listed on page 10 with attachments? 2:34:57PM
2	Q. At the time of the invention, the 2:31:21PM	2	Q. Right. The attachment that is 2:35:01PM
3	well accepted standard of care? 2:31:22PM	3	listed is Heier, et al -- is the Heier, et al. 2:35:03PM
4	MR. BERL: Objection, lack of 2:31:25PM	4	paper from 2003 that I have given you as DX911, 2:35:07PM
5	foundation. 2:31:25PM	5	right? 2:35:12PM
6	A. I'm sorry, you're referring to the 2:31:32PM	6	MR. BERL: Objection, lack of 2:35:12PM
7	statement where? 2:31:33PM	7	foundation. You examined the witness who 2:35:13PM
8	Q. Sure. In DX910 under -- in the 2:31:37PM	8	wrote this. Why are you asking him about 2:35:16PM
9	Double Patenting Rejection, fifth paragraph 2:31:41PM	9	this? This has nothing to do with him. 2:35:18PM
10	down, it says, "At the time of the invention 2:31:44PM	10	Objection, lack of foundation. 2:35:22PM
11	the well accepted standard of care for the 2:31:46PM	11	A. I am just noting that this document 2:35:29PM
12	treatment," et cetera, et cetera. Do you 2:31:49PM	12	clearly refers to multiple Heier, et al. 2:35:33PM
13	know -- and it refers to the Heier paper from 2:31:52PM	13	papers, only one of which is this one. So, do 2:35:40PM
14	2003. Do you know whether the time of the 2:31:57PM	14	you read on page 7 where it says the attached 2:35:43PM
15	invention, the standard of care was circa 2003 2:32:02PM	15	Heier, et al. published paper in December 2012, 2:35:45PM
16	standards? 2:32:08PM	16	which is clearly not this attached paper which 2:35:49PM
17	MR. BERL: Objection, vague, lack of 2:32:09PM	17	is 2003, so that there are multiple Heier, et 2:35:53PM
18	foundation, misstated the document. 2:32:11PM	18	al. publications that are referred to here. 2:35:57PM
19	A. Was this the Heier paper that is 2:32:21PM	19	So, it's impossible to tell which one is being 2:36:01PM
20	being referred to in this other document? 2:32:24PM	20	referred to and which sections because they are 2:36:04PM
21	Q. Yep. If you take a look at page 10, 2:32:31PM	21	all referred to as Heier, et al. 2:36:08PM
22	it says attachment -- it refers to the 2:32:37PM	22	Q. Well, let me give you as Defendant's 2:36:10PM
23	attachments and it gives that 2003 citation, 2:32:39PM	23	Exhibit 912, the 2012 Heier, et al. paper 2:36:12PM
24	which we marked as DX911. 2:32:42PM	24	titled "Intravitreal Aflibercept in Wet 2:36:16PM
25	A. So what was the question? 2:33:19PM	25	Age-related Macular Degeneration", which has 2:36:21PM
Page 123		Page 125	
1	Q. The state of the art at the time of 2:33:21PM	1	production numbers RGN-BYLEA-MYLAN 13918 2:36:25PM
2	your invention was certainly beyond this 2:33:25PM	2	through 13929. 2:36:28PM
3	treatment description that is set forth in the 2:33:29PM	3	(Whereupon Exhibit 912 was marked 2:36:34PM
4	2003 Heier paper we've marked as DX911, right? 2:33:32PM	4	for identification.) 2:36:34PM
5	MR. BERL: Objection, lack of 2:33:37PM	5	MR. BERL: The last one was 912, no? 2:36:34PM
6	foundation, vague. 2:33:39PM	6	MS. MAZZOCHI: No, the last one was 2:36:37PM
7	A. I'm very confused because I'm seeing 2:33:48PM	7	911. 2:36:39PM
8	references to the attached Heier, et al., 2:33:54PM	8	MR. BERL: You announced that as 912 2:36:41PM
9	published paper in December of 2012 in 2:33:58PM	9	on the record. Okay, sorry. 2:36:42PM
10	ophthalmology and as you say on page 10, it 2:34:02PM	10	Q. You're a coauthor on this paper that 2:36:47PM
11	just refers to this. So, there's multiple 2:34:06PM	11	we've marked as Defendant's Exhibit 912, 2:36:49PM
12	Heier papers. So, I don't know which one is 2:34:11PM	12	correct? 2:36:52PM
13	actually being referred to, because clearly, 2:34:13PM	13	A. Yes, I recognize this paper. 2:36:59PM
14	the one that is being referred to in this 2:34:16PM	14	Q. Now, what is the basis for your 2:37:06PM
15	document is not the one that you are referring 2:34:18PM	15	assertion or for the assertion that -- well, 2:37:14PM
16	to that is attached on page 10 because it's a 2:34:20PM	16	actually, let me take a step back. Do you 2:37:18PM
17	different paper. 2:34:28PM	17	agree that by the time you filed this patent 2:37:21PM
18	Q. Well, look at the last page -- 2:34:28PM	18	application, ranibizumab dosed monthly was the 2:37:23PM
19	A. No, I realize on page 10 -- 2:34:32PM	19	only standard of care when it came to dosing 2:37:30PM
20	Q. Right. 2:34:33PM	20	ranibizumab? 2:37:39PM
21	A. It says that, but if you read the 2:34:33PM	21	MR. BERL: Objection. 2:37:43PM
22	text in the document, okay, it refers, to a 2:34:37PM	22	A. What was the question again because 2:38:24PM
23	Heier, et al. published in December of 20 -- 2:34:42PM	23	I'm just reminding myself reviewing this paper 2:38:27PM
24	"The attached Heier et al. paper published in 2:34:47PM	24	that I haven't seen in more than 10 years? 2:38:29PM
25	December of 2012." Okay. And so that -- where 2:34:50PM	25	Q. At the time you filed your patent -- 2:38:32PM

Page 126		Page 128	
1	your first patent application in this family 2:38:33PM	1	that the VEGF-Trap Eye or EYLEA could actually, 2:42:07PM
2	back in January 2011, was it scientifically 2:38:37PM	2	with half the treatment burden, match the 2:42:11PM
3	accurate to say that only dosing Lucentis once 2:38:43PM	3	outcomes of monthly ranibizumab, providing a 2:42:16PM
4	a month -- that dosing Lucentis once a month 2:38:49PM	4	huge benefit, as we said before, to all the 2:42:19PM
5	was the only treatment standard of care? 2:38:51PM	5	patients who were so desperate to maintain or 2:42:24PM
6	MR. BERL: Objection. 2:38:56PM	6	save their vision, but now they could do it 2:42:28PM
7	Q. In the field? 2:38:59PM	7	with half the number of visits to go to 2:42:32PM
8	A. Well, I would not say only because 2:39:04PM	8	there -- these elderly patients to go to their 2:42:37PM
9	individual doctors with individual patients 2:39:07PM	9	retinal specialists and get injections in the 2:42:41PM
10	have the liberty to do what they might think is 2:39:09PM	10	eye, which, obviously, one would want to avoid 2:42:44PM
11	best for that individual patient, but it's 2:39:14PM	11	if you could maintain the benefit, which is 2:42:48PM
12	pretty clear, as is nicely summarized in this 2:39:20PM	12	what EYLEA provided these individuals. 2:42:50PM
13	Heier, et al. reference, which might be the one 2:39:24PM	13	Q. Did the PRN ranibizumab treatment 2:42:54PM
14	that was referred to in the paragraph that you 2:39:27PM	14	protocol have -- was it less expensive to the 2:43:00PM
15	read before. As I read here from the 2:39:29PM	15	patient? 2:43:06PM
16	discussion, it says here, "Because the CATT 2:39:31PM	16	MR. BERL: Objection, lack of 2:43:11PM
17	highlighted the inability -- because the CATT 2:39:46PM	17	foundation. 2:43:16PM
18	trials highlighted the inability of other 2:39:51PM	18	A. Honestly, my expertise is in 2:43:20PM
19	regimens, including, most notably, PRN 2:39:55PM	19	inventing and developing these medicines. I 2:43:23PM
20	ranibizumab, to match the retinal thickness and 2:40:02PM	20	don't honestly know the exact prices nor how 2:43:25PM
21	retinal fluid improvement seen with bimonthly 2:40:05PM	21	the cost is covered by the patient and what the 2:43:29PM
22	ranibizumab," and then it also goes on in the 2:40:09PM	22	ultimate cost to the patient is. As we know, 2:43:34PM
23	next paragraph to explain the details of why 2:40:12PM	23	for many of these patients on Medicare with 2:43:37PM
24	"The PRN regimens produced numerically smaller 2:40:16PM	24	supplemental aid, the cost of the drugs can be 2:43:42PM
25	gains in visual acuity with poor anatomic 2:40:21PM	25	entirely covered, so. But I don't know the 2:43:45PM
Page 127		Page 129	
1	outcomes." It goes on to say, switching from a 2:40:26PM	1	details of that. 2:43:48PM
2	monthly to a PRN regimen during the second 2:40:27PM	2	Q. Was the ranibizumab PRN regimen that 2:43:49PM
3	year of the CATT trial significantly worsened 2:40:28PM	3	was known at the time you filed your patent 2:43:52PM
4	visual acuities and anatomic end points. It 2:40:33PM	4	application, one that would be less painful to 2:43:56PM
5	concludes that the standard of care or at least 2:40:36PM	5	the patient relative to monthly dosing? 2:43:59PM
6	the best standard of care to achieve the best 2:40:38PM	6	MR. BERL: Objection. 2:44:03PM
7	results is demonstrated in all of these trials 2:40:42PM	7	A. One would have to go back and look 2:44:13PM
8	is that nothing could match monthly ranibizumab 2:40:47PM	8	at the details of the studies. I believe that 2:44:16PM
9	until the results of this trial and it points 2:40:53PM	9	the point of the PRN regimen is that they tried 2:44:21PM
10	out how the ability of decreasing the treatment 2:40:59PM	10	to use less injections by giving them so-called 2:44:25PM
11	burden by half provides such a meaningful 2:41:09PM	11	as needed, but as needed meant that you let the 2:44:30PM
12	benefit to patients while maintaining that 2:41:12PM	12	patient slip a little before you treated them 2:44:34PM
13	ability to give people back their vision or 2:41:16PM	13	and those trials, as summarized in the 2:44:42PM
14	maintain their vision as well as monthly 2:41:20PM	14	discussion that I just read, resulted in 2:44:46PM
15	ranibizumab. So, that is, I guess, the major 2:41:24PM	15	numerically worse visual and anatomic outcomes 2:44:48PM
16	conclusion of this paper which is consistent 2:41:27PM	16	than treating with regular, monthly 2:44:52PM
17	with the notion, as it was written at the time, 2:41:30PM	17	ranibizumab. So, they may have reduced the 2:44:55PM
18	that monthly ranibizumab was the gold standard 2:41:34PM	18	treatment burden but at the cost of causing 2:44:58PM
19	and nothing had ever shown that these other 2:41:41PM	19	loss of vision, of costing vision for these 2:45:07PM
20	regimens that lowered the treatment burden 2:41:45PM	20	patients and that's why they were not 2:45:11PM
21	could actually match monthly ranibizumab. 2:41:48PM	21	considered a gold standard, and, in fact, many 2:45:13PM
22	There was enormous effort in the 2:41:51PM	22	such as myself, felt that it was improper 2:45:17PM
23	field, including studies like CATT and HARBOR 2:41:54PM	23	medical care to deliver to a patient to try to 2:45:25PM
24	that they refer to here, and that's why it was 2:42:00PM	24	use a PRN regimen to lower the treatment, lower 2:45:29PM
25	such a huge advance when we were able to show 2:42:02PM	25	the treatment burden but result in loss to 2:45:32PM

Page 130

1 vision for the patients. 2:45:37PM

2 Q. But we can agree that the PRN dosing 2:45:40PM

3 method of ranibizumab, which was in place 2:45:46PM

4 before you filed your patent application, would 2:45:49PM

5 subject the patient to fewer potential adverse 2:45:54PM

6 effects such as infection with each treatment 2:45:59PM

7 as compared to monthly ranibizumab, right? 2:46:02PM

8 MR. BERL: Objection. 2:46:07PM

9 A. We can agree that if we did not 2:46:10PM

10 treat any patients, they would not have any 2:46:14PM

11 side effects from the treatment burden of 2:46:17PM

12 infection into their eyes, but on average, they 2:46:21PM

13 would go legally blind within a year or so. 2:46:24PM

14 Q. That wasn't really my question. Can 2:46:31PM

15 you agree that the risk to patients, such as 2:46:33PM

16 infection from the injection, was less in the 2:46:40PM

17 ranibizumab PRN dosing regimen in place before 2:46:45PM

18 you filed your patents as compared to the 2:46:48PM

19 ranibizumab monthly regimen? 2:46:51PM

20 MR. BERL: Vague as to "such as." 2:46:54PM

21 A. I think we can agree that regardless 2:46:57PM

22 of the treatment -- let's say you have a 2:47:00PM

23 treatment to treat cancer that causes really 2:47:02PM

24 bad side effects but cures the cancer, if you 2:47:08PM

25 gave less treatments, you would cause less 2:47:12PM

Page 131

1 chemotherapy associated side effects but at the 2:47:17PM

2 cost of more people dying. So, of course, if 2:47:20PM

3 you have a treatment that involves injections 2:47:24PM

4 into the eyes that results in side effects, if 2:47:27PM

5 you avoid those injections, you'll have less of 2:47:30PM

6 the side effects, but the point of the story 2:47:35PM

7 here is that when people try to do that, when 2:47:40PM

8 they try to decrease the number of injections 2:47:44PM

9 to spare the side effects but not only the side 2:47:47PM

10 effects, the treatment burden. These are 2:47:50PM

11 elderly patients. 2:47:52PM

12 I know my mother had age-related 2:47:54PM

13 macular regeneration. I had to take her to the 2:47:56PM

14 hospital. I would have to take a whole day off 2:48:00PM

15 from work to take her, but I was doing it 2:48:03PM

16 because it's my mother and I was trying to save 2:48:05PM

17 her vision. It was an enormous burden to take 2:48:07PM

18 my 91-year-old mother to the doctor regularly 2:48:10PM

19 for treatments. If you had told me that I only 2:48:14PM

20 had to take her once every two months instead 2:48:18PM

21 of once a month, it would have been great for 2:48:21PM

22 both of us, but if you told me that the cost of 2:48:23PM

23 taking her half as often was that she would go 2:48:26PM

24 blind, I would never do that. 2:48:30PM

25 Q. Right, but -- 2:48:32PM

Page 132

1 A. So, the point here is, of course -- 2:48:32PM

2 what is nicely summarized in both the documents 2:48:35PM

3 that you gave me is that the gold standard at 2:48:40PM

4 the time of our approach and infection was 2:48:44PM

5 monthly ranibizumab because that's the only one 2:48:50PM

6 that was shown to optimally gain and maintain 2:48:52PM

7 vision for these patients who would otherwise 2:48:55PM

8 go blind at the cost of the burden of monthly 2:48:58PM

9 treatment forever. 2:49:02PM

10 What we were able to show is that we 2:49:04PM

11 could actually, for the first time in history, 2:49:08PM

12 maintain statistically the same exact benefit 2:49:10PM

13 but by cutting the treatment burden in half, 2:49:19PM

14 which all these studies, like these CATT 2:49:22PM

15 studies and so forth that are referred to here, 2:49:26PM

16 they tried to do. They could not actually even 2:49:28PM

17 reduce the treatment burden by as much as we 2:49:30PM

18 reduced the treatment burden but the costs of 2:49:35PM

19 their attempts to reduce the treatment burden 2:49:37PM

20 was blindness and loss of vision. 2:49:40PM

21 Q. All right. You're exaggerating 2:49:42PM

22 because you're -- 2:49:43PM

23 MR. BERL: Were you done, 2:49:44PM

24 Dr. Yancopoulos? No, you can't interrupt 2:49:44PM

25 him. You cannot interrupt the witness. 2:49:46PM

Page 133

1 Q. Your own paper -- your own paper -- 2:49:49PM

2 MR. BERL: Dr. Yancopoulos, were you 2:49:49PM

3 finished with your answer or not? 2:49:50PM

4 Q. Your own paper, page 25 -- 2:49:56PM

5 A. I'm sorry, I was interrupted and I 2:49:59PM

6 lost my train of thought, but I was not 2:50:01PM

7 exaggerating. 2:50:04PM

8 Q. Your own paper admits that monthly 2:50:05PM

9 ranibizumab versus the PRN regimens in the CATT 2:50:10PM

10 study, that the PRN regimen was non-inferior 2:50:15PM

11 statistically when it came to the visual acuity 2:50:19PM

12 measurements, correct? 2:50:22PM

13 A. No, that's incorrect. If you read 2:50:24PM

14 the -- 2:50:25PM

15 Q. Page 2538. 2:50:27PM

16 A. If you read the paper -- let me read 2:50:28PM

17 it again, okay. If you understand how 2:50:30PM

18 non-inferiority studies work, it depends on the 2:50:35PM

19 margin, on the margin that is set and those are 2:50:40PM

20 set by the investigators. They are not 2:50:46PM

21 necessarily what the standard of care is or 2:50:49PM

22 what people would believe. So, the CATT and 2:50:53PM

23 HARBOR studies arbitrarily used non-inferiority 2:50:57PM

24 margins from baseline BCVA of five letters for 2:51:02PM

25 the CATT study. What does that mean? 2:51:07PM

Page 134		Page 136	
1	That means five letters is a whole 2:51:09PM	1	you dosing instructions for Lucentis that the 2:54:10PM
2	line of vision on an eye chart and what this 2:51:11PM	2	European regulatory authorities approved, 2:54:14PM
3	means is that they tolerated -- they tolerated 2:51:20PM	3	correct? 2:54:18PM
4	patients losing up to five letters and they 2:51:23PM	4	A. This appears to be referring to 2:55:14PM
5	still called it non-inferiority. What we were 2:51:26PM	5	dosing instructions that were released by the 2:55:16PM
6	able to show in our studies is that our regimen 2:51:30PM	6	European authorities. 2:55:20PM
7	was within 0.3 letters of the gold standard. 2:51:33PM	7	Q. So, you knew by 2007 that the 2:55:23PM
8	That is a totally different goal to set and 2:51:39PM	8	European regulatory authorities allowed -- had 2:55:27PM
9	that is why, as is written here in the papers, 2:51:48PM	9	approved dosing instructions for Lucentis where 2:55:31PM
10	it shows even though they met this arbitrarily 2:51:50PM	10	there were three monthly loading doses and then 2:55:37PM
11	set non-inferiority margin, these PRN regimens 2:51:55PM	11	the treatment interval could go longer than 2:55:40PM
12	produced numerically smaller gains in BCVA, up 2:52:01PM	12	monthly dosing, right? 2:55:45PM
13	to 2.6, almost three letters, with poor 2:52:06PM	13	MR. BERL: Objection. 2:55:48PM
14	anatomic outcomes. 2:52:09PM	14	A. Approval of this regimen by the 2:55:55PM
15	Moreover, when you switch from 2:52:10PM	15	European authorities was very highly 2:55:58PM
16	monthly to a PRN regimen during the second 2:52:12PM	16	controversial because it was actually not based 2:56:01PM
17	year, vision and anatomic outcomes 2:52:16PM	17	on any clinical data and it was largely 2:56:05PM
18	significantly worsened. So, that is what we 2:52:20PM	18	intended as a way to save costs and not 2:56:08PM
19	said here. That -- and what largely the field 2:52:23PM	19	prioritize patients' outcomes. Moreover, this 2:56:13PM
20	understood, which is why almost nobody uses PRN 2:52:27PM	20	regimen still demanded that the patients come 2:56:19PM
21	dosing anymore because it was realized that it 2:52:31PM	21	in on a monthly basis to get full evaluations 2:56:24PM
22	was actually therapeutically inferior costing 2:52:34PM	22	to decide whether or not they should be 2:56:29PM
23	people vision. We've done calculations in the 2:52:40PM	23	treated. This was an attempt to prevent too 2:56:32PM
24	past, enormous numbers of patients -- it's not 2:52:44PM	24	much vision loss that you would get by not 2:56:37PM
25	an exaggeration -- I believe, became blind, 2:52:50PM	25	regularly treating them. 2:56:40PM
Page 135		Page 137	
1	went legally blind, because they were poorly 2:52:52PM	1	So, in many ways the impact on 2:56:42PM
2	treated with PRN regimens, which the data shows 2:52:55PM	2	treatment burden that I described, the fact 2:56:47PM
3	are clearly not as good as the gold standard at 2:53:00PM	3	that these elderly patients and their care 2:56:49PM
4	the time, which was monthly ranibizumab 2:53:02PM	4	givers now have to go to the doctor's office, 2:56:52PM
5	delivering a new treatment and demonstrating 2:53:07PM	5	and in many cases take the whole day in order 2:56:54PM
6	that it could be regularly used every two 2:53:11PM	6	to do this, that was still -- the treatment 2:56:58PM
7	months, and on average, keep people to have 2:53:14PM	7	burden here still is monthly, yet subsequent 2:57:01PM
8	almost exactly the same amount of vision gain 2:53:16PM	8	studies like we just described which were done 2:57:04PM
9	is not an exaggeration if you known a mother or 2:53:19PM	9	the same way demonstrated that this exact 2:57:06PM
10	had a relative who is going blind from 2:53:24PM	10	regimen, as described here, resulted in 2:57:11PM
11	age-related macular degeneration. It's truly a 2:53:27PM	11	inferior vision and anatomic outcomes and was 2:57:15PM
12	Godsend and it's not an exaggeration. 2:53:30PM	12	clearly a mistake if you're taking patients' 2:57:19PM
13	Q Well, we'll get to that in a minute. 2:53:32PM	13	vision and their outcomes as a priority. 2:57:23PM
14	I am giving you a document that I marked as 2:53:34PM	14	So, it was very controversial at the 2:57:25PM
15	defendant's Exhibit 913, which has production 2:53:36PM	15	time that a European agency would release or 2:57:29PM
16	numbers RGN-EYLEA-MYLAN 525081 through 083, and 2:53:39PM	16	indicate a dosing instruction in the absence of 2:57:36PM
17	can you confirm that the top e-mail is an 2:53:46PM	17	data and subsequently was proofed to be a big 2:57:41PM
18	e-mail from Avner Ingerman to you and others 2:53:48PM	18	mistake because subsequent studies I just 2:57:46PM
19	dated February 5th, 2007? 2:53:52PM	19	referred to showed that this resulted in loss 2:57:50PM
20	(Whereupon Exhibit 913 was marked 2:53:55PM	20	of vision, increased blindness, and if you 2:57:56PM
21	for identification.) 2:53:55PM	21	calculate what -- for example, a five to six 2:58:00PM
22	A Well, I agree that it is a document 2:53:57PM	22	average letter loss in a population does for 2:58:04PM
23	that says it's on that date from Avner Ingerman 2:54:01PM	23	millions of people, the number of individuals 2:58:08PM
24	to myself and others. 2:54:05PM	24	who on the outer part of the bell curve and are 2:58:11PM
25	Q And Mr. Ingerman was forwarding to 2:54:07PM	25	legally blind is unfortunately very, very 2:58:16PM

Page 138 1 large. 2:58:19PM 2 Q. Well, whether you agreed with it or 2:58:20PM 3 not, your attorneys didn't tell the PTO when 2:58:21PM 4 they were tauting various standards of care 2:58:26PM 5 that the European regulatory authorities had 2:58:29PM 6 allowed Lucentis dosing at treatment intervals 2:58:32PM 7 that were longer than once per month, right? 2:58:37PM 8 MR. BERL: Objection, lack of 2:58:41PM 9 foundation. Are you referring to that one 2:58:42PM 10 document you showed earlier or the entire 2:58:47PM 11 prosecution history which he hasn't 2:58:50PM 12 reviewed? 2:58:52PM 13 MS. MAZZOCHI: Yes, that's what I 2:58:53PM 14 said. 2:58:53PM 15 MR. BERL: Objection. 2:58:54PM 16 A. I can't speak to whether even this 2:58:56PM 17 was still even utilized in Europe or elsewhere 2:58:59PM 18 at the time of the filings. I also can't speak 2:59:04PM 19 to whether or not our patent attorneys provided 2:59:08PM 20 any of this information or not to the patent 2:59:17PM 21 office. 2:59:21PM 22 Q. Have you ever heard of the PAT 2:59:23PM 23 Survey that is done by the American Society of 2:59:27PM 24 Retina Specialists? 2:59:28PM 25 A. Let me just get myself some water 2:59:31PM	Page 140 Regeneron Protected Material
Page 139 1 for a second. 2:59:31PM Regeneron Protected Material	Page 141 Regeneron Protected Material

Regeneron Protected Material

Regeneron Protected Material

Regeneron Protected Material

Regeneron Protected Material

37 (Pages 142 - 145)

6 Regeneron Protected Material	Page 148 1 could reflect many different kinds of PRN 3:13:05PM 2 regimens. 3:13:10PM 3 MR. BERL: We have been going for 3:13:11PM 4 about an hour, counsel, so let's take a 3:13:12PM 5 break soon. 3:13:14PM 6 Q. Sure. If you thought PRN regimens 3:13:16PM 7 were so inferior, why did you include PRN 3:13:18PM 8 regimens in your '601 and '572 patents? 3:13:21PM 9 MR. BERL: Objection. 3:13:27PM 10 Q. As regimens you consider to be part 3:13:27PM 11 of your present invention? Column 16. 3:13:29PM 12 A. Can you point me to which patent we 3:13:36PM 13 are talking about? 3:13:38PM 14 Q. Either one, '601 patent or '572 3:13:40PM 15 patent, column 16. 3:13:44PM 16 A. (Witness reviewing document.) 3:14:08PM 17 Q. Dr. Yancopoulos, you see that your 3:16:49PM 18 example seven includes a whole host of PRN 3:19:07PM 19 dosing regimens, right? 3:19:11PM 20 A. We are going back a long time and 3:19:13PM 21 I'm trying to remind myself about all this, but 3:19:15PM 22 what I do see is that this is specifically in 3:19:21PM 23 the section dealing with or following the 3:19:26PM 24 section on CRVO where the trial design dosing 3:19:34PM 25 regimens were much different than what were 3:19:41PM
Page 147 Regeneron Protected Material M	Page 149 1 used in the AMD and the DME settings, which 3:19:45PM 2 were limited amount of loads then followed by 3:19:53PM 3 every eight week dosing. In this trial, in 3:19:59PM 4 CRVO -- 3:20:03PM 5 Q. I'm not asking about example six. 3:20:06PM 6 I'm asking about example seven. 3:20:08PM 7 MR. BERL: What is the question 3:20:13PM 8 exactly? 3:20:14PM 9 Q. Example seven. 3:20:15PM 10 MR. BERL: What about it? 3:20:16PM 11 Q. You put a whole series of PRN dosing 3:20:17PM 12 regimens in example seven as within the scope 3:20:20PM 13 of your present invention, right? 3:20:24PM 14 A. And what I was trying to say is that 3:20:54PM 15 these dosing regimens encompass the ways it was 3:20:57PM 16 utilized and the VEGF-Trap was utilized and 3:21:06PM 17 shown to have efficacy in these various 3:21:10PM 18 settings. In this specific example right 3:21:13PM 19 before these dosing regimens is a trial where 3:21:17PM 20 it was used exactly in that manner. And so, 3:21:19PM 21 these dosing regimens encompass both loading 3:21:22PM 22 followed by regular dosing, as well as loading 3:21:29PM 23 followed by PRN dosing. 3:21:34PM 24 Q. Are you saying that the example 3:21:38PM 25 seven dosing regimens are supposed to be 3:21:40PM

38 (Pages 146 - 149)

Page 150		Page 152	
1	limited to just the CRVO indication? 3:21:43PM	1	of variations in this patent. I do see that 3:26:23PM
2	MR. BERL: Objection, misstates 3:21:48PM	2	directly in the paragraphs before the paragraph 3:26:28PM
3	testimony. And let's take a break after 3:21:49PM	3	that you are referring to, it refers to the 3:26:31PM
4	this question. We have been going for 3:21:51PM	4	fact that physicians and other qualified 3:26:34PM
5	well over an hour. 3:21:53PM	5	medical professionals can use their own 3:26:39PM
6	A. What I was saying was that we have 3:21:54PM	6	judgment to utilize any of these dosing 3:26:43PM
7	many examples of different regimens used in 3:22:00PM	7	regimens and even create further variations 3:26:46PM
8	different trials and the last example right 3:22:04PM	8	based on their own assessments. So, I don't 3:26:50PM
9	before the dosing regimens is one example where 3:22:09PM	9	know if this section is referring to that or 3:26:55PM
10	one is using loading followed by PRN. The 3:22:13PM	10	what it is exactly referring to. I don't 3:26:59PM
11	example seven dosing regimens are trying to 3:22:16PM	11	understand the legal phraseology here and why 3:27:02PM
12	include or encompass examples of the dosing 3:22:20PM	12	all of these are included herein. 3:27:05PM
13	regimen that were covered by all of the 3:22:25PM	13	MR. BERL: Okay, let's take a break. 3:27:08PM
14	previous trials, including both regular dosing 3:22:28PM	14	MS. MAZZOCHI: We can take a break. 3:27:14PM
15	followed by regular dosing or regular dosing 3:22:34PM	15	THE VIDEOGRAPHER: We are going off 3:27:16PM
16	followed by PRN dosing as we had clinical trial 3:22:37PM	16	the record at 3:27 p.m. 3:27:17PM
17	data using many of these approaches. 3:22:41PM	17	(Off the record.) 3:27:20PM
18	Q. Including for AMD, right? 3:22:44PM	18	THE VIDEOGRAPHER: We are back on 3:40:37PM
19	MR. BERL: Objection. 3:22:49PM	19	the record at 3:40 p.m. 3:40:38PM
20	A. For AMD the data that we showed -- 3:22:50PM	20	Q. Dr. Yancopoulos, the ophthalmology 3:40:41PM
21	if we turn back to it -- 3:22:54PM	21	manuscript, DX912, that you published with 3:40:45PM
22	Q. Well, didn't you say column 17, 3:22:58PM	22	Dr. Heier in 2012, you originally tried to have 3:40:49PM
23	lines 16 to 20, that, "Any of the foregoing 3:23:00PM	23	that published in the New England Journal of 3:40:53PM
24	administration regimens may be used for the 3:23:09PM	24	Medicine, right? 3:41:00PM
25	treatment of e.g., age-related macular 3:23:11PM	25	A. That's quite possible but I don't 3:41:06PM
Page 151		Page 153	
1	degeneration (e.g., wet AMD, exudative AMD)," 3:23:15PM	1	really remember. 3:41:27PM
2	et cetera? 3:23:20PM	2	Q. Well, let me give you a document 3:41:28PM
3	A. I don't believe I said that. What I 3:23:21PM	3	that I will mark as Defendant's Exhibit 915, 3:41:29PM
4	was saying -- 3:23:22PM	4	which has production numbers RGN-EYLEA-MYLAN 3:41:31PM
5	Q. Column 17. 3:23:23PM	5	501236 through 501248. And can you confirm 3:41:38PM
6	A. Column 17. 3:23:23PM	6	that at the -- that the top e-mail in this is 3:41:49PM
7	Q. Yep. Starting at line 16. Do you 3:23:23PM	7	from you dated January 19, 2012, subject "Re: 3:41:55PM
8	see where it says, "Any of the foregoing 3:23:34PM	8	From Drs. Brown and Kaiser- FW: Decision 3:42:01PM
9	administration regimens may be used for the 3:23:36PM	9	regarding VIEW ms," meaning manuscript, "New 3:42:05PM
10	treatment of, e.g., age-related macular 3:23:39PM	10	England Journal of Medicine, 11-13378?" 3:42:08PM
11	degeneration (e.g., wet AMD, exudative AMD)," 3:23:44PM	11	(Whereupon Exhibit 915 was marked 3:42:15PM
12	et cetera? Do you see that language? 3:23:50PM	12	for identification.) 3:42:15PM
13	A. I see where it says that. 3:23:53PM	13	A. Yes, that's what it says. 3:42:15PM
14	Q. All right. So, that's referring to 3:23:54PM	14	Q. All right. And if you can go to the 3:42:17PM
15	all of the dosing regimens in example seven as 3:23:57PM	15	second page of the exhibit this is an e-mail 3:42:20PM
16	well, right? 3:24:00PM	16	from the -- on behalf of the Editorial Board of 3:42:30PM
17	MR. BERL: Objection. 3:24:04PM	17	the New England Journal of Medicine, right, 3:42:34PM
18	A. (Witness reviewing document.) I'm 3:25:00PM	18	dated January 17, 2012? 3:42:37PM
19	not sure what the question is. 3:25:39PM	19	A. Say that again, please. 3:42:42PM
20	Q. The dosing regimens that included 3:25:43PM	20	Q. Second page of Exhibit 915, it's an 3:42:43PM
21	PRN dosing in example seven apply to AMD, 3:25:46PM	21	e-mail from the -- on behalf of The Editorial 3:42:48PM
22	age-related macular degeneration treatments, 3:25:54PM	22	Board of the New England Journal of Medicine 3:42:52PM
23	right? 3:26:00PM	23	dot org sent Tuesday January 17, 2012? 3:42:55PM
24	A. I'm not sure I appreciate or 3:26:12PM	24	A. That's what it says, yes. 3:42:58PM
25	understand the intention of including all sorts 3:26:16PM	25	Q. And the subject is again, 3:43:00PM

Page 154		Page 156	
1	"VEGF-Trap- Eye vs. Ranibizumab in Two Phase 3 3:43:01PM	1	in risk of endophthalmitis and retinal 3:46:17PM
2	Studies of Age-Related Macular Degeneration" 3:43:07PM	2	detachment achieved by reducing the number of 3:46:21PM
3	A. Yes. 3:43:11PM	3	injections in year 1 by 5 for the VTE 2q8 3:46:24PM
4	Q All right. And if we go forward to 3:43:11PM	4	group." That is referring to the every other 3:46:30PM
5	the page that ends in 2139, we see that the 3:43:14PM	5	month dosing group, right? 3:46:34PM
6	individual representing the New England Journal 3:43:21PM	6	A. Well, perhaps I should read this 3:46:38PM
7	of Medicine who signed off on this letter was 3:43:24PM	7	document because it's been a long time. 3:46:40PM
8	Elizabeth Phimister, Ph.D., Deputy Editor? 3:43:27PM	8	Q. Well, 2Q8 is referring to the every 3:46:43PM
9	A. Where do you see page numbers on 3:43:43PM	9	other month dosing, right? 3:46:46PM
10	this? 3:43:45PM	10	A. I just would like to familiarize 3:46:49PM
11	Q Lower right-hand corner, the one 3:43:45PM	11	myself with this whole document before I answer 3:46:50PM
12	that ends in 239. 3:43:48PM	12	questions about it. (Witness reviewing 3:46:54PM
13	A. Oh, I see. Yes, Yours Truly. 3:43:51PM	13	document.) 3:47:01PM
14	Elizabeth G. Phimister. 3:43:58PM	14	Q. Are you ready, Doctor? 3:55:58PM
15	Q. Do you know who she is? 3:44:00PM	15	A. Almost. Okay. 3:55:59PM
16	A. It says that she is deputy editor, 3:44:02PM	16	Q. So, we are in DX915 at 501241 and I 3:57:36PM
17	New England Journal of Medicine. 3:44:05PM	17	was pointing you to point number 18 from 3:57:42PM
18	Q. Have you ever met her before? 3:44:06PM	18	reviewer number one talking about your 3:57:44PM
19	A. I may have. I don't remember. 3:44:12PM	19	submitted manuscript page 11. And midway down, 3:57:45PM
20	Q. And one of the -- if you go back to 3:44:13PM	20	the reviewer was talking about the number of 3:57:51PM
21	the top of the e-mail sent to Ursula 3:44:20PM	21	injections in the VTE 2q8 group. 2q8 is 3:57:56PM
22	Schmidt-Erfuth from the New England Journal of 3:44:27PM	22	referring to every other week -- I'm sorry, 3:58:03PM
23	Medicine she says, "Dear Dr. Schmidt-Erfuth, 3:44:30PM	23	every other month dosing or every eight week's 3:58:05PM
24	Your manuscript "VEGF Trap-Eye vs Ranibizumab 3:44:34PM	24	dosing, right? 3:58:08PM
25	in Two Phase 3 Studies of Age-Related Macular 3:44:38PM	25	A. Yes. 3:58:09PM
Page 155		Page 157	
1	"Degeneration" has been evaluated by outside 3:44:42PM	1	Q. And the VTE is referring to 3:58:09PM
2	reviewers, one of our internal statisticians, 3:44:45PM	2	afibercept? 3:58:12PM
3	and by the editors. We do not find it 3:44:48PM	3	A. Yes. 3:58:13PM
4	acceptable for publication in its present form. 3:44:50PM	4	Q. And if we look at the last four 3:58:13PM
5	We share the concerns of the reviewers 3:44:53PM	5	lines from the New England Journal of 3:58:18PM
6	regarding the interpretation of the results of 3:44:55PM	6	Medicine's comment, the reviewer said, "While 3:58:19PM
7	the studies that you describe, and those 3:44:58PM	7	the argument of decreased burden for the 3:58:26PM
8	published studies." So, does this help refresh 3:44:59PM	8	patient by eliminating 5 monitoring visits in 3:58:29PM
9	your recollection that you submitted a 3:45:03PM	9	the first year is solid, the argument for 3:58:32PM
10	manuscript about the VIEW 1/VIEW 2 studies to 3:45:05PM	10	increased patient safety is overstated, 3:58:34PM
11	the New England Journal of Medicine and they 3:45:09PM	11	particularly relatively to ranibizumab PRN." 3:58:38PM
12	rejected it? 3:45:11PM	12	Do you see that? 3:58:42PM
13	A. Well, the next line says, "We would 3:45:23PM	13	A. Yes, I see that. 3:58:44PM
14	be willing to consider a substantially revised 3:45:25PM	14	Q. And that argument of your regimen 3:58:45PM
15	version that responds to the enclosed 3:45:28PM	15	having increased patient safety is the one that 3:58:48PM
16	comments." So, this is not a rejection. But 3:45:32PM	16	we saw your attorneys making to the PTO as to 3:58:51PM
17	it does remind me that yes, we did submit it to 3:45:38PM	17	why you're dosing regimen was nonobvious, 3:58:56PM
18	the New England Journal of Medicine. 3:45:43PM	18	right? 3:59:00PM
19	Q. Let's take a look at reviewer one's 3:45:46PM	19	MR. BERL: Objection. 3:59:01PM
20	comment, point number 18, that appears on the 3:45:51PM	20	A. I think this referee's comments have 3:59:22PM
21	page ending in 241. Let me know when you are 3:45:57PM	21	to be taken into context. It relates to what 3:59:28PM
22	there. 3:46:02PM	22	we were discussing before. PRN, which was 3:59:31PM
23	A. Yes. 3:46:10PM	23	controversial at the time because some 3:59:38PM
24	Q. The reviewer wrote regarding page 3:46:12PM	24	physicians believed in it but has largely 3:59:43PM
25	11, "The authors repeatedly cite the decrease 3:46:13PM	25	failed the test of time because it's now an 3:59:47PM

Page 158		
1	obsolete treatment modality because physicians	3:59:51PM
2	recognize it results in suboptimal efficacy for	3:59:55PM
3	the patients. So, it is true that if you give	4:00:02PM
4	patients less injections as you would with PRN,	4:00:05PM
5	because you're getting less injections, you	4:00:08PM
6	have less of a safety concern but you're not	4:00:12PM
7	delivering as good efficacy as has been proven	4:00:17PM
8	by the test of time and that's why nobody uses	4:00:21PM
9	PRN dosing anymore or very few people use it.	4:00:24PM
10	So, as I said before if you don't	4:00:30PM
11	treat patients, you're not going to get the	4:00:34PM
12	safety burden that comes with an injection into	4:00:39PM
13	the eye. On the other hand, if you don't treat	4:00:42PM
14	patients, you're going to lose vision. So,	4:00:46PM
15	it's somewhat of an irrelevant comparison	4:00:49PM
16	unless it's put into that context. So --	4:00:54PM
17	Q. Okay.	4:00:58PM
18	A. Let me finish my answer. So, if you	4:00:59PM
19	compare it to what was then and what was proven	4:01:01PM
20	to be over time the gold standard of treatment	4:01:05PM
21	that best results in return and maintenance of	4:01:10PM
22	vision, which was at the time monthly	4:01:14PM
23	ranibizumab, then as correctly stated in the	4:01:18PM
24	paper, you're saving five injections and the	4:01:21PM
25	need for five monthly visits to the hospital	4:01:26PM

Page 159		
1	for the first year which results in traumatic	4:01:31PM
2	decrease in the treatment burden and the saving	4:01:36PM
3	of all the associated potential safety events	4:01:39PM
4	associated with saving all those injections	4:01:43PM
5	while maintaining the gold standard efficacy	4:01:46PM
6	result equivalent to monthly ranibizumab.	4:01:52PM
7	Q. Well, if we look at the comments	4:01:54PM
8	from reviewer two on the next page, 501242 in	4:01:57PM
9	DXN15, starting the fifth line down, first full	4:02:01PM
10	sentence. This reviewer said, "The primary	4:02:06PM
11	finding that may differentiate VEGF-Trap as	4:02:09PM
12	compared to the many prior reports is an	4:02:14PM
13	apparently noninferior semi-monthly dosing	4:02:16PM
14	schedule as opposed to monthly dosing.	4:02:21PM
15	Although clearly of burden benefit to patients	4:02:25PM
16	and physicians, this is not a major conceptual	4:02:29PM
17	advance." Do you see that?	4:02:32PM
18	A. I see that.	4:02:38PM
19	Q. Okay. So, this reviewer from the	4:02:38PM
20	New England Journal of Medicine didn't quite	4:02:41PM
21	find this outcome as Earth shattering as	4:02:45PM
22	apparently you did; is that fair?	4:02:49PM
23	MR. BERL: Objection.	4:02:52PM
24	A. Well, I think you have to read the	4:03:00PM
25	next sentence to understand what they mean by a	4:03:03PM

Page 160		
1	conceptual advance. So, what they say is that,	4:03:06PM
2	"It is clearly a burden benefit to patients and	4:03:09PM
3	physicians." The question is is that	4:03:14PM
4	conceptual. This individual is not calling	4:03:20PM
5	that a conceptual advance because they are in	4:03:23PM
6	the next paragraph talking about the fact that	4:03:26PM
7	VEGF-Trap and ranibizumab are, "Both antiVEGF	4:03:30PM
8	agents with high affinity for VEGF." So, "it's	4:03:35PM
9	not surprising that they have similar clinical	4:03:38PM
10	effects." So, that's what they refer to. It's	4:03:41PM
11	not as if we and we never claimed that we	4:03:45PM
12	discovered how the anti-VEGF can really have a	4:03:49PM
13	benefit in this disease. That's what they are	4:03:57PM
14	referring to as a conceptual advance	4:03:59PM
15	understanding defining the mechanism of action	4:04:01PM
16	of this class of drugs. That is their	4:04:05PM
17	definition of a conceptual advance. They are	4:04:08PM
18	pointing out -- they are merely not calling it	4:04:11PM
19	a conceptual advance. That it is clearly a	4:04:15PM
20	burden benefit to patients and physicians, and	4:04:18PM
21	if you're focusing on treatment burden, I	4:04:21PM
22	think, as this reviewer states, he or she and	4:04:28PM
23	essentially everybody else would agree that it	4:04:36PM
24	is clearly a burden benefit to patients and	4:04:39PM
25	physicians.	4:04:42PM

Page 161		
1	Q. Right. And the reviewer, however,	4:04:42PM
2	again, didn't consider it to be particularly	4:04:45PM
3	Earth shattering because in the last paragraph	4:04:47PM
4	reviewer two said, "Although these data	4:04:51PM
5	certainly indicate that VEGF-Trap Eye can be	4:04:53PM
6	essentially as beneficial as ranibizumab in	4:04:56PM
7	treatment of neovascular AMD (and perhaps at a	4:05:01PM
8	modest reduced treatment frequency), its	4:05:06PM
9	mechanism of action, molecular target," et	4:05:09PM
10	cetera, "are not surprising." So, again, the	4:05:12PM
11	reviewer thought that this reduction in	4:05:15PM
12	treatment burden was, in the grand scheme of	4:05:18PM
13	things modest, not anything Earth shattering or	4:05:22PM
14	ground breaking, right?	4:05:26PM
15	MR. BERL: Objection, misstates the	4:05:27PM
16	document.	4:05:29PM
17	A. It's hard to judge subjective	4:05:33PM
18	comments and what that reflects in terms of	4:05:36PM
19	societal and patient and physician burden	4:05:43PM
20	issues. The author states that this is clearly	4:05:46PM
21	a burden benefit to patients and physicians,	4:05:54PM
22	and their major point is that it is not a	4:05:57PM
23	conceptual advance because the mechanism of	4:06:05PM
24	action in the molecular target are not	4:06:08PM
25	surprising based on the previous results. So,	4:06:11PM

Page 162

1 it is a matter of -- 4:06:16PM
2 Q. Right. And the burden is modest? 4:06:16PM
3 A. Well, it's a matter of -- 4:06:17PM
4 MR. BERL: Just let him answer. 4:06:17PM
5 (crosstalk). 4:06:17PM
6 A. Well, it's a matter of a subjective 4:06:20PM
7 assessment when in one paragraph they say it's 4:06:27PM
8 clearly a burden benefit, then they describe it 4:06:31PM
9 differently in another paragraph, it turns out 4:06:34PM
10 that ultimately physicians and patients spoke 4:06:38PM
11 with their choices and the vast majority of 4:06:44PM
12 physicians and patients over time have taken 4:06:47PM
13 advantage of what they see is the clear burden 4:06:49PM
14 benefit while maintaining the efficacy gains. 4:06:57PM
15 And so, they have spoken by rapidly adopting 4:07:04PM
16 EYLEA to become the leading gold standard of 4:07:11PM
17 care. 4:07:14PM
18 Q. Now, reviewer number 3, first full 4:07:15PM
19 paragraph, last five lines, criticized your 4:07:18PM
20 paper as saying, "The paper also lacks balance 4:07:22PM
21 and is much too heavy handed in its treatment 4:07:25PM
22 of every two month dosing, so much so that it 4:07:27PM
23 comes off as the beginning of a marketing 4:07:31PM
24 campaign. There were two other arms of the 4:07:34PM
25 study that are barely discussed. Regeneron Protected Material

Regeneron Protected Material

Page 163

Regeneron Protected Material

Page 165

Regeneron Protected Material

Page 166		Page 168	
Regeneron Protected Material			
2 Q. Let's go back to DX915 and go to	4:13:00PM	1 similar is somewhat irrelevant to what the	4:16:25PM
3 page 501244. This is, again, reviewer number	4:13:04PM	2 actual results were, and the test of time has	4:16:28PM
4 three comments. This time item 9, page 7. The	4:13:09PM	3 shown the field has pretty much abandoned the	4:16:33PM
5 reviewer characterized your non-inferiority	4:13:15PM	4 so-called PRN dosing because it is accepted	4:16:39PM
6 margin of 10 percent as, "Very loose, an easy	4:13:19PM	5 that they yield inferior results in the	4:16:42PM
7 margin to hit." Do you see that?	4:13:24PM	6 side-by-side comparisons in terms of numerical	4:16:47PM
8 A. I see those words.	4:13:27PM	7 numbers they were ten times worse.	4:16:52PM
9 Q. All right. And the reviewer said a	4:13:31PM	8 Q. Right. Well, if we take a look at	4:16:54PM
10 couple of lines down, "This wide margin becomes	4:13:33PM	9 page 501245, the bottom of the page, reviewer	4:16:56PM
11 problematic for you when you try to compare	4:13:36PM	10 three comment, paragraph 21, also talking about	4:17:00PM
12 your study to other trials, because if they had	4:13:39PM	11 your page 11 arguments that one of the other	4:17:04PM
13 used it, they too would have been non-inferior	4:13:42PM	12 reviewers had objected to. Again, this line —	4:17:08PM
14 for all groups. For example, if CATT had used	4:13:45PM	13 I'm sorry, this number of letter argument that	4:17:10PM
15 the same definition, all four of the treatment	4:13:49PM	14 you are making in comparisons to other PRN	4:17:13PM
16 arms would have easily been non-inferior. So,	4:13:52PM	15 regimens or CATT, the reviewer says, "You imply	4:17:17PM
17 you have no basis for stating or implying that	4:13:55PM	16 that the numerically smaller gains with PRN	4:17:22PM
18 other treatments in other trials were less	4:13:59PM	17 dosing (less than 1.7 and less than 2.6) in	4:17:24PM
19 successful, including the PRN arms of HARBOR	4:14:02PM	18 CATT are important, and yet the differences	4:17:28PM
20 and CATT when their definition of	4:14:07PM	19 between treatment groups and your own study are	4:17:31PM
21 non-inferiority was much tighter than your	4:14:08PM	20 of the exact same magnitude and you accept that	4:17:33PM
22 own." Do you see that?	4:14:12PM	21 they are equivalent or not important." So the	4:17:36PM
23 A. The non-inferiority margins that we	4:14:22PM	22 reviewers were actually objecting to that	4:17:39PM
24 used were actually set by the FDA. When you	4:14:25PM	23 argument that you just — throughout there,	4:17:42PM
25 are trying to do cross-study comparisons,	4:14:31PM	24 right, that you can't say, for example, that	4:17:45PM
		25 the number of letter differences when the	4:17:47PM
Page 167		Page 169	
1 you're not doing it based on the preset margins	4:14:34PM	1 variability between your own same trial arms	4:17:49PM
2 that were used or were set, but actually by the	4:14:42PM	2 can vary so much to then turn around and say	4:17:54PM
3 actual results, and what the actual results	4:14:45PM	3 that similar numbers are meaningful, and, for	4:17:58PM
4 showed was this regimen that we talk about in	4:14:50PM	4 example, the CATT study, you can't have it both	4:18:00PM
5 the largest and most convincing dataset. Let e	4:14:54PM	5 ways, you can't have your cake and eat it too?	4:18:03PM
6 take you — integrated analysis that was shown	4:14:56PM	6 MR. BERL: Objection, compound,	4:18:06PM
7 in the studies, viewer one studies, and	4:15:00PM	7 vague. You misread the document. You're	4:18:08PM
8 described in the ophthalmology paper.	4:15:08PM	8 not showing him the underlying data. You	4:18:10PM
9 The every two months regimen	4:15:13PM	9 haven't shown him the manuscript even.	4:18:13PM
10 resulted in vision gains within .3 letters of	4:15:15PM	10 This is all improper. It's useless too	4:18:15PM
11 the monthly regimens, whereas in CATT, for	4:15:24PM	11 but it's improper. I'm leave the	4:18:18PM
12 example, they had ten times the loss of vision	4:15:31PM	12 objection at that.	4:18:20PM
13 when measured in letters. So, it's not about	4:15:37PM	13 A. Well, I would just add the comment	4:18:25PM
14 the margins that you set going in, but it's	4:15:40PM	14 that the data that we felt and that the field	4:18:27PM
15 about the results that you get going out. So,	4:15:43PM	15 has felt over time was the best data set	4:18:34PM
16 you get numerically, it was pointed out in the	4:15:46PM	16 representing our data was what we called the	4:18:41PM
17 paper, much greater loss of vision and time.	4:15:53PM	17 integrated dataset where we have created the	4:18:44PM
18 Once again, the test of time has shown that	4:15:58PM	18 largest overall dataset by actually combining	4:18:47PM
19 with PRN, the results only get worse and worse	4:16:01PM	19 multiple studies, and therein the differences,	4:18:51PM
20 and worse, whereas our longer-term results with	4:16:05PM	20 and we used the largest dataset because it is	4:18:57PM
21 our every two month regimen have stood the test	4:16:10PM	21 true, as pointed out here, that when you take	4:19:01PM
22 of time.	4:16:14PM	22 individual studies in smaller numbers of	4:19:04PM
23 So, I'm trying to say that, oh, the	4:16:14PM	23 patients, you can get individual variation.	4:19:06PM
24 results, you know, are similar because the	4:16:18PM	24 But to get at the truth, because we are at	4:19:08PM
25 non-inferior margins that were preset were	4:16:21PM	25 truth seeking here, you combine your datasets	4:19:13PM

Page 170		Page 172	
1	to create the largest most convincing dataset. 4:19:15PM	1	to monthly ranibizumab as the "gold standard." 4:22:35PM
2	And in the integrated analysis, the 4:19:18PM	2	I would avoid this phrase since if it is truly 4:22:39PM
3	differences are tiny between the every two 4:19:21PM	3	the gold standard, why do so very few 4:22:43PM
4	month groups and the monthly dose groups. And 4:19:28PM	4	clinicians use it." Do you see that? 4:22:46PM
5	furthermore, as I said, when you follow the 4:19:33PM	5	MR. BERL: You misread it again. 4:22:49PM
6	test of time, the PRN results just continue to 4:19:35PM	6	Objection. 4:22:50PM
7	diverge and get worse for monthly dosing while 4:19:39PM	7	A. Could you point me to the section? 4:22:51PM
8	the every two month regimen of EYLEA maintains 4:19:44PM	8	Q. Yes. It's about -- 4:22:54PM
9	its benefit with time. 4:19:49PM	9	A. I'm sorry, what page are we on? 4:22:59PM
10	So, what we said we saw here has 4:19:50PM	10	Q. Page 501246 in DX915, reviewer 4:23:02PM
11	stood up to follow-up analyses and follow-up 4:19:55PM	11	three, about 19 lines -- 18, 19 lines down, the 4:23:10PM
12	data, and what we said about PRN has also stood 4:19:57PM	12	reviewer states, "In the next sentence, you 4:23:15PM
13	up, which is why the field has largely 4:20:02PM	13	refer to monthly ranibizumab as the "gold 4:23:19PM
14	abandoned it. And I should point out that it 4:20:04PM	14	standard." I would avoid this phrase since if 4:23:26PM
15	is very likely that at least one, if not all of 4:20:07PM	15	it is truly the gold standard, why do so very 4:23:29PM
16	the reviewers here, were participants in the 4:20:11PM	16	few clinicians use it." Do you see that? 4:23:33PM
17	CATT trials and these PRN trials and were very 4:20:16PM	17	MR. BERL: Objection. You continue 4:23:40PM
18	conflicted in their points of views which is 4:20:20PM	18	to misread it. I can only conclude that 4:23:42PM
19	probably why they were trying to -- 4:20:23PM	19	you are doing that on purpose to mislead 4:23:47PM
20	Q. You don't know that? 4:20:26PM	20	the witness. Is it random that you 4:23:51PM
21	MR. BERL: Objection. Let him 4:20:27PM	21	continue to misread it in the same way? 4:23:52PM
22	finish his answers. Were you done, 4:20:28PM	22	MS. MAZZOCHI: No, I'm reading it 4:23:52PM
23	Dr. Yancopoulos? 4:20:31PM	23	verbatim. 4:23:53PM
24	A. I was just going to add that in 4:20:33PM	24	MR. BERL: You are not. The record 4:23:54PM
25	general, the way journals work is they send 4:20:37PM	25	will reflect that you are not. You are 4:23:56PM
Page 171		Page 173	
1	your articles to the people who have competing 4:20:43PM	1	adding words, both times the same word. 4:23:58PM
2	points of views to get those competing points 4:20:46PM	2	So, I'll take you at your word that it was 4:24:01PM
3	of views and try to put things into 4:20:48PM	3	a mistake and you're not intentionally 4:24:04PM
4	perspective. It's very likely, and we have 4:20:51PM	4	trying to mislead the witness. Objection, 4:24:05PM
5	even had other reasons to believe, that people 4:20:57PM	5	misstates the document. 4:24:08PM
6	involved in the CATT and the PRN studies were 4:21:01PM	6	A. Well, we refer to it as the gold 4:24:14PM
7	involved in reviewing this process. And so, 4:21:05PM	7	standard in terms of providing the best care to 4:24:17PM
8	they were conflicted as they were trying to 4:21:09PM	8	the patient as supported by all the data we 4:24:25PM
9	protect the point of view, which as I said, the 4:21:11PM	9	believed at the time in which I said has been 4:24:29PM
10	test of time has shown has failed. 4:21:14PM	10	now confirmed by additional years of follow-up 4:24:33PM
11	Q. Do you have any evidence that any of 4:21:16PM	11	that -- which is why PRN has largely been 4:24:38PM
12	the reviewers from the New England Journal of 4:21:17PM	12	rejected by the community that they recognize, 4:24:45PM
13	Medicine participated in the CATT or other 4:21:19PM	13	regardless of how many might be using it at a 4:24:48PM
14	trials and had a conflict of interest when it 4:21:24PM	14	given point in time or not, that it is now 4:24:50PM
15	came to reviewing your manuscript? 4:21:27PM	15	recognized. It was not the optimal way to 4:24:54PM
16	MR. BERL: Objection, compound. 4:21:30PM	16	treat patients because it resulted in profound 4:24:57PM
17	A. Any -- any such evidence would be 4:21:52PM	17	loss of vision, and if you integrated over the 4:25:01PM
18	considered -- other than looking at the points 4:22:07PM	18	millions of patients who were receiving 4:25:05PM
19	that were in here and how they were phrased and 4:22:09PM	19	treatment, it was leading to very large numbers 4:25:08PM
20	so forth, other than that, they would be 4:22:11PM	20	of patients losing vision and even going 4:25:11PM
21	considered hearsay. 4:22:16PM	21	legally blind. So, the gold standard should 4:25:14PM
22	Q. One of the other items that reviewer 4:22:18PM	22	refer to not what might be the most common 4:25:17PM
23	three mentioned -- and this is on page 501246, 4:22:23PM	23	usage at the time. The gold standard refers to 4:25:22PM
24	about a third of the way down the page, the 4:22:25PM	24	what delivers the best benefit to the patients 4:25:24PM
25	reviewer said, "In the next sentence you refer 4:22:32PM	25	in this case, the best ability to restore, and 4:25:30PM

Page 174		Page 176	
1	save and maintain their precious vision. 4:25:34PM	1	paper in Ophthalmology 2012 when patients were 4:29:08PM
2	Q. But when your attorneys were in 4:25:37PM	2	put on or switched to PRN regimens, they 4:29:15PM
3	front of the PTO arguing that monthly 4:25:39PM	3	progressively lost vision compared to monthly 4:29:18PM
4	ranibizumab was the standard of care, you 4:25:42PM	4	ranibizumab, which was then the gold standard 4:29:23PM
5	equate that to the gold standard, not 4:25:45PM	5	because the PRN regimens kept just getting 4:29:26PM
6	necessarily what most clinicians were actually 4:25:48PM	6	worse and worse in comparison over time. 4:29:29PM
7	doing in the field? 4:25:51PM	7	Whereas, in our studies, the every 4:29:31PM
8	MR. BERL: Objection, lack of 4:25:53PM	8	other month regimen of EYLEA managed to stay 4:29:38PM
9	foundation. 4:25:54PM	9	flat and within very tiny differences compared 4:29:44PM
10	A. I don't know what our lawyers are 4:26:00PM	10	to the monthly regimens. So yes, the preset 4:29:47PM
11	referring to when they are making various 4:26:03PM	11	ways of assessing non-inferiority were 4:29:52PM
12	arguments. I'm referring to what I mean when I 4:26:07PM	12	different but the results were also very 4:29:55PM
13	say the gold standard. 4:26:11PM	13	different. With PRN dosing, you continue to 4:29:58PM
14	Q. If you can take a look at the next 4:26:16PM	14	lose benefit compared to monthly ranibizumab 4:30:02PM
15	page where we get into comments from reviewer 4:26:19PM	15	over time, whereas we were able to show with 4:30:05PM
16	four. This is on page 501247 in DX915, their 4:26:22PM	16	every other month EYLEA, you're able to 4:30:08PM
17	point number eight. Again, they criticized 4:26:26PM	17	maintain that benefit with time. 4:30:11PM
18	your statements on page 11 in the draft 4:26:33PM	18	Q. If you thought PRN dosing was going 4:30:13PM
19	manuscript and said, "Since the non-inferiority 4:26:35PM	19	to be so awful at the time, why did you agree 4:30:17PM
20	assessment was made only for moderate vision 4:26:39PM	20	to let PRN dosing be the regimen for the second 4:30:20PM
21	loss (avoiding loss of 15 letters or more), the 4:26:43PM	21	year of the VIEW 1 and VIEW 2 study? 4:30:23PM
22	study design was not the same as CATT. The 4:26:47PM	22	MR. BERL: Objection. 4:30:27PM
23	margin chosen for non-inferiority was chosen as 4:26:51PM	23	A. If people could go back to those 4:30:37PM
24	10 percent for the primary endpoint, 5 percent 4:26:55PM	24	times, and I'm sure people could find them part 4:30:43PM
25	was selected as clinical equivalence. These 4:26:59PM	25	of the record, I was a very vocal, even prior 4:30:47PM
Page 175		Page 177	
1	were all quite different from the CATT design. 4:27:02PM	1	to our studies, opponent to PRN, because 4:30:51PM
2	The authors should clarify on page 11." Do you 4:27:05PM	2	literally, you only treat people when they are 4:30:55PM
3	agree that the CATT design had a more stringent 4:27:09PM	3	starting to fail, and essentially, I equate it 4:30:58PM
4	letter standard than the one that was in your 4:27:14PM	4	to just continuously, you know, try to make up 4:31:01PM
5	non-inferiority trial comparing your eight-week 4:27:18PM	5	for failure. That's not a great strategy for 4:31:04PM
6	dosing regimen to monthly ranibizumab? 4:27:24PM	6	success. I thought that a regular treatment 4:31:07PM
7	MR. BERL: Objection. 4:27:27PM	7	that stayed ahead of failure would have a 4:31:10PM
8	A. Nowhere in here does it say what you 4:27:41PM	8	better outcome. However, there was a 4:31:13PM
9	said. What it merely says here is the criteria 4:27:44PM	9	controversy and when one needs to engage a lot 4:31:19PM
10	for non-inferiority were all quite different 4:27:48PM	10	of cites and a lot of in investigators to be 4:31:28PM
11	from the CATT design. In the CATT design, they 4:27:52PM	11	able to carry out your studies, the design 4:31:32PM
12	were using a non-inferiority margin of letter 4:27:58PM	12	sometimes is a negotiation. This is why in 4:31:44PM
13	differences. The FDA mandated end point which 4:28:04PM	13	some parts of the study, we used regimens that 4:31:48PM
14	is what we were required to use based on our 4:28:08PM	14	we thought maybe might not be as effective but 4:31:51PM
15	discussions with the FDA was the number of 4:28:22PM	15	it was part of trying to engage and include as 4:31:55PM
16	individuals losing 15 or more letters. And so, 4:28:26PM	16	many cites and investigators as possible. 4:32:01PM
17	yes, it's very true that as is stated, not in 4:28:33PM	17	Q. Well, which cites and investigators 4:32:04PM
18	your question but in this paragraph, that the 4:28:39PM	18	wanted to ensure there was going to be PRN 4:32:06PM
19	non-inferior margins were all prospectively set 4:28:41PM	19	dosing? Were they the ones on the Bayer side? 4:32:09PM
20	quite differently in our trials as from the 4:28:47PM	20	MR. BERL: Objection. 4:32:12PM
21	CATT design. That does not in any way, shape 4:28:50PM	21	A. Well, all the investigators and so 4:32:14PM
22	nor form change the outcome of what was 4:28:53PM	22	forth, I mean, they are all independent. I 4:32:17PM
23	observed both in the first year but also with 4:28:56PM	23	don't know if they are on one side or another. 4:32:19PM
24	subsequent follow-up that, as was described 4:28:59PM	24	They are essentially independent academic 4:32:22PM
25	nicely, in the discussion of the Heier, et al. 4:29:03PM	25	investigators. 4:32:26PM

Page 178			Page 180		
1	Q. Okay. Which of your academic	4:32:27PM	1	dated Saturday, June 9, 2012?	4:40:14PM
2	investigators who are going -- who you were	4:32:30PM	2	A. That's what it says on this	4:40:17PM
3	relying on to conduct VIEW 1, VIEW 2 clinical	4:32:31PM	3	document.	4:40:20PM
4	studies were insistent that there had to be a	4:32:37PM	4	Q. All right. And can you confirm as	4:40:20PM
5	PRN dosing regiment component?	4:32:40PM	5	part of this e-mail thread, you saw the	4:40:22PM
6	MR. BERL: Objection.	4:32:43PM	6	additional round of New England Journal of	4:40:24PM
7	A. All these years later, it's	4:32:53PM	7	Medicine reviewer comments after you	4:40:25PM
8	impossible for me to remember and it's not as	4:32:55PM	8	resubmitted a revised manuscript?	4:40:29PM
9	if they were insisting. It was what they were	4:33:00PM	9	A. Yes.	4:40:40PM
10	negotiating so as to be participating or	4:33:04PM	10	Q. And the New England Journal of	4:40:41PM
11	participants in the trial.	4:33:13PM	11	Medicine said that, "Although the paper has	4:40:41PM
12	Q. Now, you have been talking about	4:33:24PM	12	clearly improved we must decline the manuscript	4:40:45PM
13	the, quote/unquote, gold standard back then.	4:33:26PM	13	as it currently stands," right?	4:40:48PM
14	Would you agree that the gold standard now is	4:33:28PM	14	A. Yes, I see that.	4:40:54PM
15	actually not fixed dosing, it's treat and	4:33:33PM	15	Q. And again, if we look at the	4:41:03PM
16	extend?	4:33:36PM	16	comments from reviewer number four, the bulk of	4:41:05PM
17	MR. BERL: Objection.	4:33:46PM	17	which appear on page 493993, again, the	4:41:09PM
18	A. I believe that treat and extend is a	4:34:37PM	18	reviewer took issue with how you were	4:41:14PM
19	major improvement over so called PRN dosing,	4:34:41PM	19	discussing letter improvements within VIEW	4:41:16PM
20	though I believe if you are going to use gold	4:34:45PM	20	1/VIEW 2 and comparing and contrasting with the	4:41:20PM
21	standard and by the definition of trying to	4:35:06PM	21	results in the CATT study, right?	4:41:25PM
22	deliver the best care to the most number of	4:35:10PM	22	A. These are the same concerns we	4:41:40PM
23	patients, I believe that it may still be the	4:35:14PM	23	discussed before.	4:41:41PM
24	case that regular dosing regimens can deliver	4:35:18PM	24	Q. Right. So, after the New England	4:41:42PM
25	better results until proven otherwise. As far	4:35:24PM	25	journal of Medicine passed, according to DX916,	4:41:45PM
Page 179			Page 181		
1	as I'm aware, there haven't been clinical	4:35:29PM	1	the e-mail on the cover page from Peter Kaiser	4:41:50PM
2	trials to show that treat and extend can	4:35:32PM	2	sent Saturday, June 9th, 2012, to Jeffrey Heier	4:41:54PM
3	outperform regular dosing.	4:35:35PM	3	and you and others, he said, "Idiots... I guess	4:42:00PM
4	Q. What percentage of physicians who	4:35:38PM	4	Ursula screwed us all, but we cannot let the	4:42:04PM
5	were using EYLEA for AMD are actually using the	4:35:39PM	5	VIEW2 team derail us from being published	4:42:08PM
6	treat and extend protocol?	4:35:44PM	6	quickly... Get Andy to publish this in	4:42:10PM
7	MR. BERL: Objection, lack of	4:35:45PM	7	Ophthalmology and get this nightmare behind us	4:42:13PM
8	foundation.	4:35:46PM	8	(he has already said he would without year 2)." 4:42:15PM	
9	A. I'm sure people have done surveys	4:35:55PM	9	Do you see that?	4:42:18PM
10	but I'm not aware of those results.	4:35:57PM	10	A. Could you keep reading, please?	4:42:19PM
11	Q. I'm going to mark as Defendant's	4:35:58PM	11	Q. "Trying for Lancet with the" -- I	4:42:20PM
12	Exhibit 916 a document with production numbers	4:36:00PM	12	don't want to say the word, "Editor in chief is	4:42:25PM
13	RGN-EYLEA-Mylan 493989 through 994. And can	4:36:02PM	13	a very bad idea, and I am sure he will ask for	4:42:28PM
14	you confirm that top e-mail in this thread is	4:36:14PM	14	the same stuff delaying us further. Enough."	4:42:31PM
15	one from Quan Nguyen dated Saturday, June 9,	4:36:16PM	15	A. He is implying incompetence with the	4:42:34PM
16	2012, to Peter Kaiser, Jeff Heier and cc'ing	4:36:22PM	16	word that he used, and this is what I was also	4:42:37PM
17	you and others?	4:36:26PM	17	referring to in these various documents if you	4:42:41PM
18	(Whereupon Exhibit 916 was marked	4:36:27PM	18	read it in the next line. "Despite I am not	4:42:45PM
19	for identification.)	4:36:27PM	19	paranoid, there is something wrong we do not	4:42:49PM
20	A. (Witness reviewing document.) I was	4:36:56PM	20	know or understand what this paper in the New	4:42:52PM
21	reviewing the document. So was there a	4:40:04PM	21	England Journal of Medicine I would suggest	4:42:54PM
22	question?	4:40:05PM	22	that we submit to another journal," and this is	4:42:56PM
23	Q. Sure. All I was asking you is can	4:40:06PM	23	what I was referring to before. The	4:42:59PM
24	you confirm that the covering e-mail in this	4:40:08PM	24	sophisticated authors who are leaders in the	4:43:04PM
25	thread was from Quan Nguyen to you and others	4:40:11PM	25	field on our paper felt that there was some	4:43:07PM

Page 182			Page 184		
1	sort of bias and the hearsay that I was	4:43:11PM	1	ranibizumab, right?	4:46:10PM
2	referring to about the conflicts of interest in	4:43:16PM	2	MR. BERL: Objection.	4:46:11PM
3	some of the referees.	4:43:18PM	3	A. You asked that question very out of	4:46:11PM
4	The major point that the New England	4:43:21PM	4	context. There is five pages of reviewers'	4:46:13PM
5	Journal of Medicine pointed to in terms of why	4:43:23PM	5	comments and one of the authors is simply	4:46:18PM
6	they were declining the manuscript, if you read	4:43:27PM	6	referring to some and I don't think which data	4:46:21PM
7	the next line, is that it's because they took	4:43:29PM	7	or criticism as being valid, not that they are	4:46:26PM
8	so long in the whole review process, they now	4:43:33PM	8	all valid, and as we pointed out before,	4:46:29PM
9	state that, now, "Two of the reviewers refer to	4:43:36PM	9	reviewer four makes the mistake of not focusing	4:46:33PM
10	data acquired during the second year of the	4:43:43PM	10	on the largest dataset, the integrated	4:46:39PM
11	study," and "we would only be interested in a	4:43:45PM	11	analysis, which essentially shows almost no	4:46:43PM
12	resubmission that includes the year-2 data."	4:43:47PM	12	measurable differences between our every other	4:46:46PM
13	This review process has taken so long that they	4:43:50PM	13	month dosing arm, which is very different than	4:46:50PM
14	now want to further delay it by asking and	4:43:53PM	14	what they saw in CATT and not only the first	4:46:53PM
15	awaiting second-year data. This is despite the	4:43:55PM	15	year but in the second year of CATT. And that	4:46:59PM
16	fact that the first comments among reviewer	4:43:59PM	16	point of view is certainly and the possibility	4:47:02PM
17	number one is that -- let me read it. His	4:44:02PM	17	that some people were conflicted here was	4:47:05PM
18	first comment is, "The authors prove results	4:44:11PM	18	vindicated by the publication in a separate	4:47:08PM
19	from two similarly-designed clinical trials	4:44:23PM	19	peer reviewed paper that allowed all those	4:47:12PM
20	for 4 active treatments for choroidal	4:44:30PM	20	comments to be included in the paper.	4:47:15PM
21	neovascularization secondary to age-related	4:44:35PM	21	Q. Well, it sounds like Peter Kaiser --	4:47:20PM
22	macular degeneration. The finding that dosing	4:44:38PM	22	I mean, he said, get Andy to publish this in	4:47:21PM
23	every 2 months provides outcomes similar to the	4:44:42PM	23	Ophthalmology. It sounded like they'd already	4:47:26PM
24	standard of monthly dosing with ranibizumab is	4:44:46PM	24	prediscussed that Andy, one of the editors at	4:47:29PM
25	important." That's the first comment from the	4:44:49PM	25	Ophthalmology, was just going to publish it and	4:47:32PM
Page 183			Page 185		
1	first reviewer and there are similar comments	4:44:52PM	1	let it pass, right?	4:47:35PM
2	among the other reviewers.	4:44:55PM	2	MR. BERL: Objection.	4:47:37PM
3	Despite this, now they are asking to	4:44:57PM	3	A. I don't know who Andy is and I don't	4:47:45PM
4	wait to get additional year two data. This is	4:44:59PM	4	know what he means by his statements in this	4:47:48PM
5	why the comments from the sophisticated retinal	4:45:03PM	5	other than his statement that he is claiming,	4:47:53PM
6	specialists who are coauthors indicate the fact	4:45:07PM	6	as you read before, that the editors in chief	4:47:56PM
7	that they are paranoid or fear that there is	4:45:10PM	7	involved in reviewing it so far were	4:48:03PM
8	some underlying reason and they suggest that we	4:45:15PM	8	incompetent.	4:48:05PM
9	go to another journal.	4:45:17PM	9	Q. What -- which journal has the higher	4:48:06PM
10	MR. BERL: We've been going more	4:45:21PM	10	prestige ranking amongst physicians in the	4:48:12PM
11	than an hour, so.	4:45:23PM	11	United States, the New England Journal of	4:48:15PM
12	Q. Let's finish up with this document.	4:45:24PM	12	Medicine or Ophthalmology?	4:48:16PM
13	Reviewer number four, though, again, was	4:45:25PM	13	MR. BERL: Objection, vague.	4:48:27PM
14	criticizing your -- what she called or what she	4:45:29PM	14	A. I don't know how any of these	4:48:53PM
15	called the or what he called the, "Fundamental	4:45:33PM	15	rankings relate to quality or believability of	4:48:54PM
16	problem of making comparisons between either	4:45:36PM	16	data in publications in the various journals.	4:49:02PM
17	CATT or HARBOR and VIEW 1/VIEW 2" and one of	4:45:38PM	17	Q. Have you ever gotten any of your	4:49:05PM
18	the covering responsive e-mails from Bernd	4:45:43PM	18	papers published in the New England Journal of	4:49:07PM
19	Kirchof, he said, "The reviewer's comments are	4:45:47PM	19	Medicine?	4:49:10PM
20	valid." So, you know, while I understand	4:45:51PM	20	A. Yes, I have.	4:49:12PM
21	you're assuming that there is a conflict of	4:45:54PM	21	Q. And how many?	4:49:12PM
22	interest, it could also be that the reviewer's	4:45:57PM	22	A. I don't know the exact number.	4:49:18PM
23	comments were valid and they didn't like the	4:45:59PM	23	Q. Did any of them involve clinical	4:49:20PM
24	statistical or the comparisons you were making	4:46:02PM	24	trial data?	4:49:23PM
25	between your VIEW 1/VIEW 2 results and CATT	4:46:04PM	25	A. Yes.	4:49:24PM

Page 186			Page 188		
1	Q. And did they involve conceptual	4:49:24PM	1	Q. All right. But you don't dispute	5:08:37PM
2	ground breaking advances or no?	4:49:31PM	2	that in November -- November 22, 2010,	5:08:38PM
3	MR. BERL: Objection, vague, lack of	4:49:36PM	3	Regeneron issued a press release to announce	5:08:40PM
4	foundation.	4:49:40PM	4	the results of the phase three studies from the	5:08:46PM
5	A. What you are referring to, which may	4:49:44PM	5	VIEW 1 and VIEW 2 trials?	5:08:50PM
6	be relevant here as articulated by one of the	4:49:46PM	6	A. It's quite likely that we did.	5:08:53PM
7	referees, when we describe a new mechanism of	4:49:51PM	7	Q. Can you confirm that this date,	5:08:56PM
8	action, a new way a drug works in terms of it	4:49:57PM	8	Monday, November 22, 2010, is before you filed	5:08:59PM
9	attacks a target, a new target, that type of	4:49:59PM	9	any of your patent applications relating to the	5:09:03PM
10	so-called conceptual advance when it	4:50:04PM	10	'601 and '572 patents in this case?	5:09:07PM
11	scientifically defines a new mechanism for a	4:50:08PM	11	A. Sorry, the print on this document is	5:09:12PM
12	disease is more likely to get it into New	4:50:12PM	12	pretty small. Let me just look at it for a	5:09:13PM
13	England Journal of Medicine where they are	4:50:16PM	13	second. (Witness reviewing document.) Okay.	5:09:16PM
14	looking for those sorts of new mechanistic	4:50:20PM	14	Q. Can you confirm that this press	5:12:54PM
15	incites because they consider themselves more	4:50:23PM	15	release went out before you filed any of your	5:12:57PM
16	focused on science and mechanisms than just	4:50:26PM	16	patent applications leading to the '601 or '572	5:13:00PM
17	pure clinical data. Some of the other journals	4:50:30PM	17	patent in this case?	5:13:04PM
18	focus on the importance of the clinical results	4:50:36PM	18	A. Yes, I don't really know the exact	5:13:07PM
19	and what it may mean to patient care and so	4:50:40PM	19	dates where things were filed and how to	5:13:09PM
20	forth, although the results may not be	4:50:43PM	20	compare them.	5:13:11PM
21	considered as sexy as identifying a new	4:50:46PM	21	Q. All right. Well, if you take a look	5:13:12PM
22	mechanism, they may end up being just as, if	4:50:51PM	22	at the second page of Defendant's Exhibit 4,	5:13:13PM
23	not more important, in terms of how it changes	4:50:55PM	23	which is the '601 patent -- actually, if you	5:13:17PM
24	the practice in medicine and the treatment of	4:50:58PM	24	want to look at the provisional, that's fine.	5:13:36PM
25	patients.	4:51:01PM	25	The first date --	5:13:39PM
Page 187			Page 189		
1	MS. MAZZOCHI: All right. Let's go	4:51:02PM	1	A. This is the provisional that I'm	5:13:40PM
2	ahead and take a break.	4:51:03PM	2	looking at?	5:13:42PM
3	THE VIDEOGRAPHER: We are going off	4:51:05PM	3	Q. Yes. The first date -- the filing	5:13:43PM
4	the record at 4:51 p.m.	4:51:06PM	4	date for the provisional application 61432245	5:13:44PM
5	(Off the record.)	4:51:07PM	5	was filed on January 13, 2011, right?	5:13:49PM
6	THE VIDEOGRAPHER: We are back on	5:07:21PM	6	A. You must be right but I don't know	5:13:53PM
7	the record at 5:07 p.m.	5:07:22PM	7	where to read that on the document.	5:14:09PM
8	Q. Dr. Yancopoulos, I'm giving you a	5:07:24PM	8	Q. There you go. You see the entry	5:14:30PM
9	document that I have marked as Defendant's	5:07:26PM	9	that says receipt date January 13, 2011?	5:14:32PM
10	Exhibit 917, which has production numbers	5:07:28PM	10	A. Yes.	5:14:35PM
11	RGN-EYLEA-MYLAN 504690 through 693. Can you	5:07:31PM	11	Q. All right. So, we can agree that	5:14:35PM
12	confirm please that this is an e-mail to you	5:07:39PM	12	November 22, 2010, is before January 2011,	5:14:37PM
13	from newsdesk@broadcast shareholder.com dated	5:07:43PM	13	right?	5:14:41PM
14	Monday, November 22, 2010, 5:06 a.m.?	5:07:49PM	14	A. Yes, I agree.	5:14:41PM
15	(Whereupon Exhibit 917 was marked	5:07:52PM	15	Q. All right. And can we also agree	5:14:42PM
16	for identification.)	5:07:52PM	16	that you -- that Regeneron disclosed in this	5:14:47PM
17	A. That's what the header says.	5:07:54PM	17	November 22, 2010, press release, the VIEW 1,	5:14:50PM
18	Q. And was it common for you to receive	5:07:56PM	18	VIEW 2 monthly -- VIEW 1, VIEW 2 dosing	5:14:57PM
19	Regeneron's press releases to your e-mail?	5:08:00PM	19	schedule that included three monthly doses of	5:15:01PM
20	A. I'm not familiar with the "from"	5:08:22PM	20	2 milligrams of aflibercept followed by every	5:15:04PM
21	address that says	5:08:24PM	21	eight week dosing?	5:15:09PM
22	newsdesk@broadcast shareholder.com. I don't	5:08:25PM	22	MR. BERL: Objection.	5:15:11PM
23	know if that's some sort of Regeneron e-mail	5:08:29PM	23	A. Can you restate the question?	5:15:15PM
24	address. I'm not familiar with getting too	5:08:33PM	24	Q. Sure. Can you confirm that in this	5:15:17PM
25	many e-mails from that address.	5:08:35PM	25	press release, Regeneron disclosed the dosing	5:15:19PM

Page 190	Page 192
1 regimen of receiving 2 milligrams of 5:15:24PM 2 aflibercept every two months — I'm sorry, 5:15:29PM 3 monthly for three months followed by dosing 5:15:32PM 4 every two months? 5:15:36PM 5 MR. BERL: Objection. 5:15:40PM 6 A. I'm just going to wait for that to 5:15:45PM 7 pass. When you refer to dosing regimen, the 5:15:49PM 8 dosing regimen encompasses a great number and a 5:15:53PM 9 set of details in addition to just the broad 5:15:59PM 10 frequency of injections and it's the collection 5:16:08PM 11 of all the criteria, inclusion criteria, 5:16:14PM 12 exclusion criteria, how you select the patients 5:16:18PM 13 and so forth and so on that encompasses the 5:16:21PM 14 dosing regimen. And so, I would say no, it's 5:16:23PM 15 not correct that the dosing regimen was 5:16:27PM 16 disclosed in this press release, just the 5:16:30PM 17 general characteristics of the numbers of 5:16:33PM 18 injections. 5:16:36PM 19 Q. Let's try to get at it this way. 5:16:37PM 20 Let's turn to the page that is in DX917 that 5:16:39PM 21 has got the number 691 on the bottom. 5:16:45PM 22 A. Yes. 5:16:52PM 23 Q. All right. And do you see in the 5:16:52PM 24 second paragraph it says -- it describes what 5:16:53PM 25 was happening in the studies and one of the 5:16:57PM	1 this way. The studies that you were 5:18:30PM 2 publicizing involved human subjects, right? 5:18:33PM 3 A. These were human clinical trials. 5:18:37PM 4 Q. Right. And the disease that was 5:18:39PM 5 being treated was a type of age-related macular 5:18:43PM 6 degeneration, right? 5:18:48PM 7 A. Yes, the disease being studied in 5:18:50PM 8 these clinical trials was wet age-related 5:18:52PM 9 macular degeneration. 5:18:57PM 10 Q. And you gave doses to patients 5:18:59PM 11 intravitreally, right? 5:19:01PM 12 A. Yes. 5:19:03PM 13 Q. And one of the types of doses that 5:19:04PM 14 was given to patients was 2 milligrams of 5:19:07PM 15 aflibercept approximately every four weeks for 5:19:11PM 16 the first three months, right? 5:19:13PM 17 A. One of the dosing arms involved 5:19:19PM 18 included giving 2 milligrams of aflibercept 5:19:23PM 19 every month for the first three months. 5:19:27PM 20 Q. And that was then followed by giving 5:19:29PM 21 aflibercept once every eight weeks or once 5:19:34PM 22 every two months, right? 5:19:38PM 23 A. For that dosing arm, as I said 5:19:43PM 24 these, refer to the general dosing schedules 5:19:46PM 25 but are not really referred to as the overall 5:19:48PM
Page 191	Page 193
1 dosing arms is listed as 2 milligrams every two 5:17:00PM 2 months following three monthly loading doses. 5:17:05PM 3 Do you see that regimen? 5:17:08PM 4 MR. BERL: Objection. 5:17:13PM 5 A. I see what you just read. 5:17:17PM 6 Q. Okay. Now, in -- that dosing arm 5:17:18PM 7 was used in a method for treating wet AMD, 5:17:25PM 8 right? 5:17:30PM 9 MR. BERL: Objection. 5:17:32PM 10 A. Well, if you just read the next 5:17:35PM 11 sentence, for example, just to make it obvious, 5:17:36PM 12 it says as needed PRN dosing would be used in 5:17:39PM 13 the second year of the studies, and as you 5:17:43PM 14 know, PRN dosing means as needed as judged by a 5:17:46PM 15 variety of treatment criteria. There is an 5:17:52PM 16 enormous list of treatment criteria by which 5:17:55PM 17 you judge whether to give the PRN dosing or not 5:17:59PM 18 and that's all part of the regimen. So, this 5:18:03PM 19 is just a global description that doesn't 5:18:06PM 20 really encompass what you would need to know to 5:18:11PM 21 understand in full the dosing regimen. So, 5:18:14PM 22 what this does in this brief paragraph is just 5:18:17PM 23 summarize broadly the injection approaches and 5:18:21PM 24 frequencies in the different arms. 5:18:27PM 25 Q. All right. Let's try to get at it 5:18:29PM	1 dosing regimen which includes all of the other 5:19:52PM 2 details that are not included. 5:19:55PM 3 Q. Fine. And the patients that 5:19:57PM 4 received the 2 milligrams aflibercept every two 5:19:59PM 5 months following three monthly loading doses, 5:20:03PM 6 they were also treated for wet AMD, right? 5:20:05PM 7 A. Everybody enrolled in the studies 5:20:16PM 8 was selected and only included various 5:20:20PM 9 criteria. We did not try to treat all forms of 5:20:24PM 10 wet AMD and so forth. This was, you know, 5:20:28PM 11 restricted by all the exclusion and inclusion 5:20:31PM 12 criteria to certain categories of patients, but 5:20:34PM 13 all those categories of patients include 5:20:37PM 14 patients who were suffering from wet 5:20:40PM 15 age-related macular degeneration. 5:20:44PM 16 Q. Now, if we look at the VIEW 1 and 5:20:47PM 17 VIEW 2 results that were publicized, I'd like 5:20:48PM 18 to look at the numbers that were recorded for 5:20:53PM 19 have VEGF-Trap Eye for every two months, so the 5:20:55PM 20 right-hand most column. Do you have that one? 5:21:02PM 21 A. Right, yes. 5:21:03PM 22 Q. All right. Did the patients gain at 5:21:04PM 23 least 15 letters of best corrected visual 5:21:06PM 24 acuity score in that dosing, in that arm? 5:21:10PM 25 A. I'm sorry, I don't understand what 5:21:25PM

Page 194

1 you mean by "did the patients." 5:21:27PM

2 Q. According to the data presented 5:21:29PM

3 here, did the patients achieve gains of at 5:21:31PM

4 least 15 letters of best corrected visual 5:21:37PM

5 acuity score in either of the -- in either VIEW 5:21:41PM

6 1 or VIEW 2? 5:21:46PM

7 A. There is no way of telling from the 5:21:57PM

8 data that is presented here whether patients in 5:21:58PM

9 any particular arm gained -- whether any 5:22:02PM

10 patients in any of these arms gained 15 letters 5:22:09PM

11 of vision or not. 5:22:12PM

12 Q. Well, are there any steps that a 5:22:14PM

13 doctor can take to ensure that their patient is 5:22:16PM

14 going to gain 15 letters or more in best 5:22:20PM

15 corrected visual acuity score when they are 5:22:24PM

16 dosing with aflibercept? 5:22:26PM

17 MR. BERL: Objection, vague. 5:22:29PM

18 Q. For wet AMD? 5:22:30PM

19 MR. BERL: Objection, vague. 5:22:36PM

20 A. Could you -- could you restate the 5:22:37PM

21 question? 5:22:38PM

22 Q. Sure. Is there any step that a 5:22:39PM

23 doctor can take to ensure that their patient 5:22:41PM

24 actually does gain 15 letters of best corrected 5:22:43PM

25 visual acuity when they are being dosed with 5:22:47PM

Page 195

1 aflibercept for a wet AMD? 5:22:50PM

2 MR. BERL: Objection, vague. 5:22:52PM

3 A. I'm really not sure I understand 5:22:58PM

4 what you are asking. 5:23:01PM

5 Q. What steps could a doctor take when 5:23:03PM

6 they are dosing their patient with aflibercept 5:23:05PM

7 to make sure that after they've done the three 5:23:08PM

8 loading doses and then are dosing every eight 5:23:13PM

9 weeks to make sure that their patient does 5:23:16PM

10 actually gain 15 letters of BCVA score? 5:23:18PM

11 MR. BERL: Objection, vague. 5:23:26PM

12 A. So, you just asked before whether 5:23:48PM

13 any patient in the studies gained 15 letters 5:23:51PM

14 and I said it was impossible to tell from this 5:23:55PM

15 table, and now you're asking is it possible to 5:23:58PM

16 ensure that any particular patient gains 15 5:24:01PM

17 letters from baseline? 5:24:05PM

18 Q. Yes, is there anything that a doctor 5:24:07PM

19 can do when they are dosing aflibercept 5:24:09PM

20 2-milligram after three loading doses and then 5:24:11PM

21 dosing every other month to make sure that 5:24:16PM

22 their patient is going to get across a 5:24:18PM

23 threshold of gaining 15 letters of BCVA score? 5:24:21PM

24 MR. BERL: Objection, vague. 5:24:28PM

25 A. From their baseline pretreat? 5:24:29PM

Page 196

1 Q. Sure. 5:24:33PM

2 MR. BERL: Objection. 5:24:34PM

3 A. I'm not sure I totally understand 5:24:34PM

4 the question, but I believe that the answer is 5:24:36PM

5 for any particular patient treated with any 5:24:42PM

6 drug using any regimen, it's not possible to 5:24:52PM

7 predict how much that individual patient will 5:24:57PM

8 gain. 5:25:04PM

9 Q. Why not? 5:25:09PM

10 MR. BERL: Objection. 5:25:16PM

11 A. Well, I believe in general it's true 5:25:16PM

12 for almost any disease with any treatment that 5:25:44PM

13 individual patients will respond differently 5:25:49PM

14 and the goal of clinical trials is to establish 5:25:58PM

15 the average result across a defined sub set of 5:26:02PM

16 patients using a defined treatment approach. 5:26:10PM

17 Q. Okay. Well, can you say on average 5:26:16PM

18 the VIEW 1, VIEW 2 patient cohorts who got 5:26:24PM

19 aflibercept 2 milligrams every two months after 5:26:30PM

20 three loading doses, on average, did they get 5:26:33PM

21 a -- do they gain at least 15 letters of BCVA 5:26:37PM

22 score? 5:26:43PM

23 A. Well, reading from this table, it 5:26:47PM

24 says the mean improvement in vision in letters 5:26:50PM

25 at 52 weeks versus baseline was about eight to 5:26:55PM

Page 197

1 nine letters for the 2-milligram dosing arms -- 5:27:04PM

2 sorry, was -- did you ask for individual arms? 5:27:12PM

3 Q. Either or combined. 5:27:28PM

4 A. Okay. For the fourth arm in this 5:27:30PM

5 table, it would be roughly eight to nine 5:27:33PM

6 letters was the mean improvement in vision in 5:27:36PM

7 letters at 52 weeks versus baseline. 5:27:40PM

8 Q. Well, can you say at any time any of 5:27:45PM

9 these patients actually gained 15 letters of 5:27:49PM

10 BCVA score? 5:27:53PM

11 MR. BERL: Objection, lack of 5:27:55PM

12 foundation. 5:28:01PM

13 A. Not from the data that is in this 5:28:03PM

14 table. One would have to go to the individual 5:28:07PM

15 patient data over time. 5:28:09PM

16 Q. Well, we are going to provide you 5:28:14PM

17 with a document that was previously marked as 5:28:15PM

18 Defendant's Exhibit 520A, which is the current 5:28:17PM

19 most recent prescribing information for EYLEA 5:28:25PM

20 last revised August of 2022. And if you could 5:28:29PM

21 turn to Table 4, which is on page 712304, is it 5:28:37PM

22 fair to say that in the VIEW 1 and VIEW 2 5:28:59PM

23 studies less than a majority of patients 5:29:02PM

24 managed to gain at least 15 letters of vision 5:29:06PM

25 from baseline? 5:29:11PM

Page 198

1 A. Let me just read this relevant 5:29:13PM
2 section here (witness reading document). Could 5:29:14PM
3 you just ask the question again now that I 5:30:20PM
4 familiarized myself? 5:30:22PM
5 Q. Sure. From the data presented in 5:30:24PM
6 Table 4, is it fair to say that less than a 5:30:25PM
7 majority of patients who took EYLEA 5:30:30PM
8 2 milligrams every eight weeks after three 5:30:35PM
9 monthly loading doses actually attained at 5:30:42PM
10 least 15 letters of vision gain from baseline? 5:30:48PM
11 A. Now, you're saying -- you're asking 5:30:57PM
12 just to be clear, you're asking whether they 5:31:00PM
13 gained or the number or percentage gained at 5:31:04PM
14 any point during their treatment or only at the 5:31:09PM
15 52-week time point? 5:31:13PM
16 Q. Well, from the data of presented 5:31:14PM
17 here in Table 4. 5:31:16PM
18 A. Okay. So, what you are asking is -- 5:31:17PM
19 you want to know roughly what percentage of 5:31:19PM
20 patients achieved at least a 15 letter of 5:31:22PM
21 vision gained from baseline at the 52-week time 5:31:25PM
22 point? 5:31:30PM
23 Q. Sure. Whatever data you think is 5:31:31PM
24 available in Table 4, can you say that -- 5:31:35PM
25 A. Well, that is what's -- the data 5:31:38PM

Page 199

1 that is available is that one specific time 5:31:40PM
2 frame, the 52-week time point. It says that 5:31:43PM
3 over the various treatment arms, 29 to 5:31:48PM
4 38 percent gained 50 letters of vision from 5:31:51PM
5 baseline at the 52-week time point. It does 5:31:56PM
6 not speak to whether more may have gained it 5:32:00PM
7 across different points in the trial. 5:32:04PM
8 Q. What can a doctor do to make sure 5:32:06PM
9 their patient crosses that threshold of being a 5:32:10PM
10 patient who gained at least 15 letters of 5:32:13PM
11 vision from baseline? 5:32:16PM
12 MR. BERL: Objection. 5:32:17PM
13 Q. If they are taking EYLEA every other 5:32:21PM
14 month? 5:32:23PM
15 MR. BERL: Objection. 5:32:24PM
16 A. As I said before, as with, I 5:32:38PM
17 believe, almost any treatment for any disease, 5:32:42PM
18 it's impossible to guarantee any particular 5:32:45PM
19 outcome for any one patient from that treatment 5:32:48PM
20 in that disease. 5:32:51PM
21 Q. Take a look at your '601 patent, 5:32:53PM
22 column 21, claim 5. So DX4, column 21, claim 5:32:57PM
23 No. 5. Do you have that? 5:33:16PM
24 A. Column 21, claim No. 5? 5:33:27PM
25 Q. Yeah. Do you see the reference 5:33:29PM

Page 200

1 there to the method of claim 2 wherein the 5:33:31PM
2 patient gains at least 15 letters of best 5:33:33PM
3 corrected visual acuity BCVA score? 5:33:37PM
4 A. Yes, I see that. 5:33:43PM
5 Q. When does the BCVA score have to be 5:33:45PM
6 measured? 5:33:47PM
7 MR. BERL: Objection. 5:33:50PM
8 Q. To assess for 15 letters? 5:33:51PM
9 MR. BERL: Objection. 5:33:56PM
10 A. In this particular line that you are 5:34:00PM
11 referring to? 5:34:03PM
12 Q. Yes. 5:34:04PM
13 A. It does not speak to the when. 5:34:05PM
14 Q. Does it have to be at the 52-week 5:34:10PM
15 mark? 5:34:13PM
16 MR. BERL: Objection. 5:34:13PM
17 A. Not according to what is written 5:34:20PM
18 here. 5:34:21PM
19 Q. Does it have to be by the time 5:34:22PM
20 you've taken your first every other month dose? 5:34:25PM
21 MR. BERL: Objection. 5:34:28PM
22 A. (Witness reviewing document.) I'm 5:35:30PM
23 sorry, what is the question again? 5:35:35PM
24 Q. Does it have to be by the -- does it 5:35:37PM
25 have to be measured by the time you've taken 5:35:38PM

Page 201

1 your first every other month dose? 5:35:41PM
2 MR. BERL: Objection, calls for a 5:35:45PM
3 legal conclusion. 5:35:50PM
4 A. I'm not sure what the legal 5:35:55PM
5 interpretation of all of these -- you know, 5:35:57PM
6 this particular language is. It's not clear to 5:35:59PM
7 me within what time frame or respect to what 5:36:06PM
8 point in treatment that refers. 5:36:12PM
9 Q. Does the BCVA score have to be 5:36:16PM
10 measured at a distance of 2 meters? 5:36:18PM
11 MR. BERL: Objection, calls for a 5:36:24PM
12 legal conclusion. 5:36:25PM
13 A. If you're trying to get at the 5:37:09PM
14 definition or implications legally of all this 5:37:11PM
15 claim language in here, I don't think I am the 5:37:16PM
16 appropriate person to try to interpret these. 5:37:19PM
17 Q. Well, this is your patent. I just 5:37:21PM
18 want to understand when you are talking about 5:37:23PM
19 assessing somebody according to BCVA score, do 5:37:26PM
20 they do it at the 2-meter mark, the 3-meter 5:37:29PM
21 mark, the 4-meter mark? 5:37:34PM
22 MR. BERL: Objection, calls for a 5:37:36PM
23 legal conclusion. 5:37:38PM
24 A. Like I said, I don't understand the 5:37:40PM
25 legal or otherwise implication of the language 5:37:45PM

Page 202		Page 204	
1	in these claims. 5:37:49PM	1	A. That's what it says. 5:40:38PM
2	Q. Well, as a scientist, is the rule 5:37:53PM	2	Q. All right. And do you know who 5:40:38PM
3	supposed to be that you measured at the 2-meter 5:37:55PM	3	Jamie Danz is of WCG? 5:40:40PM
4	mark, 3-meter mark, or the 4-meter mark? 5:37:59PM	4	A. No, I do not. 5:40:48PM
5	MR. BERL: Objection. 5:38:03PM	5	Q. Are they an advertising and PR firm? 5:40:49PM
6	Q. Can you do it at any of those three? 5:38:04PM	6	A. I don't recognize that e-mail. 5:40:53PM
7	MR. BERL: Objection. 5:38:14PM	7	Q. Do you dispute that you received 5:40:55PM
8	A. Well, if you want, I can go through 5:38:15PM	8	this e-mail? 5:40:57PM
9	the patent and see whether we specify anywhere 5:38:17PM	9	A. I couldn't tell you whether I 5:40:59PM
10	more specifically how these assessments should 5:38:23PM	10	received this e-mail or not. It's more than 10 5:41:00PM
11	be made. 5:38:27PM	11	years ago. 5:41:04PM
12	Q. Well, as a scientist, are you going 5:38:27PM	12	Q. Well, is there anything that would 5:41:06PM
13	to get different letter gain results if the 5:38:29PM	13	cause you to believe that you wouldn't get a 5:41:07PM
14	patient is standing at 2 meters, 3 meters, or 4 5:38:32PM	14	copy of this e-mail in your inbox? 5:41:09PM
15	meters away -- 5:38:36PM	15	A. There is no reason to believe that I 5:41:10PM
16	MR. BERL: Objection. 5:38:40PM	16	got it, I didn't got it, whether it got into my 5:41:13PM
17	Q. -- from the chart? 5:38:41PM	17	spam or not, or whether I read, you know, any 5:41:15PM
18	MR. BERL: Objection, calls for a 5:38:43PM	18	one of, you know, a couple of hundred e-mails I 5:41:19PM
19	legal conclusion, vague, lack of 5:38:44PM	19	get every day. 5:41:24PM
20	foundation. 5:38:46PM	20	Q. Well, she is reporting to you that 5:41:25PM
21	Q. Independent of the patent, 5:38:56PM	21	the press release that Regeneron issued on the 5:41:28PM
22	Dr. Yancopoulos, do you know as a scientist 5:38:57PM	22	phase three data resulted in 41 original 5:41:33PM
23	whether if you take the measurement at 2-meter 5:39:01PM	23	articles and garnered an audience reach of more 5:41:38PM
24	mark, 3-meter mark, or 4-meter mark, you will 5:39:03PM	24	than 33 million. Do you see that? 5:41:41PM
25	get different results in terms of letter score 5:39:06PM	25	A. I do. 5:41:43PM
Page 203		Page 205	
1	on the chart? 5:39:13PM	1	Q. Is it fair to say that Regeneron was 5:41:44PM
2	MR. BERL: Objection. 5:39:14PM	2	not trying to keep its VIEW 1/VIEW 2 data 5:41:46PM
3	A. I don't know if it's been 5:39:18PM	3	results secret? 5:41:49PM
4	definitively studied. If you take -- if you do 5:39:19PM	4	MR. BERL: Objection, vague as to 5:41:51PM
5	the same patient using the same technique at 5:39:24PM	5	time. 5:41:53PM
6	baseline and the same technique at whatever 5:39:29PM	6	Q. After November 22, 2010? 5:41:57PM
7	time point you want to compare to the baseline 5:39:33PM	7	A. According to the documents that you 5:42:06PM
8	visits, whether changes in the way you conduct 5:39:36PM	8	gave me, we had issued a press release. 5:42:09PM
9	the assessment by varying any one of the 5:39:43PM	9	Q. All right. And one of the reasons 5:42:13PM
10	variables that you could vary, whether that 5:39:48PM	10	why Regeneron wanted to issue press releases 5:42:16PM
11	could systemically change the average change or 5:39:51PM	11	showing successful clinical trial results is 5:42:19PM
12	the individual change from baseline when 5:39:53PM	12	because that helped your stock, it generated 5:42:24PM
13	assessed differently. I don't know if those 5:39:55PM	13	buzz, was good for you with investors, right? 5:42:27PM
14	studies have been done. 5:39:58PM	14	A. Well, I think the major reason that 5:42:30PM
15	Q. I'm going to put before you a 5:39:59PM	15	we issue press releases is in particular when 5:42:46PM
16	document that I'm marking as Defendant's 5:40:00PM	16	there is material information that needs to be 5:42:51PM
17	Exhibit 918, which has production numbers RGN- 5:40:02PM	17	disclosed. 5:42:56PM
18	EYLEA-MYLAN 495807 through 852. Can you 5:40:05PM	18	Q. And material information that needs 5:42:59PM
19	confirm that the first page of this document is 5:40:13PM	19	to be disclosed is information that would have 5:43:02PM
20	an e-mail from Jamie Danz to you and others 5:40:16PM	20	a material effect on the Regeneron stock price, 5:43:05PM
21	dated November 22, 2010. "Subject: Wet AMD 5:40:21PM	21	right? 5:43:09PM
22	Phase 3 Data Coverage Report, 11/22/10, Final 5:40:27PM	22	MR. BERL: Objection, lack of 5:43:10PM
23	Report." 5:40:37PM	23	foundation, calls for a legal conclusion. 5:43:11PM
24	(Whereupon Exhibit 918 was marked 5:40:37PM	24	A. I think it's fair to say that 5:43:32PM
25	for identification.) 5:40:37PM	25	material information can often affect but not 5:43:33PM

Page 206

1 necessarily affect stock price. 5:43:38PM
2 Q I'm going to mark as Defendant's 5:43:53PM
3 Exhibit 919 a document with production numbers 5:44:02PM
4 RGN-EYLEA-MYLAN 539067 through 068. 5:44:07PM
5 (Whereupon Exhibit 919 was marked 5:44:14PM
6 for identification.) 5:44:14PM
7 MR. BERL: You have three minutes, 5:44:16PM
8 by the way. 5:44:17PM
9 MS. MAZZOCHI: Not if you're doing 5:44:21PM
10 redirect. 5:44:22PM
11 Q Do you see that, Dr. Yancopoulos? 5:44:24PM
12 A My eyes are beginning to fail me. 5:44:27PM
13 It's been a long day. 5:44:29PM
14 Q Can you confirm this was another 5:44:30PM
15 press release dated November 14, 2009, that was 5:44:32PM
16 sent to you confirming that enrollment had been 5:44:37PM
17 completed in Regeneron and Bayer's phase three 5:44:40PM
18 studies in VEGF-Trap Eye in wet AMD? 5:44:45PM
19 A Well, I can't confirm that, but I 5:44:50PM
20 can say that is what the document says that it 5:44:52PM
21 appears to be a press release that was sent to 5:44:54PM
22 me from an e-mail that I don't recognize that 5:44:57PM
23 refers to what appears to be a press release 5:45:04PM
24 issued on September 14, 2009. 5:45:07PM
25 Q If you look at the bottom of the 5:45:11PM

Page 207

1 page, it mentions that, "VEGF-Trap Eye is also 5:45:13PM
2 in Phase 3 development for the treatment of 5:45:18PM
3 CRVO." Do you see that, the last paragraph on 5:45:21PM
4 the first page? 5:45:28PM
5 A Let me just familiarize myself, 5:45:29PM
6 please, with this document. I haven't seen it, 5:45:31PM
7 if I have, in a long, long time. (Witness 5:45:33PM
8 reviewing document.) Okay. Sorry, what was 5:46:07PM
9 the question? 5:47:45PM
10 Q Can you confirm that the CRVO dosing 5:47:45PM
11 regimen that Regeneron publicized in this press 5:47:49PM
12 release was for six monthly intravitreal 5:47:53PM
13 injections of aflibercept at a dose of 5:47:57PM
14 2 milligrams? 5:48:00PM
15 MR. BERL: Objection. You're at 5:48:01PM
16 seven hours. You can answer this and then 5:48:07PM
17 we are done. 5:48:10PM
18 THE WITNESS: Should I answer the 5:48:11PM
19 question? 5:48:12PM
20 MR. BERL: Yes. 5:48:13PM
21 A Just -- sorry, I lost track. 5:48:18PM
22 Confirm again what was the question, can I 5:48:19PM
23 confirm what? 5:48:22PM
24 Q That Regeneron disclosed publicly it 5:48:23PM
25 was dosing patients for CRVO with 2 milligrams 5:48:26PM

Page 208

1 aflibercept with six monthly intravitreal 5:48:33PM
2 injections? 5:48:37PM
3 MR. BERL: Objection. 5:48:40PM
4 Q By September 14, 2009? 5:48:45PM
5 MR. BERL: Objection. 5:48:48PM
6 A It says here or I can confirm that 5:48:51PM
7 the overall dosing regimen, which as I said, is 5:48:54PM
8 much more complicated than just the timing of 5:48:59PM
9 the delivery of doses, but that that dosing -- 5:49:02PM
10 overall dosing regimen included six monthly 5:49:05PM
11 intravitreal injections of VEGF-Trap at a dose 5:49:09PM
12 of 2 milligrams. 5:49:15PM
13 Q Is it true that you were recently 5:49:17PM
14 booed at the conference where you were 5:49:18PM
15 serving -- 5:49:20PM
16 MR. BERL: All right. You're past 5:49:21PM
17 your time. We are done. 5:49:21PM
18 MS. MAZZOCHI: I'm just going to 5:49:23PM
19 note for the record that the witness took 5:49:24PM
20 an inordinate amount of time to read 5:49:26PM
21 rudimentary documents including his own 5:49:28PM
22 patents and that that created significant 5:49:31PM
23 delay and ate up time on the deposition. 5:49:34PM
24 The witness also gave multiple repeated 5:49:37PM
25 nonresponsive answers that were lengthy 5:49:40PM

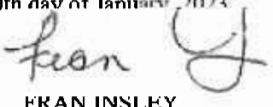
Page 209

1 narrative driven to very simple questions, 5:49:42PM
2 and if we have to go back to the Court to 5:49:45PM
3 get more time with the witness to 5:49:47PM
4 compensate for that, we will. So I just 5:49:48PM
5 want it to be clear that we are not 5:49:51PM
6 waiving our right to go back to the Court. 5:49:52PM
7 MR. BERL: All right. I'll note for 5:49:55PM
8 the record that you asked him to review 5:49:56PM
9 his patent and invited him to do it, first 5:49:58PM
10 of all. Second of all, your aspersion 5:50:01PM
11 that that is a rudimentary document is not 5:50:03PM
12 well taken. Third of all, his answers 5:50:06PM
13 were responsive to your questions, which 5:50:08PM
14 were often turgent and not well formed. 5:50:10PM
15 And fourth, this is a senior executive 5:50:12PM
16 witness and you are lucky we gave him 5:50:15PM
17 seven hours. We could have filed an apex 5:50:15PM
18 motion. We could have limited his time 5:50:18PM
19 here to less than seven hours on the 5:50:20PM
20 record. We were gracious and he 5:50:21PM
21 graciously agreed to sit here for an 5:50:23PM
22 entire day, seven hours, when you decided 5:50:26PM
23 to waste your time with things irrelevant 5:50:29PM
24 to this litigation from the DOJ 5:50:32PM
25 investigation onward. So, the notion that 5:50:32PM

Page 210

1 you are going to get more time with this 5:50:34PM
2 witness is preposterous. We are obviously 5:50:36PM
3 not going to consent to that and the 5:50:40PM
4 deposition is done. 5:50:44PM
5 MS. MAZZOCHI: Are you doing any 5:50:45PM
6 redirect? 5:50:46PM
7 MR. BERL: No. 5:50:47PM
8 THE VIDEOGRAPHER: This marks the 5:50:48PM
9 end of the deposition. We are going off 5:50:48PM
10 the record at 5:50 p.m. 5:50:50PM
11 (Time noted: 5:50 p.m.) 5:50:51PM
12 5:50:57PM
13 5:50:57PM
14 5:50:57PM
15 5:50:57PM
16 5:50:57PM
17 5:50:57PM
18
19
20
21
22
23
24
25

Page 211

1 **C E R T I F I C A T E**
2 I, FRAN INSLEY, hereby certify that the
3 Deposition of GEORGE D. YANCOPOULOS was held
4 before me on the 18th day of January, 2023;
5 that said witness was duly sworn before the
6 commencement of testimony; that the testimony
7 was taken stenographically by myself and then
8 transcribed by myself; that the party was
9 represented by counsel as appears herein;
10 That the within transcript is a true
11 record of the Deposition of said witness;
12 That I am not connected by blood or
13 marriage with any of the parties; that I am not
14 interested directly or indirectly in the
15 outcome of this matter; that I am not in the
16 employ of any of the counsel.
17 IN WITNESS WHEREOF, I have hereunto set
18 my hand this 20th day of January, 2023
19 
20 FRAN INSLEY
21
22
23
24
25

Page 212

1 Veritext Legal Solutions
2 1100 Superior Ave
3 Suite 1820
4 Cleveland, Ohio 44114
5 Phone: 216-523-1313
6
7 January 20, 2023
8 To: David Berl, Esq.
9
10 Case Name: Regeneron Pharmaceuticals, Inc. v.
11 Mylan Pharmaceuticals, Inc.
12 Veritext Reference Number: 5650063
13 Witness: George D. Yancopoulos Deposition Date: 1/18/2023
14
15 Dear Sir/Madam:
16
17 Enclosed please find a deposition transcript. Please have the witness
18 review the transcript and note any changes or corrections on the
19 included errata sheet, indicating the page, line number, change, and
20 the reason for the change. Have the witness' signature notarized and
21 forward the completed page(s) back to us at the Production address
22 shown
23 above, or email to production-midwest@veritext.com.
24
25 If the errata is not returned within thirty days of your receipt of
this letter, the reading and signing will be deemed waived.
Sincerely,
Production Department
NO NOTARY REQUIRED IN CA

Page 213

1 **DEPOSITION REVIEW**
2 **CERTIFICATION OF WITNESS**
3
4 ASSIGNMENT REFERENCE NO: 5650063
5 CASE NAME: Regeneron Pharmaceuticals, Inc. v.
6 Mylan Pharmaceuticals, Inc.
7 DATE OF DEPOSITION: 1/18/2023
8 WITNESS NAME: George D. Yancopoulos
9 In accordance with the Rules of Civil
10 Procedure, I have read the entire transcript of
11 my testimony or it has been read to me.
12 I have made no changes to the testimony
13 as transcribed by the court reporter.
14
15 Date George D. Yancopoulos
16 Sworn to and subscribed before me, a
17 Notary Public in and for the State and County,
18 the referenced witness did personally appear
19 and acknowledge that:
20
21 They have read the transcript;
22 They signed the foregoing Sworn
23 Statement; and
24 Their execution of this Statement is of
25 their free act and deed.
I have affixed my name and official seal
this _____ day of _____, 20____.
Notary Public
Commission Expiration Date

Page 214

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

DEPOSITION REVIEW
CERTIFICATION OF WITNESS

ASSIGNMENT REFERENCE NO: 5650063

CASE NAME: Regeneron Pharmaceuticals, Inc. v. Mylan Pharmaceuticals, Inc.

DATE OF DEPOSITION: 1/18/2023

WITNESS' NAME: George D. Yancopoulos

In accordance with the Rules of Civil Procedure, I have read the entire transcript of my testimony or it has been read to me.

I have listed my changes on the attached Errata Sheet, listing page and line numbers as well as the reason(s) for the change(s).

I request that these changes be entered as part of the record of my testimony.

I have executed the Errata Sheet, as well as this Certificate, and request and authorize that both be appended to the transcript of my testimony and be incorporated therein.

Date George D. Yancopoulos

Sworn to and subscribed before me, a Notary Public in and for the State and County, the referenced witness did personally appear and acknowledge that:

They have read the transcript;
They have listed all of their corrections in the appended Errata Sheet;
They signed the foregoing Sworn Statement; and
Their execution of this Statement is of their free act and deed.

I have affixed my name and official seal
this _____ day of _____, 20____.

Notary Public

Commission Expiration Date

Page 215

1 **ERRATA SHEET**
2 **VERITEXT LEGAL SOLUTIONS MIDWEST**
3 **ASSIGNMENT NO: 5650063**
4 **PAGE/LINE(S) / CHANGE /REASON**
5 _____
6 _____
7 _____
8 _____
9 _____
10 _____
11 _____
12 _____
13 _____
14 _____
15 _____
16 _____
17 _____
18 _____
19 _____
20 _____
21 **Date** George D. Yancopoulos
22 **SUBSCRIBED AND SWORN TO BEFORE ME THIS** _____
23 **DAY OF** _____, 20_____.
24 _____
25 **Notary Public**

26 **Commission Expiration Date** _____