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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAMSUNG BIOEPIS CO., *
LTD., *
PETITIONER, * CASE IPR2023-00442
VS. * U.S. PATENT NO. 10,130,681
REGENERON *
PHARMACEUTICALS, INC., *
PATENT OWNER. *

ORAL AND VIDEOTAPED DEPOSITION OF
DR. DAVID M. BROWN
DECEMBER 13, 2023

ORAL AND VIDEOTAPED DEPOSITION OF
DR. DAVID M. BROWN, produced as a witness at the
instance of the PETITIONER, and duly sworn, was
taken in the above-styled and numbered cause on
DECEMBER 13, 2023, from 9:07 A.M. to 5:42 P.M.,
before AMY PRIGMORE, CSR, in and for the State of
Texas, reported by stenographic means, at the
offices of Arnold & Porter Kaye Scholer, LLP,
700 Louisiana Street, Suite 4000, Houston, Texas,
pursuant to the Federal Rules of Civil Procedure
and the provisions stated on the record or attached
hereto.

1 APPEARANCES 2 3 FOR THE PETITIONER: 4 Zach Summers 5 QUINN EMANUEL URQUHART & SULLIVAN, LLP 6 865 S Figueroa St, 10th Floor 7 Los Angeles CA 90017 8 zachsummers@quinnemanuel.com 9 10 FOR THE RESPONDENT: 11 Abigail Struthers 12 David Denuyl (VIA ZOOM) 13 ARNOLD & PORTER KAYE SCHOLER LLP 14 250 West 55th Street 15 New York NY 10019 16 abigail.struthers@arnoldporter.com 17 18 ALSO PRESENT: 19 Britni Stanwood, Videographer 20 Eileen Woo (VIA ZOOM) 21 22 23 24 25 Page 2	1 EXHIBIT 2131 RANDOMIZED DOUBLE MASKED 192 2 SHAM CONTROLLED TRIAL OF 3 RANIBIZUMAB FOR 4 NEOVASCULAR AGE-RELATED 5 MACULAR DEGENERATION: 6 PIER STUDY 1 7 EXHIBIT 2362 VEGF TRAP-EYE FOR 234 8 EXUDATIVE AMD 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 Page 4
1 INDEX 2 PAGE 3 APPEARANCES 2 4 STIPULATIONS 1 5 SIGNATURE AND CHANGES 266 6 REPORTER'S CERTIFICATE..... 268 7 8 EXAMINATIONS 9 DR. DAVID M. BROWN PAGE 10 EXAMINATION 6 11 BY MR. SUMMERS 12 13 EXHIBITS 14 EXHIBIT DESCRIPTION PAGE 15 EXHIBIT 2060 CURRICULUM VITAE 8 16 EXHIBIT 2055 THE EXPERT DECLARATION 14 17 OF DAVID M. BROWN, M.D. 18 EXHIBIT 1001 U.S. PATENT 10,130,681 53 19 EXHIBIT 2185 EYLEA LABEL AS OF 59 20 NOVEMBER 2011 21 EXHIBIT 2189 EYLEA DRUG LABEL FOR 60 22 MARCH 2021 23 EXHIBIT 1006 VEGF TRAP-EYE FOR THE 103 24 TREATMENT OF NEOVASCULAR 25 AGE-RELATED MACULAR DEGENERATION EXHIBIT 2212 LUCENTIS DRUG LABEL FROM 133 2006 EXHIBIT 2297 THE 1-YEAR RESULTS OF 139 CLEAR-IT 2, A PHASE 2 STUDY OF VASCULAR ENDOTHELIAL GROWTH FACTOR TRAP-EYE DOSED AS-NEEDED AFTER 12-WEEK FIXED DOSING EXHIBIT 2296 PRIMARY ENDPOINT RESULTS 141 PHASE 3 STUDY OF VASCULAR ENDOTHELIAL GROWTH FACTOR TRAP-EYE IN WET AGE-RELATED MACULAR DEGENERATION Page 3	1 PROCEEDINGS 2 * * * 3 THE VIDEOGRAPHER: Good morning. 09:08:04 4 We're going on the record at 9:07 a.m. on 09:08:05 5 12-13-2023. Please note that microphones are 09:08:09 6 sensitive and may pick up whispering and private 09:08:12 7 conversations. Please mute your phones at this 09:08:15 8 time. 09:08:18 9 Audio and video recording will 09:08:18 10 continue to take place, unless all parties agree to 09:08:20 11 go off the record. 09:08:23 12 This is Media Unit 1 on the video 09:08:23 13 record deposition of Dr. David Brown, taken by 09:08:27 14 counsel for the petitioner in the matter of Samsung 09:08:30 15 Bioepris Co. LTD versus Regeneron pharmaceuticals, 09:08:34 16 Inc., filed in the United States, patent and 09:08:40 17 trademark office, Case No. IPR, 202300442. 09:08:44 18 The location of deposition is 09:08:51 19 700 Louisiana Street, Suite 4000, Houston, Texas, 09:08:55 20 77002. My name is Britni Stanwood, representing 09:08:58 21 Veritext Legal Solutions and I'm the videographer. 09:09:03 22 The court reporter is Amy Prigmore, 09:09:05 23 from the firm Veritext Legal Solutions. 09:09:07 24 I am not related to any party in 09:09:11 25 this action, nor am I financially interested in the 09:09:13 Page 5

2 (Pages 2 - 5)

1 outcome. If there are any objections to the 09:09:15 2 proceeding, please state them at the time of your 09:09:17 3 appearance. 09:09:21 4 Counsel and all present will now 09:09:21 5 state their appearances and their affiliations for 09:09:24 6 the record, beginning with the noticing attorney. 09:09:26 7 MR. SUMMERS: Good morning. This is 09:09:28 8 Zach Summers, Quinn Emanuel, for Petitioner, 09:09:29 9 Samsung Bioepsis. 09:09:34 10 MS. STRUTHERS: And good morning. 09:09:36 11 This is Abigail Struthers, from Arnold & Porter. 09:09:37 12 I'm joined today remotely by my colleague, David 09:09:41 13 Denuyl, also from Arnold & Porter. And I believe 09:09:44 14 Eileen Woo of Regeneron is following along on 09:09:47 15 realtime. 09:09:50 16 We are here today on behalf of 09:09:51 17 Regeneron Pharmaceuticals and the witness. 09:09:53 18 THE VIDEOGRAPHER: Will the court 09:09:55 19 reporter please swear in the witness. 09:09:56 20 DR. DAVID BROWN, 09:08:28 21 having been first duly sworn, testified as follows: 22 EXAMINATION 23 BY MR. SUMMERS: 24 Q. Good morning. 09:10:07 25 A. Good morning. 09:10:07 Page 6	1 Q. From time to time, your counsel may make 09:11:19 2 objections. 09:11:22 3 Unless your counsel instructs you not to 09:11:23 4 answer the question, I ask that you please go ahead 09:11:25 5 and answer the question that's pending. 09:11:28 6 We'll take breaks as needed today. Please 09:11:32 7 let me know anytime you need a break. The only 09:11:36 8 thing I ask is if there's a question pending, that 09:11:38 9 you go ahead and finish the answer before we take a 09:11:40 10 break. 09:11:42 11 A. Sounds reasonable. 09:11:42 12 Q. So I want to start out asking -- I'm going 09:11:45 13 to hand you something that's already been marked as 09:11:49 14 Exhibit 2060. I think you'll recognize it. I 09:11:55 15 believe it's your CV that was submitted with your 09:11:57 16 report. And let me share. I've got a ways to go 09:12:00 17 across the table. 09:12:08 18 MS. STRUTHERS: Thank you. 09:12:09 19 A. Correct. 09:12:09 20 Q. (BY MR. SUMMERS) So is this your CV? 09:12:09 21 A. Yes, sir. 09:12:16 22 Q. Okay. And I want to skip you to, perhaps, 09:12:17 23 the second page. Under education and training, it 09:12:36 24 starts at 1993, University of Iowa Hospitals and 09:12:43 25 Clinics. 09:12:48 Page 8
1 Q. Dr. Brown, can you please state your name 09:10:08 2 for the record? 09:10:12 3 A. David Brown. 09:10:12 4 Q. And can you give me your business address? 09:10:14 5 A. Business address at our main office is 4460 09:10:16 6 Bellaire -- I'm sorry, 4460 Bissonnet, Bellaire, 09:10:22 7 Texas. 09:10:28 8 Q. Thank you. You're here today as an expert 09:10:28 9 on behalf of Regeneron, correct? 09:10:32 10 A. That's correct. 09:10:34 11 Q. Now, I know you've been deposed a few times 09:10:35 12 before, and I'm guessing you're relatively familiar 09:10:42 13 with the process. But I have a couple of notes 09:10:45 14 that will hopefully make this go easier for both of 09:10:48 15 us, and most importantly, for our court reporter. 09:10:52 16 First of all, do you understand that I'm 09:10:55 17 going to ask you questions today, and you need to 09:10:58 18 give me an answer, subject to your counsel's 09:11:01 19 objections? 09:11:04 20 A. Yes. 09:11:05 21 Q. Okay. And you understand it will make it 09:11:05 22 much easier for our court reporter if you can give 09:11:11 23 a verbal answer, not a head shake or a nod or a 09:11:13 24 shrug, to the extent possible? 09:11:17 25 A. Yes. 09:11:19 Page 7	1 Could you -- could you talk to me a little 09:12:48 2 bit about what you were studying when you were at 09:12:51 3 the University of Iowa? 09:12:53 4 A. Yeah. So I started in 1990 as an 09:12:56 5 ophthalmology resident, to '93. I served as a 09:13:03 6 vitreoretinal surgeon and medical retina fellow 09:13:07 7 from '93 to '95. 09:13:09 8 Q. Okay. And do you recall, was there a time 09:13:11 9 in between '90 -- 1990 and 1995, where you gave an 09:13:13 10 intravitreal injection? 09:13:17 11 A. Yes. 09:13:20 12 Q. Do you recall the first time that you were 09:13:20 13 asked to do that? 09:13:22 14 A. No. 09:13:30 15 Q. Do you recall, did you receive any training 09:13:30 16 on receiving -- or on performing an intravitreal 09:13:32 17 injection before you were asked to give that first 09:13:36 18 injection? 09:13:38 19 MS. STRUTHERS: Objection; beyond 09:13:39 20 the scope the scope. 21 A. I don't really remember. You know, as a -- 09:13:46 22 as a retina surgeon, you learn how to do 09:13:49 23 vitrectomies, where you place -- where you cut 09:13:53 24 three incisions into the pars plana of the eye, 09:13:54 25 which is the part between the -- the -- the clear 09:13:58 Page 9

3 (Pages 6 - 9)

1 parts of the cornea and then the white part. And 09:14:01 2 the pars plana is this area that's relatively a 09:14:03 3 vascular area. Used to making incisions and 09:14:07 4 operating through that area all the time. 09:14:10 5 So an intravitreal injection is just poking 09:14:11 6 a simple needle into that area. Much less 09:14:15 7 complicated than the surgical procedure itself. 09:14:18 8 So, I don't really remember intravitreal 09:14:19 9 injections being that big of a deal because I was 09:14:23 10 an vitreoretinal surgeon. 09:14:26 11 Q. Do you recall -- that raises a good 09:14:28 12 question. Do you recall what you were injecting 09:14:30 13 the first time that you gave an intravitreal 09:14:32 14 injection? 09:14:37 15 A. I don't remember. 09:14:37 16 Q. Let's presumably fast forward a little bit. 09:14:38 17 When is the first time you recall giving an 09:14:42 18 intravitreal injection for an angiogenic eye 09:14:45 19 disorder? 09:14:54 20 A. Best of my recollection, 2002 or so, the 09:15:09 21 Phase 2 ranibizumab trials. At that point in time, 09:15:15 22 they were called Rhu-Fab V2. 09:15:21 23 Q. Could you spell that by any chance? I'm not 09:15:24 24 sure. 09:15:26 25 A. Yeah, ranibizumab is R-A-N-I-B-I-Z-U-M-A-B. 09:15:26 Page 10	1 Q. And then I heard you distinguish it, 09:17:41 2 commercially available Eylea. 09:17:46 3 Do you give an injection of -- 09:17:47 4 A. I can't recall. In -- in clinical trials, 09:17:53 5 there are masked investigators and unmasked. I was 09:17:56 6 usually masked, because I was a principal 09:18:01 7 investigator, which means I didn't actually give 09:18:03 8 the injection. 09:18:04 9 You know, did we have an open label before 09:18:05 10 CLEAR-IT? I don't remember. 09:18:11 11 Q. Thank you. That's -- that's helpful. 09:18:12 12 Did you -- when you gave your first 09:18:37 13 intravitreal injection for Lucentis, did you have 09:18:41 14 to retrain yourself to give an intravitreal 09:18:43 15 injection? 09:18:47 16 MS. STRUTHERS: Objection; beyond 09:18:48 17 the scope the scope. 09:18:54 18 A. Yeah, I don't discuss it in my declaration, 09:18:54 19 but I don't remember. 09:18:57 20 Q. (BY MR. SUMMERS) And -- 09:18:57 21 A. At that point, I had done several thousand 09:18:59 22 vitrectomies. So a needle in the pars plana 09:19:09 23 isn't -- wasn't that memorable. 09:19:12 24 Q. Is it the case -- you say you've done -- 09:19:14 25 you've -- you've done -- and I missed the term you 09:19:18 Page 12
1 At the time it was called Rhu-Fab V2, R-H-U, dash, 09:15:33 2 F-A-B, V-2. 09:15:37 3 Q. So at least to the best of your 09:15:39 4 recollection, the first intravitreal injection you 09:15:49 5 gave for an angiogenic eye disorder was 09:15:51 6 ranibizumab. 09:15:56 7 Is that correct? 09:15:56 8 A. It was an experimental formulation that led 09:15:56 9 to the formation of ranibizumab. 09:16:08 10 Q. Okay. And did -- have you given 09:16:11 11 intravitreal injections of Avastin? 09:16:21 12 A. Yes. 09:16:25 13 Q. And when was the first time you recall 09:16:25 14 giving an intravitreal injection of Avastin? 09:16:27 15 A. I don't exactly recall, but it probably 09:16:39 16 would have been 2005. 09:16:42 17 Q. And when is the first time -- or well, have 09:16:51 18 you given intravitreal injections of Eylea? 09:16:54 19 A. Yes, I have. 09:17:01 20 Q. And do you recall when the first time you 09:17:02 21 would have given an intravitreal injection of Eylea 09:17:06 22 was? 09:17:12 23 A. Commercially available Eylea would have been 09:17:14 24 shortly after their launch. We can look up the 09:17:37 25 date, but 2011-ish. 09:17:39 Page 11	1 used actually. You said a thousand -- what was -- 09:19:23 2 what was the word you used? 09:19:26 3 A. Pars plana vitrectomies, which are 09:19:27 4 operations where we remove the individual patients, 09:19:32 5 after making incisions in the pars plana. And the 09:19:34 6 pars plana is where you inject an intravitreal 09:19:37 7 injection. 09:19:40 8 Q. Okay. So you say you've done several 09:19:40 9 thousand pars plana vitrectomies. 10 Is -- is it the case that the procedure for 09:19:49 11 the injections is the same as the one that you 09:19:52 12 apply when you give an intravitreal injection for 09:19:54 13 an Anti-VEGF agent? 09:19:57 14 MS. STRUTHERS: Objection to form, 09:20:04 15 beyond the scope the scope. 09:20:05 16 A. It's several orders of magnitude easier than 09:20:05 17 an intravitreal injection. 09:20:12 18 Q. (BY MR. SUMMERS) Can you walk me through 09:20:24 19 the steps that you take when you ready a patient to 09:20:30 20 received an intravitreal injection today? 09:20:34 21 MS. STRUTHERS: Objection; beyond 09:20:40 22 the scope the scope. 09:20:40 23 A. Can I see my declaration? 09:20:40 24 Q. (BY MR. SUMMERS) Sure. I'm going to hand 09:20:46 25 you what has been previously marked as 09:20:58 Page 13

1 Exhibit 2050. It's a document with the title, 09:21:01 2 Expert Declaration of David M. Brown, the -- 09:21:07 3 actually, strike that. Because I would be handing 09:21:12 4 you the wrong declaration. I think that's the one. 09:21:14 5 A. That one looked too thick. 09:21:17 6 Q. That one. I agree. This will look better. 09:21:22 7 I'm going to hand you what previously -- 09:21:43 8 MR. SUMMERS: Just for the record, I 09:21:44 9 didn't hand Exhibit 2050 to Dr. Brown just yet. 09:21:45 10 Q. (BY MR. SUMMERS) I'm going to hand you 09:21:49 11 what's previously marked Exhibit 2055, also titled, 09:21:49 12 The Expert Declaration of David M. Brown, M.D. 09:21:54 13 (The witness peruses the document.) 09:22:55 14 A. Can you repeat the question? 09:27:17 15 Q. (BY MR. SUMMERS) Sure. Can you walk me 09:27:18 16 through the steps you take when you ready a patient 09:27:20 17 to receive an intravitreal injection today? 09:27:22 18 MS. STRUTHERS: Objection; beyond 09:27:26 19 the scope the scope. 09:27:26 20 A. So, I reviewed my declaration. Can you 09:27:26 21 point to me in the declaration where I go through 09:27:31 22 the mechanisms of offering the drug? 09:27:33 23 Q. (BY MR. SUMMERS) No, I can't. That's why 09:27:35 24 I'm asking. I'm here to depose you today, which 09:27:38 25 means I'm going to ask you some questions outside 09:27:41 Page 14	1 asking you for some facts, which is what steps you 09:29:09 2 take to prepare a patient to receive an 09:29:12 3 intravitreal injection. I'm going to ask you 09:29:15 4 again. 09:29:17 5 What steps do you take to prepare a patient 09:29:21 6 to receive an intravitreal injection today? 09:29:23 7 MS. STRUTHERS: Objection; beyond 09:29:26 8 the scope the scope. 09:29:27 9 Counsel, if you have questions for 09:29:27 10 the witness on the declaration, he'll be happy to 09:29:30 11 answer them. If you don't, we should consider 09:29:33 12 wrapping it up because we can't do this all day. 09:29:35 13 Q. (BY MR. SUMMERS) The question is pending. 09:29:37 14 Please answer. 09:29:40 15 MS. STRUTHERS: Same objection; 09:29:41 16 beyond the scope the scope. 09:29:43 17 A. I discuss a lot who to treat and when to 09:29:43 18 treat. I don't go into the mechanisms of how the 09:29:46 19 sausage is made. I don't offer an opinion, and I 09:29:49 20 don't -- don't feel prepared to offer one today. 09:29:52 21 Q. (BY MR. SUMMERS) You've given an opinion on 09:30:00 22 a -- a patent from Regeneron. It's U.S. Patent 09:30:24 23 10,130,681, correct? 09:30:29 24 A. 10,130,681. That is correct. 09:30:35 25 Q. Okay. Will you understand what I'm 09:30:38 Page 16
1 of what's in your declaration. So, I'm going to 09:27:43 2 ask you the question again. 09:27:47 3 If you know the answer to it, I'm going to 09:27:48 4 remind you that you're under oath. So please go 09:27:50 5 ahead and answer. 09:27:54 6 Can you walk me through the steps you take 09:27:55 7 when you ready a patient to receive an intra -- 09:28:02 8 intravitreal injection today? 09:28:04 9 MS. STRUTHERS: Objection; beyond 09:28:07 10 the scope the scope. 09:28:07 11 A. I didn't offer an opinion on the mechanisms 09:28:07 12 of how to give the drugs, and I'm not prepared to 09:28:16 13 do so today. 09:28:18 14 Q. (BY MR. SUMMERS) So you -- it's your 09:28:19 15 testimony you can't tell me today what steps you 09:28:22 16 take to prepare a patient to receive an 09:28:27 17 intravitreal injection? 09:28:30 18 MS. STRUTHERS: Objection; 09:28:31 19 mischaracterized the testimony and beyond the scope 09:28:32 20 the scope. 09:28:33 21 A. I'm a careful witness. I spend a lot of 09:28:33 22 time with all the words. I didn't offer an 09:28:41 23 opinion, and I'm not prepared to do so today. 09:28:45 24 Q. (BY MR. SUMMERS) All right. I'm not -- to 09:28:54 25 be clear, I'm not asking you for an opinion. I'm 09:29:03 Page 15	1 referring to, if I refer to that as the '681 09:30:39 2 patent? 09:30:43 3 A. Yes, sir. 09:30:44 4 Q. And you read the claims of the '681 patent 09:30:44 5 in order to prepare your declaration, correct? 09:30:52 6 A. Yes, I did. 09:30:57 7 Q. Okay. The claims in the '681 patent refer 09:30:57 8 to something known as an exclusion criteria, 09:31:03 9 correct? 09:31:07 10 A. Can I see the '681 patent? 09:31:10 11 Q. They're reproduced in your report at 09:31:12 12 page 45, which you already have in front of you. 09:31:15 13 Why don't you go ahead and pull that up? 09:31:18 14 (The witness peruses the document.) 09:31:34 15 Q. (BY MR. SUMMERS) So I'm going to repeat my 09:31:53 16 question. 09:31:54 17 The claims of the '681 patent refer to 09:31:54 18 something known as exclusion criteria, correct? 09:31:58 19 A. I see that. 09:32:00 20 Q. Okay. What is an exclusion criteria? 09:32:01 21 MS. STRUTHERS: Objection; beyond 09:32:03 22 the scope. 09:32:08 23 (The witness peruses the document.) 09:32:08 24 A. I'm a physician, not an attorney. And while 09:32:34 25 I see the words exclusion criteria for the patient 09:32:45 Page 17

5 (Pages 14 - 17)

1 in this, I didn't offer an opinion as to what that 09:32:48 2 means or -- and I'm not prepared to do so today. 09:32:51 3 Q. (BY MR. SUMMERS) Do you have an 09:32:56 4 understanding, sitting here today, what exclusion 09:32:58 5 criteria means in the claims of the '681 patent? 09:33:00 6 MS. STRUTHERS: Objection; beyond 09:33:06 7 the scope. 8 And I'd reiterate, Counsel, that if 09:33:07 9 you're not going to ask questions about the 09:33:10 10 opinions in his declaration, we should wrap this 09:33:12 11 up. 09:33:14 12 A. Again, top of my med school class. A lot of 09:33:14 13 kids went to law school; I didn't. I can't give 09:33:19 14 you a definition of exclusion criteria within the 09:33:21 15 patent. I didn't offer an opinion, and not 09:33:24 16 prepared to do so today. 09:33:28 17 Q. (BY MR. SUMMERS) So you -- you are not 09:33:30 18 prepared to give me today your understanding of the 09:33:31 19 word, exclusion criteria, as it appears in the 09:33:33 20 claim of the '681 patent. 09:33:36 21 Is that correct? 09:33:41 22 MS. STRUTHERS: Objection; asked and 09:33:41 23 answered and beyond the scope. 09:33:43 24 A. I didn't offer an opinion, and I'm not 09:33:44 25 prepared to do so today. 09:33:46 Page 18	1 A. So I understand that reasonable expectation 09:36:47 2 of success is a legal term. I state, page 47, 09:37:16 3 paragraph 101: The POSA would not have had a 09:37:21 4 reasonable expectation of successfully achieving 09:37:25 5 the Q8 dosing regimen claimed by the '681 patent 09:37:27 6 until after Regeneron conducted its VIEW 1, VIEW 2 09:37:31 7 trials. 09:37:34 8 As discussed in Section V1C, the prior art 09:37:34 9 was littered with failed attempts to develop an 09:37:38 10 extended dosing regimen for the treatment of wet 09:37:40 11 AMD. 09:37:43 12 Many of these features were only recognized 09:37:44 13 after the trial was completed or upon post hoc 09:37:47 14 analysis, which contributed to a general skepticism 09:37:51 15 by the POSA, regarding whether a prospective fixed 09:37:55 16 extended dosing regimen would be successful until 09:37:59 17 the results were recognized. 09:38:02 18 In addition, here, the Phase 2 results of 09:38:03 19 the VEGF Trap-Eye in CLEAR-IT 2 would have created 09:38:08 20 uncertainty if the VEGF Trap-Eye would be effective 09:38:11 21 if dosed on a Q8 regimen. 09:38:14 22 Q. Is that your complete answer? 09:38:16 23 A. Yes. 09:38:28 24 MR. SUMMERS: So I'm going to move 09:38:31 25 to strike that as nonresponsive. 09:38:35 Page 20
1 Q. (BY MR. SUMMERS) Okay. Did you read the 09:33:47 2 claims of the '681 patent before you submitted your 09:33:47 3 declaration? 09:33:50 4 A. I read the claims multiple times. 09:33:50 5 Q. Okay. And you saw the word, exclusion 09:33:57 6 criteria, in those claims, right? 09:33:59 7 A. I saw the words and see the words as they're 09:34:00 8 in front of me today. 09:34:05 9 Q. Okay. What is your understanding of those 09:34:06 10 words? 09:34:07 11 MS. STRUTHERS: Objection; asked and 09:34:09 12 answered, beyond the scope. 09:34:09 13 A. Didn't offer an opinion on their meaning 09:34:10 14 or -- and not prepared to do so today. 09:34:19 15 Q. (BY MR. SUMMERS) You give an opinion in 09:34:20 16 your declaration on reasonable expectation of 09:34:25 17 success as it relates to some prior art grounds for 09:34:30 18 the '681 patent, correct? 09:34:36 19 A. Can you repeat the question? 09:34:38 20 Q. You give an opinion, in your declaration, on 09:36:27 21 reasonable expectation of success as it relates to 09:36:31 22 some prior art grounds for the '681 patent, 09:36:34 23 correct? 09:36:38 24 A. That is correct. 09:36:38 25 Q. What is a reasonable expectation of success? 09:36:39 Page 19	1 Q. (BY MR. SUMMERS) I'm just going to ask you 09:38:37 2 again. 09:38:39 3 What is your understanding of a reasonable 09:38:39 4 expectation of success? 09:38:44 5 MS. STRUTHERS: Objection; asked and 09:38:46 6 answered. 09:38:48 7 A. I -- in layman's terms, to me, and again, 09:38:48 8 I'm not a lawyer, reasonable expectation of success 09:38:58 9 is if we would have thought it would have worked. 09:39:00 10 As it pertains to this patent, after -- 09:39:05 11 having probably more intimate knowledge of CLEAR-IT 09:39:09 12 than almost anyone in the -- the country, I didn't 09:39:12 13 think it would work. So I didn't think it would 09:39:16 14 have a reasonable expectation of success. And if 09:39:18 15 that meets the legal definition, I'm not sure, but 09:39:20 16 that's the way I interpret it. 09:39:23 17 Q. (BY MR. SUMMERS) Okay. Do you understand 09:39:24 18 that a reasonable expectation of success requires 09:39:26 19 certainty that a method will work? 09:39:28 20 A. Repeat that. 09:39:34 21 MS. STRUTHERS: Object -- 09:39:35 22 A. Repeat that. 09:39:36 23 Q. (BY MR. SUMMERS) Do you understand that a 09:39:36 24 reasonable expectation of success requires 09:39:37 25 certainty that a method will work? 09:39:39 Page 21

1 MS. STRUTHERS: Objection; calls for 09:39:42 2 speculation. 09:39:44 3 A. Repeat your question one more time. So 09:39:44 4 it's -- it requires certainty? 09:39:51 5 Q. (BY MR. SUMMERS) Yeah, sure. Do you 09:39:52 6 understand that a reasonable expectation of success 09:39:53 7 requires certainty that a method will work? 09:39:55 8 MS. STRUTHERS: Objection; calls for 09:39:58 9 speculation. 09:40:00 10 A. You have to have all the data in each 09:40:00 11 circumstance to figure that out, I think, if you 09:40:13 12 were certain that something would work. Like... 09:40:19 13 Q. (BY MR. SUMMERS) What do you mean by you 09:40:25 14 have to have all the data? 09:40:26 15 MS. STRUTHERS: Again, objection; 09:40:34 16 calls for speculation. 09:40:35 17 A. It seems reasonable that a -- that a 09:40:35 18 reasonable expectation of success would require 09:40:54 19 that you were -- required certainty. I don't know 09:40:56 20 if those are legal terms or not. Again, I'm not a 09:41:00 21 lawyer. But it seems reasonable to me that you 09:41:02 22 have to have certainty. 09:41:07 23 Q. (BY MR. SUMMERS) And -- and in forming your 09:41:08 24 opinion for the purposes of this declaration, did 09:41:10 25 you apply that understanding of a reasonable 09:41:15 Page 22	1 expectation of success requires? 09:43:05 2 MS. STRUTHERS: Object -- objection 09:43:14 3 to form; mischaracterizes the testimony. 09:43:14 4 (The witness peruses the document.) 09:43:45 5 A. Paragraph 101, I state, part way through the 09:45:32 6 next page: In addition, here, the Phase 2 results 09:45:37 7 of VEGF Trap-Eye in CLEAR-IT 2 would have created 09:45:43 8 uncertainty that VEGF Trap-Eye could be effective 09:45:46 9 if dosed on a Q8 regimen. 09:45:50 10 Page 50, paragraph 107, I state: Thus, 09:45:53 11 prior failures to achieve an effective extended 09:45:57 12 dosing regimen demonstrate that there was great 09:46:00 13 uncertainty as to whether Regeneron's fixed 09:46:05 14 extending dosing regimen with greater than or equal 09:46:08 15 to eight weeks maintenance dosing would work until 09:46:10 16 the VIEW -- results of VIEW 1 and 2 studies were 09:46:12 17 reported. 09:46:15 18 Page 52, paragraph 110: Moreover, 09:46:21 19 Regeneron's VIEW 1, 2 study design confirms that 09:46:23 20 there was great uncertainty as to whether an 09:46:25 21 extended dosing regimen would be successful. 09:46:27 22 Specifically, the VIEW trials included study arms 09:46:31 23 with 2-milligram and .5-milligram administered on a 09:46:34 24 four-week dosing regimen, in addition to the two Q8 09:46:37 25 arms. 09:46:41 Page 24
1 expectation of success? 09:41:17 2 MS. STRUTHERS: Objection; 09:41:18 3 mischaracterizes the testimony, and calls for 09:41:19 4 speculation. 09:41:22 5 A. What I state is: In addition here, the 09:41:22 6 Phase 2 results of the VEGF Trap-Eye in CLEAR-IT 2 09:42:08 7 would have created uncertainty that VEGF Trap-Eye 09:42:13 8 would be effective if dosed on a Q8 regimen. 09:42:17 9 Q. (BY MR. SUMMERS) Right. And you gave me 09:42:23 10 your understanding of a reasonable expectation of 09:42:24 11 success. My question is, in forming your opinion 09:42:27 12 for the purposes of this declaration, did you apply 09:42:32 13 that understanding, in determining whether there 09:42:36 14 was an reasonable expectation of success here? 09:42:38 15 MS. STRUTHERS: Objection to form; 09:42:39 16 mischaracterizes the testimony. 09:42:43 17 A. Repeat your question. 09:42:44 18 Q. (BY MR. SUMMERS) So, my question is, 09:42:45 19 because I don't think your answer is responsive to 09:42:53 20 it. So let me ask you this again. 09:42:55 21 MS. STRUTHERS: And I object to that 09:42:56 22 characterization, but please ask your question. 09:42:57 23 Q. (BY MR. SUMMERS) Okay. In forming your 09:42:58 24 opinions for the purposes of your declaration, did 09:43:00 25 you apply your understanding of what a reasonable 09:43:02 Page 23	1 The additional study arms increased the 09:46:41 2 number of patients and time needed to conduct the 09:46:43 3 clinical trial, as well as the cost of the studies. 09:46:45 4 At the time Regeneron was designing its Phase 3 09:46:49 5 trials, it was out of funds, needed to seek a 09:46:53 6 collaborative PRN to -- in order to fund the trial. 09:46:55 7 If Regeneron had been able to save the time 09:46:58 8 and expense of recruiting foreign redundant 09:47:00 9 additional study arms -- in other words if it had a 09:47:05 10 reasonably certain that a Q8 maintenance dosing 09:47:07 11 would work, it would have every incentive to drop 09:47:10 12 the four-week VEGF Trap-Eye dosing arms from the 09:47:13 13 VIEW studies. 09:47:19 14 Again, in page 122, I state: The published 09:47:19 15 results of CLEAR-IT 2 in this clinical trial 09:47:23 16 designed for VIEW 1 and 2 demonstrate that there 09:47:26 17 was great uncertainty as to whether Regeneron's 09:47:28 18 extended fixed dosing regimen, open parentheses, 09:47:31 19 with greater than or equal to eight weeks 09:47:35 20 maintenance dosing, after only three monthly 09:47:36 21 loading doses would be successful and the results 09:47:39 22 of the VIEW 1, 2 study were completed. 09:47:41 23 So I've cited five or six times in this 09:47:43 24 section on reasonable -- reasonable expectations of 09:47:45 25 success, the term certain and uncertainty. And I 09:47:59 Page 25

7 (Pages 22 - 25)

1 certainly thought about whether we thought it was 09:48:05 2 possible to happen, and I state it in my 09:48:08 3 declaration. 09:48:15 4 Q. (BY MR. SUMMERS) So I take it, in pointing 09:48:15 5 me to those passages referring to uncertainty, you 09:48:28 6 applied your understanding that a reasonable 09:48:31 7 expectation of success requires certainty in 09:48:34 8 forming your opinions? 09:48:35 9 MS. STRUTHERS: Objection; 09:48:36 10 mischaracterizes the testimony, calls for a legal 09:48:38 11 conclusion. 09:48:41 12 A. Repeat the question. 09:48:41 13 Q. (BY MR. SUMMERS) Sure. I take it, in 09:48:53 14 pointing me to these passages in your declaration 09:48:56 15 referring to uncertainty that you employed your 09:49:00 16 understanding that a reasonable expectation of 09:49:03 17 success requires certainty in forming your 09:49:05 18 opinions? 09:49:06 19 MS. STRUTHERS: Objection; 09:49:07 20 mischaracterizes the testimony, calls for a legal 09:49:07 21 conclusion. 09:49:09 22 A. Repeat the question. 09:49:09 23 Q. (BY MR. SUMMERS) Sure. I take it, in 09:50:10 24 pointing me to these passages in your declaration 09:50:11 25 referring to uncertainty that you employed your 09:50:13 Page 26	1 Q. Okay. I -- I read through these. I didn't 09:52:08 2 see anything defining for you what a reasonable 09:52:10 3 expectation of success is. 09:52:16 4 Can you go ahead and confirm that's true? 09:52:17 5 (The witness peruses the document.) 09:52:21 6 MS. STRUTHERS: Objection; document 09:52:23 7 speaks for itself. 09:52:24 8 A. It doesn't -- doesn't -- doesn't talk about 09:52:45 9 it. 09:52:47 10 Q. (BY MR. SUMMERS) Okay. So what I'm trying 09:52:48 11 to get at is what the understanding of a reasonable 09:52:49 12 expectation of success requires that you applied 09:52:54 13 when you provided this declaration, because it's 09:52:57 14 not here. And I need to know that, in order to 09:53:02 15 understand the basis for your analysis. 09:53:08 16 So, let me ask you a couple more questions 09:53:11 17 up front. 09:53:14 18 Did -- did you understand, in forming your 09:53:15 19 opinions, that conclusive proof of efficacy was 09:53:17 20 required, in order to have a reasonable expectation 09:53:26 21 of success? 09:53:28 22 MS. STRUTHERS: Objection; 09:53:28 23 mischaracterizes the testimony, calls for 09:53:35 24 speculation. 09:53:36 25 A. Repeat the question. 09:53:36 Page 28
1 understanding that a reasonable expectation of 09:50:18 2 success requires certainty in forming your 09:50:21 3 opinions? 09:50:23 4 MS. STRUTHERS: Objection; 09:50:24 5 mischaracterizes the testimony, calls for a legal 09:50:24 6 conclusion. 09:50:25 7 A. Again, I'm not a lawyer. And the exact 09:50:25 8 term, certainty, in the legal terminology, I can't 09:50:29 9 tell you I could recite. 09:50:37 10 I can tell you, in medical trials, we look 09:50:40 11 at the totality of the data, which I did in making 09:50:43 12 an opinion of whether the POSA would have a 09:50:49 13 reasonable expectation of success that the claimed 09:50:52 14 eight-week dosing regimen would be effective. 09:50:58 15 Q. (BY MR. SUMMERS) Let's try this. Please 09:51:01 16 turn, in your declaration, to page 6. 09:51:22 17 A. What page? 09:51:44 18 Q. Page 6, please. 09:51:44 19 A. Page 6. 09:51:45 20 Q. And you have some legal standards here, 09:51:52 21 correct? 09:51:59 22 A. Beg your pardon? 09:52:00 23 Q. You have some legal standards here on 09:52:00 24 page 6, from paragraphs 17 to 24. 09:52:02 25 A. Correct. 09:52:05 Page 27	1 Q. (BY MR. SUMMERS) Did you understand, in 09:53:37 2 forming your opinions, that conclusive proof of 09:53:38 3 efficacy was required in order to have a reasonable 09:53:41 4 expectation of success? 09:53:45 5 MS. STRUTHERS: Same objections. 09:53:45 6 Calls for speculation. 09:53:47 7 A. You're going to have to restate your 09:53:47 8 question. I don't quite understand it. 09:53:57 9 Q. (BY MR. SUMMERS) Sure. Did you understand, 09:53:58 10 in forming your opinions, that conclusive proof of 09:54:00 11 efficacy was required in order to have a reasonable 09:54:03 12 expectation of success? 09:54:09 13 MS. STRUTHERS: Same objections. 09:54:09 14 Calls for a legal conclusion. 09:54:10 15 A. Again, and I'm not a lawyer, and don't know 09:54:11 16 if conclusive proof of efficacy is a legal term. I 09:54:37 17 can tell you, in clinical trials, we generally 09:54:42 18 require two randomized, well-controlled, large 09:54:48 19 trials to prove efficacy, at least to the agency, 09:54:51 20 when trying to get a drug approved. So... 09:54:55 21 Q. (BY MR. SUMMERS) Is -- is that the standard 09:55:02 22 that you applied in determining whether there was a 09:55:08 23 reasonable expectation of success for the purposes 09:55:14 24 of giving your opinions in your declaration? 09:55:14 25 MS. STRUTHERS: Objection; 09:55:18 Page 29

1 mischaracterizes the testimony, calls for a legal 09:55:19 2 conclusion. 09:55:22 3 A. The standard I applied was based on my 09:55:22 4 experience as one of the leading anti-VEGF 09:55:45 5 researchers in the world, having intimate knowledge 09:55:52 6 at the time of the CLEAR-IT data, and whether I 09:55:56 7 personally thought it would work on a Q8 dosing 09:56:01 8 regimen, which I did not. 09:56:08 9 Q. (BY MR. SUMMERS) I just want to understand 09:56:09 10 your testimony. So the standard you applied was 09:56:26 11 whether you personally thought it would work at the 09:56:28 12 time. 09:56:30 13 Is that right? 09:56:30 14 MS. STRUTHERS: Objection; asked and 09:56:33 15 answered. 09:56:34 16 A. The hypothetical POSA, who has access to 09:56:34 17 everything in the world, literature that probably 09:56:45 18 even I don't have access to, presumably, all I can 09:56:48 19 do is put myself in his place as an ordinary skill 09:56:52 20 of the art, and would that person, after seeing 09:56:56 21 what I was seeing, would assume the same thing. 09:56:59 22 That's what I used. I used my standard as 09:57:02 23 an expert, having intimate knowledge of the trial 09:57:05 24 and all the data at the time. 09:57:10 25 Q. (BY MR. SUMMERS) And you said earlier that 09:57:12 Page 30	1 VEGF Trap-Eye might last six weeks, but had great 09:59:05 2 skepticism that it would be non-inferior to 09:59:10 3 Lucentis on an eight-week fixed dosing regimen. 09:59:12 4 While we thought monthly dosing of VEGF 09:59:17 5 Trap-Eye would likely work, non-inferior to 09:59:19 6 Lucentis monthly dosing, we viewed the Q8 arm as a 09:59:24 7 long shot. Indeed, as discussed above, when 09:59:27 8 Regeneron ranked its dosing regimens for 09:59:29 9 statistical reporting, it ranked the 2 Q8 arm below 09:59:31 10 the 2 Q4 arm and the 0.5-milligram Q4 dosing arms, 09:59:36 11 indicating that Regeneron believed both Q4 dosing 09:59:38 12 arms were more likely than the Q8 dosing arm to hit 09:59:42 13 their primary implants. 09:59:45 14 Q. (BY MR. SUMMERS) Dr. Brown, when you formed 09:59:49 15 your opinion about reasonable expectation of 09:59:56 16 success in your report, was one of the requirements 09:59:59 17 that you applied that there may be two randomized, 10:00:03 18 well-controlled, large trials to prove efficacy? 10:00:09 19 MS. STRUTHERS: Objection; 10:00:13 20 mischaracterizes the testimony, asked and answered. 10:00:13 21 A. Yeah, I didn't say that. I said that's what 10:00:14 22 FDA requires to approve a drug. 10:00:18 23 Q. (BY MR. SUMMERS) Right. I'm not -- I'm not 10:00:20 24 actually characterizing your testimony at all. I'm 10:00:22 25 asking you a question about the standards you 10:00:24 Page 32
1 for clinical trials, you require two randomized, 09:57:16 2 well-controlled, large trials to prove efficacy, 09:57:18 3 correct? 09:57:23 4 A. The agency requires that for approval of an 09:57:24 5 FDA-approved drug. 09:57:29 6 Q. And is that also the standard you personally 09:57:30 7 applied in looking at the data? 09:57:34 8 MS. STRUTHERS: Objection; 09:57:38 9 mischaracterizes the testimony, asked and answered. 09:57:39 10 A. The reasonable expectation of success 09:57:41 11 section deals with the Phase 2 CLEAR-IT trial, 09:57:56 12 which informed the Phase 3 designs. It led to 09:57:59 13 these Phase 3 trials, which led to approval of 09:58:03 14 aflibercept, Eylea. I personally used my knowledge 09:58:12 15 of what was available at the time in the CLEAR-IT 09:58:15 16 trial of whether I thought it would work or not, on 09:58:18 17 a Q8-week dosing. 09:58:22 18 And paragraph 121, page 60, I say: In fact, 09:58:23 19 I recall discussing the design of the Regeneron's 09:58:42 20 Phase 3 VIEW trials with co-investigator, Jeff 09:58:46 21 Heier, before initiation of the VIEW trials. At 09:58:50 22 that time we only had preliminary Phase 2 data from 09:58:53 23 CLEAR-IT 2. And I recall that looking at the 09:58:57 24 mean -- looking at the rise and mean CRT, which is 09:58:59 25 central retinal thickness. We both thought that 09:59:01 Page 31	1 applied. So let me try that again. 10:00:26 2 Dr. Brown, when you formed your opinion 10:00:28 3 about reasonable expectation of success in this 10:00:33 4 declaration, was one of the requirements that you 10:00:34 5 applied that there needed to be two randomized, 10:00:37 6 well-controlled, large trials to prove efficacy? 10:00:41 7 MS. STRUTHERS: Objection; asked and 10:00:44 8 answered. 10:00:45 9 A. The section on reasonable expectation of 10:00:45 10 success deals with CLEAR-IT 2, which is the Phase 2 10:01:02 11 trial. 10:01:05 12 Phase 2 trial informs Phase 3 trials, which 10:01:06 13 would lead to that, and what you're talking about, 10:01:09 14 which is what the agency requires, I didn't have 10:01:12 15 that data then. I had what was available in 10:01:14 16 CLEAR-IT 2, as a world expert on anti-VEGF trials, 10:01:17 17 intimately involved in the trial, first author of 10:01:27 18 CLEAR-IT 2 primary outcome, and whether I thought 10:01:29 19 it would work or not. 10:01:31 20 And based on the data predominantly from the 10:01:32 21 OCT data, I did not think it was likely to work on 10:01:35 22 a Q8-week dosing regimen, compared to ranibizumab 10:01:40 23 monthly. 10:01:51 24 Q. (BY MR. SUMMERS) With all due respect, this 10:01:53 25 is a yes or no question. Let me try it again. 10:02:04 Page 33

1 When you formed your opinion about the 10:02:09 2 reasonable expectation of success in your 10:02:11 3 declaration, was one of the requirements that you 10:02:13 4 applied that there needed to be two randomized, 10:02:17 5 well-controlled, large trials to show efficacy? 10:02:22 6 MS. STRUTHERS: Objection; asked and 10:02:27 7 answered. 10:02:29 8 A. That data wasn't available with the 10:02:29 9 CLEAR-IT 2 study, and that's what the section of 10:02:38 10 reasonable expectation of success entails. So 10:02:41 11 didn't have that data. 10:02:47 12 Q. (BY MR. SUMMERS) And it would be required 10:02:48 13 to show a reasonable expectation of success, in 10:02:51 14 your opinion. 10:02:53 15 Is that correct? 10:02:53 16 MS. STRUTHERS: Objection. 10:02:54 17 A. That is not correct. 10:02:55 18 Q. (BY MR. SUMMERS) So, let me come at it 10:02:58 19 again, because I -- I looked at your declaration, 10:03:22 20 Dr. Brown. 10:03:24 21 What is the understanding of reasonable 10:03:24 22 expectation of success that you applied in forming 10:03:26 23 the opinions in your declaration? 10:03:28 24 MS. STRUTHERS: Objection; asked and 10:03:30 25 answered. 10:03:31 Page 34	1 be successful in a Q8-week dosing regimen, and 10:04:53 2 wasn't proved otherwise until we conducted the 10:05:01 3 VIEW 1, VIEW 2 trials. 10:05:05 4 Q. (BY MR. SUMMERS) I understand that those 10:05:06 5 are the facts you say you relied on here. What I 10:05:16 6 want to know is what is the standard that you 10:05:21 7 applied to those facts in determining whether they 10:05:22 8 showed a reasonable expectation of success. 10:05:24 9 MS. STRUTHERS: Objection; asked and 10:05:29 10 answered. 10:05:29 11 A. The section on reasonable expectation of 10:05:29 12 success deals with the CLEAR-IT 2 trial. And in 10:05:44 13 paragraph 101, I state: The POSA would not have 10:05:47 14 had a reasonable expectation of successfully 10:05:51 15 achieving the Q8 dosing regimen claimed by the '681 10:05:54 16 patent until after Regeneron conducted its VIEW 1, 10:05:58 17 VIEW 2 trials. As discussed in Section V1.C, the 10:06:02 18 prior art was littered with failed attempts of 10:06:05 19 efforts, sorry, to deliver -- or attempts, to 10:06:07 20 deliver an extended dosing regimen for the 10:06:10 21 treatment of wet AMD. 10:06:13 22 Many of these failures were only recognized 10:06:15 23 after the trial was completed or upon post hoc 10:06:18 24 analysis, which would have contributed to a general 10:06:21 25 skepticism by the POSA regarding whether a 10:06:25 Page 36
1 A. So the section of reasonable expectation of 10:03:31 2 success, as I state: The POSA would not have a 10:03:44 3 reasonable expectation of successfully achieving 10:03:47 4 the Q8-week dosing regimen claimed by the '681 10:03:49 5 patent until Regeneron conducted its VIEW 1 and 10:03:53 6 VIEW trials. 10:03:56 7 The prior art was littered with failed 10:03:57 8 attempts to develop an extended dosing regimen for 10:03:59 9 the treatment of wet AMD. Many of these failures 10:04:02 10 were only recognized after the trial was completed 10:04:05 11 or upon post hoc analysis. And it would -- 10:04:08 12 contributed to a general skepticism whether a 10:04:11 13 prospective fixed extending dosing regimen would be 10:04:15 14 successful. 10:04:17 15 In addition here, the Phase 2 results of the 10:04:17 16 VEGF Trap-Eye in CLEAR-IT 2 would have created 10:04:21 17 uncertainty that the VEGF Trap-Eye would be 10:04:24 18 effective if dosed on a Q8 regimen. 10:04:25 19 I applied the totality of the data from the 10:04:28 20 CLEAR-IT 2 study, of which I was a principal 10:04:33 21 investigator, primary author of the primary 10:04:36 22 manuscript, and a worldwide anti-VEGF research 10:04:40 23 expert on whether I thought it would be successful 10:04:45 24 or not. 10:04:47 25 I personally did not think it would likely 10:04:50 Page 35	1 prospective fixed extending dosing regimen would be 10:06:27 2 successful until the results were recognized. 10:06:29 3 In addition, here, the Phase 2 results of 10:06:32 4 the VEGF Trap-Eye in CLEAR-IT 2 would have created 10:06:36 5 uncertainty that VEGF Trap-Eye could be effective 10:06:40 6 if dosed on a Q8 regimen. 10:06:42 7 The data I used was the totality of the data 10:06:45 8 from the CLEAR-IT 2 trial, as -- as an intimate 10:06:48 9 member of that trial design and first author of the 10:06:56 10 primary data outcome. 10:07:02 11 And the question is whether I thought it had 10:07:02 12 a likelihood of being successful, and I didn't 10:07:04 13 think it was likely to be successful on a Q8-week 10:07:09 14 dosing regimen, when compared to ranibizumab 10:07:13 15 0.5 milligrams monthly, and wasn't convinced 10:07:19 16 otherwise until we actually ran the horse race, 10:07:22 17 conducted the VIEW 1, VIEW 2 trials and saw the 10:07:24 18 results. 10:07:37 19 Q. (BY MR. SUMMERS) Are you able, sitting 10:07:37 20 here, to tell me what standard you applied to the 10:07:39 21 facts that you just recited in trying to determine 10:07:41 22 whether they showed a reasonable expectation of 10:07:44 23 success? 10:07:46 24 MS. STRUTHERS: Objection; asked and 10:07:46 25 answered. 10:07:51 Page 37

1 A. In the section on reasonable expectation of 10:07:51 2 success, it deals with the CLEAR-IT trial. And I 10:07:54 3 state in paragraph 101: The POSA would not have 10:08:00 4 had a reasonable expectation of successfully 10:08:03 5 achieving the Q8-week dosing regimen claimed in the 10:08:06 6 '681 patent until Regeneron conducted its VIEW 1, 10:08:11 7 VIEW 2 trials. 8 As discussed in Section V1.C, the prior art 10:08:14 9 was littered with failed attempts to develop an 10:08:18 10 extended dosing regimen for the treatment of wet 10:08:21 11 AMD. Many of those failures were only recognized 10:08:25 12 after the trial was completed or upon post hoc 10:08:27 13 analysis, which would have contributed to a general 10:08:29 14 skepticism by the POSA regarding whether a 10:08:33 15 prospective fixed extended dosing regimen would be 10:08:35 16 successful until the results were recognized. 10:08:38 17 In addition, here, the Phase 2 results of 10:08:40 18 the VEGF Trap-Eye in CLEAR-IT 2 would have created 10:08:45 19 uncertainty that the VEGF Trap-Eye would be 10:08:48 20 effective if dosed as a Q8 regimen. 10:08:52 21 What I used was the totality of the data of 10:08:54 22 the CLEAR-IT 2 study, having intimate knowledge of 10:08:57 23 the study, being the primary author of its -- of 10:09:01 24 its -- the primary publication, and being involved 10:09:04 25 in that study. 10:09:06 Page 38	1 MS. STRUTHERS: Asked and answered. 10:10:18 2 A. Relied on the totality of the data and the 10:10:18 3 trial. 10:10:24 4 Q. (BY MR. SUMMERS) So let's -- let's come 10:10:24 5 back a little bit. You can go back to page 45 of 10:10:26 6 your opinion, or your declaration. 10:10:29 7 Do you understand that a reasonable 10:10:38 8 expectation of success is a -- relates to the 10:10:39 9 entire invention that's claimed in the patent? 10:10:43 10 MS. STRUTHERS: Objection; calls for 10:10:46 11 a legal conclusion. 10:10:47 12 A. Repeat the question. 10:10:47 13 Q. (BY MR. SUMMERS) Do you understand that a 10:10:51 14 reasonable expectation of success -- well, scratch 10:10:54 15 that, actually. 10:10:56 16 To form your opinions on a reasonable 10:10:56 17 expectation of success, did you form an 10:11:00 18 understanding of what the claimed invention is? 10:11:01 19 MS. STRUTHERS: Objection to form. 10:11:07 20 A. Repeat that question, again. 10:11:07 21 Q. (BY MR. SUMMERS) To form your opinions on 10:11:10 22 reasonable expectation of success, did you form an 10:11:11 23 understanding of what the claimed invention is? 10:11:13 24 MS. STRUTHERS: Same objection. 10:11:19 25 Objection to form. 10:11:20 Page 40
1 And what I mean by that is I didn't think 10:09:07 2 that -- do I think it was going to work on a Q8 10:09:11 3 dosing regimen versus ranibizumab 0.5 milligrams 10:09:17 4 dosed monthly? I honestly didn't think it had much 10:09:21 5 of a chance, and I wasn't convinced otherwise until 10:09:24 6 we actually saw the results of the VIEW 1, VIEW 2 10:09:27 7 trials. 10:09:32 8 Q. (BY MR. SUMMERS) So outside of reading back 10:09:32 9 paragraph 101, and providing your experience with 10:09:34 10 the trials, do you have any other information to 10:09:37 11 give me about the standard for a reasonable 10:09:38 12 expectation of success that you applied, in giving 10:09:42 13 the opinions in the declaration? 10:09:44 14 MS. STRUTHERS: Objection; asked and 10:09:46 15 answered. 10:09:46 16 A. We can certainly show you the exact parts of 10:09:46 17 CLEAR-IT 2 that made me skeptical. We can 10:09:53 18 certainly go through the data points, which I'm 10:09:57 19 intimately involved with, and discuss in the -- in 10:10:00 20 the -- in the declaration, and happy to do that. 10:10:03 21 Q. (BY MR. SUMMERS) Okay. Those are the data 10:10:04 22 points on which you relied. I'm asking you for the 10:10:09 23 standard that you applied for a reasonable 10:10:13 24 expectation of success. 10:10:15 25 Do you have any further information on that? 10:10:15 Page 39	1 A. I certainly read the entire patent and 10:11:20 2 looked at the claims and read the entire patent and 10:11:28 3 understood what the invention was. 10:11:39 4 Q. (BY MR. SUMMERS) Okay. And as part of 10:11:40 5 forming that understanding, what did you understand 10:11:42 6 exclusion criteria to mean? 10:11:46 7 MS. STRUTHERS: Objection; beyond 10:11:48 8 the scope. 10:11:48 9 A. One more time. What was the question? I'm 10:11:48 10 sorry. Repeat. 10:11:50 11 Q. (BY MR. SUMMERS) As a part of forming that 10:11:51 12 understanding, what did you understand the term, 10:11:52 13 exclusion criteria, to mean? 10:11:56 14 MS. STRUTHERS: Objection; beyond 10:11:58 15 the scope, asked and answered. 10:11:59 16 (The witness peruses the document.) 10:12:07 17 A. While I cite the entire Claim 1, just as if 10:13:18 18 I didn't offer an opinion on the amino acid 10:13:26 19 sequences, I don't offer an opinion on anything 10:13:31 20 about exclusion, and I'm not prepared to do so 10:13:34 21 today. 10:13:36 22 Q. (BY MR. SUMMERS) You -- you also give some 10:13:37 23 opinions about what you refer to as objective 10:13:46 24 indicia of nonobviousness, correct, viewed in 10:13:51 25 paragraph 24, for instance? 10:13:53 Page 41

1 A. What paragraph are we on? 10:13:54 2 Q. 24. 10:13:57 3 A. 24. 10:13:58 4 (The witness peruses the document.) 10:14:44 5 MS. STRUTHERS: Is there a question 10:15:24 6 pending? 10:15:26 7 MR. SUMMERS: There is, yeah. 10:15:26 8 MS. STRUTHERS: Oh. Could you 10:15:27 9 repeat the question? I'm sorry. 10:15:28 10 Q. (BY MR. SUMMERS) You give some opinions 10:15:29 11 about what you refer to as objective indicia of 10:15:34 12 nonobviousness, correct, Dr. Brown? 10:15:40 13 A. That is correct. 10:15:42 14 Q. Okay. You say here, in paragraph 24: I've 10:15:43 15 been informed that objective indicia of 10:15:47 16 nonobviousness should have a nexus to the claimed 10:15:50 17 invention; that is, a link to the claimed 10:15:53 18 invention. 10:15:56 19 Do you see that? 10:15:57 20 A. I do. 10:15:57 21 Q. And you go on to say: I am informed that 10:15:57 22 such a nexus may exist when the objective indicia 10:16:00 23 are tied to a product that embodies the claimed 10:16:05 24 invention, or a product whose use embodies the 10:16:09 25 claimed invention. 10:16:12 Page 42	1 commercial success of the claimed invention, also 10:17:34 2 support the conclusion that the method of treating 10:17:34 3 patients with an angiogenic eye disorder are Q8 10:17:37 4 maintenance dosing schedule, as claimed in the '681 10:17:42 5 patent, was not obvious before Regeneron completed 10:17:45 6 its Phase 3 trials. 10:17:47 7 I go on to have sections on long-felt need 10:17:48 8 for extending dosing regimen. That's also in the 10:17:52 9 background of the patent, if I remember right. 10:17:54 10 Persistent goal of the retina community has been 10:17:58 11 able to find an effective treatment regimen that 10:18:00 12 requires less than monthly visits. 10:18:03 13 I -- I go on to talk about the need for an 10:18:05 14 effective treatment was widely recognized, and 10:18:07 15 stated multiple times in multiple publications. 10:18:12 16 We failed multiple times with PIER and other 10:18:15 17 studies to try to have an extended dosing regimen 10:18:22 18 beyond that. The satisfaction of long-felt need, I 10:18:29 19 was informed that evidence that an invention met a 10:18:34 20 long-felt but unmet need is evidence of 10:18:38 21 nonobviousness. 10:18:41 22 In my opinion, the treatment of patients 10:18:41 23 with angiogenic eye disorders through the 10:18:43 24 intravitreal injection of Eylea every four weeks 10:18:45 25 for the first three months, followed by 10:18:47 Page 44
1 Do you see that? 10:16:13 2 A. I see that. 10:16:13 3 Q. Okay. So, you understand that for a nexus 10:16:22 4 to exist, the objective indicia have to be tied to 10:16:25 5 a product that embodies the claimed invention, 10:16:29 6 whose products whose use embodies the claimed 10:16:34 7 invention, right? 10:16:37 8 MS. STRUTHERS: Objection; the 10:16:37 9 document speaks for itself. 10:16:38 10 A. That's what it says. 10:16:39 11 Q. (BY MR. SUMMERS) Okay. In forming the 10:16:40 12 opinions on objective indicia of nonobviousness in 10:16:40 13 your declaration, did you determine whether there 10:16:45 14 was a product that embodies the claimed invention 10:16:48 15 or a product whose use embodies the claimed 10:16:51 16 invention? 10:16:58 17 A. I did. 10:16:58 18 Q. Okay. Can you point me to that analysis? 10:16:58 19 A. Yeah, if you go to section 128. 10:17:00 20 Q. You mean paragraph 128? 10:17:09 21 A. Paragraph 128, yeah. 10:17:11 22 It's my opinion that objective indicia, such 10:17:21 23 as long-felt but unmet need and failure by others 10:17:25 24 in the prior art, unexpected benefit of the claimed 10:17:30 25 invention to patients, and industry praise and 10:17:31 Page 43	1 intravitreal injection of Eylea once every eight or 10:18:45 2 more weeks, satisfied the long-felt but unmet need 10:18:51 3 for less frequent injections and the risk 10:18:55 4 associated with each procedure, and also reduced 10:18:56 5 the need for costly and time-consuming monthly 10:19:00 6 office visits, which was the primary -- the primary 10:19:04 7 big win. 10:19:06 8 I go on to talk about the approval of Eylea. 10:19:09 9 I talk about others couldn't extend it. And praise 10:19:17 10 from the -- the members of actually the FDA and -- 10:19:22 11 and -- and other KOLs, that this was a major 10:19:31 12 breakthrough. 10:19:35 13 Q. Okay. And in forming your opinions about 10:19:36 14 whether there was a product that embodies the 10:19:43 15 claimed invention, did you do an element-by-element 10:19:45 16 analysis of the claims, versus any product? 10:19:49 17 A. I'm not exactly sure what element-by-element 10:19:54 18 analysis means. I'm sorry. 10:20:00 19 Q. Sure. Let's flip back to page 45. And you 10:20:01 20 might want to start on page 44, because that's 10:20:11 21 where the claim starts. 10:20:13 22 You see Independent Claim 1 is reproduced 10:20:14 23 across page 44 and 45? 10:20:19 24 A. I see that. 10:20:21 25 Q. Okay. Did you go through and compare each 10:20:27 Page 45

12 (Pages 42 - 45)

1 element of Claim 1 to any product to determine 10:20:31 2 whether it embodies Claim 1? 10:20:36 3 MS. STRUTHERS: Objection; beyond 10:20:47 4 the scope. 10:20:47 5 THE REPORTER: What was the 10:20:50 6 objection? I'm sorry. 10:20:51 7 MS. STRUTHERS: Oh, I said beyond 10:20:53 8 the scope. 10:20:54 9 A. So everything I discuss in the indicia are 10:21:11 10 angiogenic eye treatment disorders of dosing 10:21:17 11 regimens that did not achieve the success of Eylea 10:21:22 12 three doses Q8. I looked at the totality of the 10:21:25 13 patent, not just Claim 1. 10:21:29 14 Q. (BY MR. SUMMERS) I understand that. But 10:21:30 15 did -- did you make a determination -- let me just 10:21:38 16 give you an example. 10:21:41 17 Did you make a determination whether Eylea 10:21:42 18 embodies Claim 1 of the '681 patent in forming your 10:21:46 19 opinions as to secondary considerations? 10:21:52 20 MS. STRUTHERS: Objection; asked and 10:21:56 21 answered. 10:21:56 22 A. Repeat the question. 10:21:56 23 Q. (BY MR. SUMMERS) Sure. Let me give you an 10:22:02 24 example. Did you make a determination about 10:22:04 25 whether Eylea embodies Claim 1 of the '681 patent, 10:22:07 Page 46	1 MS. STRUTHERS: Objection to form. 10:23:37 2 A. Repeat the question. 10:23:38 3 Q. (BY MR. SUMMERS) Is it your opinion that 10:23:42 4 Eylea satisfies a long-felt but unmet need? 10:23:44 5 A. Yeah. What I state is: In my opinion, the 10:23:49 6 treatment of patients with angiogenic eye disorders 10:23:53 7 through the intravitreal injection of Eylea every 10:23:57 8 four weeks for the first three months, followed by 10:23:58 9 intravitreal injection of Eylea once every eight or 10:24:01 10 more weeks, satisfied the long-felt but unmet need 10:24:06 11 for less frequent injections. 10:24:10 12 I concur with my declaration. I agree with 10:24:14 13 it. 10:24:17 14 Q. Okay. So it is your opinion that Eylea 10:24:17 15 satisfied a long-felt but unmet need? 10:24:23 16 MS. STRUTHERS: Objection; asked and 10:24:27 17 answered. 10:24:27 18 A. So, Eylea, when dosed every four weeks for 10:24:27 19 the first three months, followed by intravitreal 10:24:33 20 injection of Eylea once every eight or more weeks, 10:24:35 21 satisfied the long-felt but unmet need for less 10:24:37 22 frequent injections. 10:24:40 23 Q. (BY MR. SUMMERS) Okay. And in forming this 10:24:41 24 opinion, did you form an opinion that Eylea 10:24:43 25 practices any claim of the '681 patent? 10:24:45 Page 48
1 in forming your opinions as to objective indicia of 10:22:12 2 nonobviousness? 10:22:18 3 MS. STRUTHERS: Same objection. 10:22:19 4 A. Yeah, so the objective indicia all involve 10:22:19 5 treatments for angiogenic eye disorder, such as 10:22:23 6 Eylea at variable dosing regimens, all of which -- 10:22:26 7 none of which could succeed the -- the goal of 10:22:29 8 going beyond fixed monthly dosing to get to where 10:22:35 9 the VIEW -- three doses and then Q8, which 10:22:38 10 performed on par with -- with ranibizumab monthly 10:22:45 11 as in MARINA/ANCHOR. I looked at the totality of 10:22:49 12 the patent, not just Claim 1. 10:22:53 13 Q. (BY MR. SUMMERS) Let's get more specific. 10:22:55 14 Perhaps that will help you here. 10:23:04 15 If you go to, satisfaction of a long-felt 10:23:05 16 need. 10:23:08 17 Do you see that? 10:23:08 18 A. Where is that? 10:23:08 19 Q. In paragraph 134, on page 65 of your 10:23:09 20 declaration. 10:23:14 21 A. 134. 10:23:16 22 Q. Just let me know when you're there. 10:23:20 23 A. I'm there. 10:23:22 24 Q. So, is it your opinion that Eylea satisfied 10:23:23 25 a long-felt but unmet need? 10:23:31 Page 47	1 MS. STRUTHERS: Objection; asked and 10:24:53 2 answered. 10:24:53 3 A. So the treatment of patients with angiogenic 10:24:53 4 eye disorders given aflibercept every four weeks 10:25:09 5 for the first three months, followed by every eight 10:25:13 6 weeks, is what the claims discuss. 10:25:16 7 Q. (BY MR. SUMMERS) They discuss more than 10:25:18 8 that, though, right? 10:25:23 9 MS. STRUTHERS: Objection to form. 10:25:27 10 A. What do you mean? 10:25:27 11 Q. (BY MR. SUMMERS) For instance, the 10:25:31 12 exclusion criteria? 10:25:34 13 A. I -- exclusion criteria is there, yes. 10:25:35 14 Q. Okay. Did you form an opinion, in giving 10:25:42 15 your opinion that Eylea satisfies a long-felt need, 10:25:44 16 about whether Eylea embodies any claim of the '681 10:25:48 17 patent? 10:25:54 18 MS. STRUTHERS: Objection; asked and 10:25:54 19 answered. 10:25:55 20 A. Repeat that question one more time. 10:25:55 21 Q. (BY MR. SUMMERS) Sure. Did you form an 10:25:58 22 opinion that Eylea -- excuse me. Let me start 10:26:00 23 again. 10:26:08 24 Did you form an opinion, in giving your 10:26:08 25 opinion about long-felt need, about whether Eylea 10:26:13 Page 49

1 embodies any claim of the '681 patent? 10:26:19 2 MS. STRUTHERS: Objection to form; 10:26:24 3 asked and answered. 10:26:25 4 A. Can you pass me the '681 patent, just so I 10:26:26 5 can have it before me? 10:26:28 6 Q. (BY MR. SUMMERS) No. I've given you -- I'm 10:26:29 7 asking you a specific question about the claims. 10:26:32 8 A. Okay. 10:26:35 9 Q. So -- 10:26:35 10 A. Fine. 10:26:38 11 Q. Do you not know, sitting here right now, 10:26:38 12 whether you formed an opinion about whether Eylea 10:26:40 13 embodies any claim of the '681 patent? 10:26:46 14 MS. STRUTHERS: Objection; 10:26:47 15 mischaracterizes the testimony. 10:26:48 16 A. What was your -- I'm sorry? 10:26:48 17 Q. (BY MR. SUMMERS) Do you not know, sitting 10:26:51 18 here today, whether you formed an opinion about 10:26:52 19 whether Eylea embodied any claim of the '681 10:26:55 20 patent? 10:27:00 21 MS. STRUTHERS: Objection; 10:27:00 22 mischaracterizes the testimony. 10:27:01 23 A. Yeah, what I said is the treatment of 10:27:02 24 patients with angiogenic eye disorders with the 10:27:05 25 intravitreal injection of Eylea every four weeks. 10:27:08 Page 50	1 Q. (BY MR. SUMMERS) All right. So you made no 10:28:16 2 determination about whether Eylea practices the 10:28:17 3 exclusion criteria recited in Claim 1 of the 10:28:20 4 '681 patent? 10:28:24 5 MS. STRUTHERS: Yeah, objection; 10:28:25 6 beyond the scope. 10:28:29 7 A. I looked at the totality -- totality, sorry, 10:28:29 8 of the patent. I don't specifically discuss 10:28:37 9 implications of exclusion criteria, and I'm not 10:28:42 10 prepared to do so today. 10:28:44 11 Q. (BY MR. SUMMERS) Okay. And let me broaden 10:28:45 12 that question a little bit. 10:28:48 13 You -- you made no determination about 10:28:48 14 whether Eylea practices the exclusion criteria 10:28:50 15 recited in any claim of the '681 patent, correct? 10:28:54 16 MS. STRUTHERS: Same objection. 10:28:57 17 Beyond the scope. 10:28:58 18 A. I don't cite an opinion on that, and am not 10:28:58 19 prepared to do so today. 10:29:04 20 Q. (BY MR. SUMMERS) And that goes for all of 10:29:04 21 your opinions, as to the objective indicia of 10:29:18 22 nonobviousness, right? You -- you did not form any 10:29:23 23 determination about whether Eylea practices the 10:29:25 24 exclusion criteria of any claim in the '681 patent, 10:29:27 25 as to any of your opinions in your declaration, 10:29:30 Page 52
1 And that does go by the claims. 10:27:10 2 THE REPORTER: Say that again. 10:27:14 3 A. In my opinion, the treatment of patients 10:27:15 4 with angiogenic eye disorders through the 10:27:18 5 intravitreal injections every four weeks for the 10:27:22 6 first three months, followed by intravitreal 10:27:23 7 injection of Eylea once every eight or more weeks, 10:27:26 8 would satisfy the long-felt need, does embody the 10:27:30 9 claims. 10:27:33 10 Q. (BY MR. SUMMERS) Okay. And there's no 10:27:33 11 reference there to exclusion criteria, however, 10:27:35 12 correct? 10:27:39 13 MS. STRUTHERS: Objection; document 10:27:42 14 speaks for itself. 10:27:43 15 A. It's what it says. 10:27:43 16 Q. (BY MR. SUMMERS) Okay. Did you form an 10:27:46 17 opinion about whether the intravitreal injection 10:27:47 18 once every eight or more weeks satisfies the 10:27:50 19 limitation in Claim 1, reciting the three exclusion 10:27:56 20 criteria? 10:28:04 21 MS. STRUTHERS: Objection; beyond 10:28:04 22 the scope. 10:28:06 23 A. Yeah, I don't discuss pertinence to 10:28:06 24 exclusion criteria, and I'm not prepared to do so 10:28:13 25 today. 10:28:16 Page 51	1 correct? 10:29:32 2 MS. STRUTHERS: Same objection. 10:29:39 3 Beyond the scope. 10:29:40 4 A. Yeah, I looked at the totality of the 10:29:40 5 patent. I don't discuss specific implications with 10:29:42 6 exclusion, and am not prepared to do so today. 10:29:46 7 Q. (BY MR. SUMMERS) And you have no opinions 10:29:48 8 about the exclusion criteria to offer today. 10:29:49 9 Is that correct? 10:29:52 10 A. I have not offered any and I'm not prepared 10:29:52 11 to do so. 10:29:54 12 MR. SUMMERS: We've been going for 10:29:56 13 about an hour and 20 minutes. Let's take a break. 10:29:57 14 THE WITNESS: Let's do it. 10:30:00 15 THE VIDEOGRAPHER: Off the record at 10:30:00 16 10:29 a.m. 10:30:02 17 (Break.) 10:30:02 18 THE VIDEOGRAPHER: We're back on the 10:40:32 19 record at 10:40 a.m. 10:40:55 20 Q. (BY MR. SUMMERS) Dr. Brown, you asked 10:41:00 21 earlier for the '681 patent. I hand it over to 10:41:07 22 you. This has previously been marked Samsung 10:41:11 23 Bioepsis Exhibit 1001. 10:41:15 24 A. Thank you. 10:41:20 25 MS. STRUTHERS: Thank you. 10:41:20 Page 53

1 Q. (BY MR. SUMMERS) You've seen this document 10:41:20 2 before, I presume? 10:41:29 3 A. Yes, sir. 10:41:30 4 Q. And you recognize it as the '681 patent? 10:41:30 5 A. I do. 10:41:38 6 Q. Let me refer you, if I can. The easiest way 10:41:39 7 to do it is by the page number in the bottom corner 10:41:46 8 there. There's page 14 and 15. 10:41:48 9 A. Yeah. 10:41:51 10 Q. Can you go there? I want to confirm your 10:41:51 11 prior testimony here. 10:41:58 12 You did not make a determination about 10:42:00 13 whether any product embodies any of the claims that 10:42:02 14 are listed here on pages 14 and 15. 10:42:06 15 Is that correct? 10:42:10 16 MS. STRUTHERS: Objection; 10:42:16 17 mischaracterizes the testimony. 10:42:17 18 But you can answer. 10:42:18 19 A. Can you repeat the question one more time? 10:42:19 20 Q. (BY MR. SUMMERS) Sure. You see there are 10:42:20 21 Claims 1 through 26 here listed across pages 14 and 10:42:26 22 15? 10:42:30 23 A. I do. 10:42:30 24 Q. Okay. And you can also refer to it at the 10:42:30 25 top of Columns 21, 22, 23, and 24. 10:42:33 Page 54	1 total -- totality. And I can tell you that -- that 10:48:31 2 the examples starting in Column 7, the following 10:48:38 3 examples are put forth as to provide those with 10:48:42 4 ordinary skill in the art a complete disclosure and 10:48:45 5 description of how to make and use the methods of 10:48:47 6 composition in the invention. 10:48:48 7 Then if you go to example -- Column 13, 10:48:50 8 Example 4, Table 1. Very familiar with this, 10:48:56 9 because that's our VIEW 1, 2 synopsis study 10:49:00 10 results, which the claims essentially were created 10:49:06 11 from by the patent attorneys, I assume. 10:49:12 12 So, I don't make any other statements, other 10:49:15 13 than -- than that in my declaration. 10:49:19 14 Q. Did you compare Column 13, Example 4, to any 10:49:22 15 claim of the '681 patent to determine whether it 10:49:26 16 embodies the claim? 10:49:29 17 MS. STRUTHERS: Objection; asked and 10:49:31 18 answered. 10:49:31 19 A. Column 4? 10:49:31 20 Q. (BY MR. SUMMERS) No. Column 13, Example 4, 10:49:35 21 what you pointed to. 10:49:37 22 A. Yeah, so, again, I examined the totality of 10:49:38 23 the patent, and, you know, looking at the examples, 10:49:46 24 Table 1 is the synopsis of our VIEW 1, 2 results, 10:49:50 25 again, which seemed to be what the patent authors 10:49:56 Page 56
1 A. Yep. 10:42:36 2 Q. You did not make a determination, for the 10:42:36 3 purposes of providing your declaration in this 10:42:41 4 matter, about whether any of Claims 1 through 26 10:42:44 5 were practiced by any product. 10:42:49 6 Is that correct? 10:42:52 7 MS. STRUTHERS: Objection; 10:42:56 8 mischaracterizes the testimony. 10:42:57 9 A. I reviewed the totality of the patent for my 10:42:57 10 declaration. You want to point me to where my 10:43:10 11 declaration you're discussing or not discussing? 10:43:13 12 Q. (BY MR. SUMMERS) I -- I actually want to 10:43:19 13 know something I couldn't find in your declaration, 10:43:22 14 which is whether or not you made a determination of 10:43:26 15 any -- whether any of Claims 1 through 26 are 10:43:32 16 embodied by any product. 10:43:40 17 Did you do that or not? 10:43:41 18 (The witness peruses the document.) 10:44:55 19 A. Repeat the question. 10:48:08 20 Q. (BY MR. SUMMERS) Did you make a 10:48:09 21 determination, in forming the opinions that are set 10:48:14 22 forth in your declaration for this matter, about 10:48:17 23 whether any of Claims 1 through 26 in the '681 10:48:20 24 patent are embodied by any product? 10:48:25 25 A. So, I reviewed the '681 patent in its 10:48:27 Page 55	1 used for creating the claims. 10:50:02 2 Q. Okay. So, did -- did you make a comparison 10:50:04 3 of any claims in the '681 patent against Column 13, 10:50:08 4 Example 4, to determine whether that embodies any 10:50:13 5 claim of the '681 patent? 10:50:22 6 MS. STRUTHERS: Objection; asked and 10:50:24 7 answered. 10:50:24 8 A. Certainly read the entire patent, including 10:50:24 9 the examples. 10:50:34 10 And the Table 1, which is our VIEW results, 10:50:35 11 seems to be what the patent authors, or the legal 10:50:46 12 authors for the patent holder, used in developing 10:50:55 13 the claims. 10:50:59 14 Q. (BY MR. SUMMERS) Okay. So part of the 10:51:01 15 claims -- and let's just look at Claim 1 in the 10:51:02 16 '681 patent. It's on page 14, Column 21. 10:51:04 17 Let me know when you're there. 10:51:09 18 A. Page 14, Column 21. Okay. 10:51:10 19 Q. Okay. Claim 1 recites, around Column 21, 10:51:13 20 line 58: Wherein the exclusion criteria for the 10:51:21 21 patient include all of -- and then there's a colon. 10:51:25 22 Do you see that? 10:51:28 23 A. I see that. 10:51:30 24 Q. Okay. So, in providing your testimony just 10:51:33 25 now, that it seems that the patent authors used the 10:51:37 Page 57

15 (Pages 54 - 57)

1 data in Column 13, Example 4, to develop the 10:51:46	1 each little part of it, but make no opinion in my 10:56:53
2 claims, did you form an opinion about the exclusion 10:51:51	2 declaration of the label versus the -- specific 10:56:57
3 criteria recited in the claims? 10:51:56	3 things of the label versus the -- versus the 10:57:02
4 MS. STRUTHERS: Objection; beyond 10:51:57	4 patent. 10:57:06
5 the scope, asked and answered. 10:51:58	5 Q. (BY MR. SUMMERS) Okay. And let me then 10:57:06
6 A. Can you repeat the question? 10:52:03	6 hand you Exhibit 2189, which has also been 10:57:10
7 Q. (BY MR. SUMMERS) You see in Column 21, in 10:52:18	7 previously marked, and is identified as the Eylea 10:57:15
8 Claim 1, where it recites: Wherein the exclusion 10:52:21	8 drug label for March 2021, in your declaration. 10:57:18
9 criteria for the patient include all of. 10:52:24	9 Are you familiar with this document, 10:57:34
10 Do you see that? 10:52:27	10 Dr. Brown? 10:57:36
11 A. I see that. 10:52:27	11 (The witness peruses the document.) 10:58:01
12 Q. Okay. Did you make a determination about 10:52:31	12 A. I know that it's the Eylea label as of 2021, 10:58:46
13 whether Example 4, in Column 13 of the patent, 10:52:32	13 with the addition of diabetic retinopathy 10:58:52
14 practices the exclusion criteria that are recited 10:52:40	14 indication. I can't say that I'm as familiar with 10:58:59
15 there? 10:52:44	15 this -- the extensiveness of this label as the 10:59:01
16 MS. STRUTHERS: Objection; beyond 10:52:45	16 first one, because while versed on each edition, I 10:59:03
17 the scope, asked and answered. 10:52:46	17 don't know that I've reviewed the whole thing in 10:59:08
18 (The witness peruses the document.) 10:53:45	18 its entirety each time it was revised. So... 10:59:09
19 A. In my declaration, I spent quite a time -- 10:53:45	19 Q. (BY MR. SUMMERS) Okay. Did you make an 10:59:15
20 quite a bit of time talking about VIEW, which I'm 10:54:17	20 evaluation of Exhibit 2189 as to whether a 10:59:17
21 happy to discuss. I -- in making my opinions, I 10:54:19	21 physician following the prescribing information 10:59:22
22 reviewed it against the totality of the patent. I 10:54:23	22 would practice any claim of the '681 patent? 10:59:25
23 never discuss the significance or -- or pertinence 10:54:27	23 MS. STRUTHERS: Objection; beyond 10:59:32
24 of the exclusion criteria, and I'm not prepared to 10:54:36	24 the scope. 10:59:33
25 do so today. 10:54:39	25 A. Repeat your question. 10:59:33
Page 58	Page 60
1 Q. (BY MR. SUMMERS) Okay. Let me hand you 10:54:39	1 Q. (BY MR. SUMMERS) Sure. Did you make an 10:59:33
2 what's previously been marked as Exhibit 2185 and 10:54:45	2 evaluation of Exhibit 2189 as to whether a 10:59:41
3 is identified in your declaration as the Eylea 10:54:50	3 physician following the prescribing information 10:59:44
4 label as of November 2011. 10:54:54	4 would practice any claim of the '681 patent? 10:59:46
5 MS. STRUTHERS: Thank you. 10:55:04	5 MS. STRUTHERS: Objection; beyond 10:59:51
6 Q. (BY MR. SUMMERS) Are you familiar with this 10:55:06	6 the scope. 10:59:51
7 document, Dr. Brown? 10:55:16	7 A. I did not offer that opinion, no. 10:59:51
8 A. I am. 10:55:23	8 Q. (BY MR. SUMMERS) Thank you. Let's look at 10:59:53
9 Q. Okay. And what is this document? 10:55:23	9 those -- keep those two labels handy, if you would. 10:59:57
10 A. This is the FDA prescribing information, 10:55:27	10 But let me refer you back to 2185, first, if 11:00:02
11 following the approval by the agency of aflibercept 10:55:35	11 that's okay. Let me know when you have that in 11:00:06
12 for the first indication, neovascular age-related 10:55:42	12 front of you. 11:00:08
13 macular degeneration. 10:55:47	13 A. I'm there. 11:00:08
14 Q. There -- there was only a single indication 10:55:50	14 Q. So 2185 is the post-approval prescribing 11:00:11
15 when Eylea was initially approved, correct? 10:55:53	15 information from November 2011, correct? 11:00:17
16 A. Correct. 10:55:56	16 A. I'm there. 11:00:24
17 Q. So, did you make an evaluation of the Eylea 10:56:00	17 Q. And there was a -- there was -- as we were 11:00:25
18 label in exhibit -- I think -- strike that. 10:56:08	18 discussing earlier, there's a single indication 11:00:27
19 Did you make an evaluation of Exhibit 2185 10:56:13	19 listed on here for neovascular wet age-related 11:00:29
20 as to whether a physician following the prescribing 10:56:17	20 macular degeneration, correct? 11:00:36
21 information would practice any claim of the '681 10:56:22	21 A. Yes. 11:00:38
22 patent? 10:56:27	22 Q. And sometimes that's just referred to as 11:00:38
23 MS. STRUTHERS: Objection; beyond 10:56:27	23 AMD, or wet AMD. 11:00:40
24 the scope. 10:56:27	24 Is that right? 11:00:41
25 A. Yeah, I'm very familiar with the label and 10:56:27	25 A. Sure. 11:00:42
Page 59	Page 61

16 (Pages 58 - 61)

1 Q. Okay. As of the date of this prescribing 11:00:42 2 information, was the efficacy of Eylea established 11:00:51 3 for wet AMD? 11:00:55 4 MS. STRUTHERS: Objection to form. 11:00:59 5 A. So re -- rephrase your question. The drug 11:00:59 6 itself, or the treatment with the drug? 11:01:12 7 Q. (BY MR. SUMMERS) Thank -- thank you. Yeah, 11:01:14 8 as of the date of this prescribing information, was 11:01:15 9 the efficacy of the prescribing information for 11:01:18 10 Eylea here established for wet AMD? 11:01:24 11 MS. STRUTHERS: Again, objection to 11:01:30 12 form. 11:01:32 13 A. Certainly by the approval date, there had 11:01:34 14 been multiple presentations and publications of the 11:01:39 15 primary efficacy of the VIEW studies, as well as 11:01:42 16 the data submitted to the FDA, leading to the 11:01:49 17 approval, which demonstrated efficacy. 11:01:53 18 Q. (BY MR. SUMMERS) Okay. And if I flip over 11:01:56 19 now to Exhibit 2189, I think you made reference to 11:01:58 20 this, but there are a number of additional 11:02:04 21 indications that have been added in the interim 11:02:07 22 between 2011 and -- on this label. 11:02:11 23 A. Correct. 11:02:15 24 Q. And those include macular edema following 11:02:15 25 retinal vein occlusion, diabetic macular edema, and 11:02:21 Page 62	1 were done, I -- I do not recall. 11:04:16 2 Q. (BY MR. SUMMERS) Do you recall the names of 11:04:17 3 those trials? 4 A. The Phase -- 11:04:19 5 THE REPORTER: Say that again. 11:04:19 6 Q. (BY MR. SUMMERS) Oh, I said, do you recall 11:04:21 7 the names of those trials? 11:04:22 8 A. I honestly don't know the names of the 11:04:23 9 trials before the Phase 3 trials. The Phase 3 11:04:26 10 trials were Copernicus and Galileo. Were there 11:04:29 11 investigator-sponsored trials or smaller trials 11:04:34 12 before? I assume, but I don't remember. 11:04:36 13 Q. Let me -- let me go on, and I'll -- I'll 11:04:40 14 circle back to that. 11:05:11 15 Looking now -- again, let's take on 11:05:12 16 November 2011. 11:05:18 17 Was there any method of dosing and 11:05:18 18 administering Eylea for diabetic macular edema that 11:05:21 19 had been established to have efficacy? 11:05:24 20 MS. STRUTHERS: Objection to form. 11:05:27 21 A. Repeat the question one more time. I'm 11:05:27 22 sorry. 11:05:38 23 Q. (BY MR. SUMMERS) Sure. As of 11:05:38 24 November 2011, was there any method of dosing and 11:05:40 25 administering Eylea for diabetic macular edema that 11:05:42 Page 64
1 diabetic retinopathy. 11:02:26 2 Is that right? 11:02:28 3 A. That is correct. 11:02:28 4 Q. As of the date of Eylea's approval in 2011, 11:02:31 5 was there any -- let me try to ask you this in -- 11:02:44 6 in a more straightforward manner. 11:02:53 7 As of the date of the Eylea label, in 11:02:55 8 Exhibit 2185, was the efficacy of any method for 11:03:01 9 dosing and administering Eylea established for 11:03:10 10 macular edema following retinal vein occlusion? 11:03:13 11 MS. STRUTHERS: Objection to form. 11:03:18 12 A. Repeat the question. What date was it 11:03:18 13 exactly? I'm sorry. 11:03:21 14 Q. (BY MR. SUMMERS) Yeah, sure. 11:03:22 15 November 2011. And I'll repeat the question -- 11:03:24 16 A. Okay. 11:03:25 17 Q. -- here. 11:03:26 18 So, as of November 2011, was there any 11:03:27 19 method of dosing and administering Eylea for 11:03:34 20 macular edema following retinal vein occlusion, 11:03:39 21 that was established to have efficacy? 11:03:42 22 MS. STRUTHERS: Objection to form. 11:03:46 23 A. I honestly don't remember whether we had 11:03:47 24 done RVO trials before 2011 or not. It wasn't 11:04:11 25 approved until afterwards. But when those trials 11:04:14 Page 63	1 had been established to have efficacy? 11:05:45 2 MS. STRUTHERS: Same objection. 11:05:48 3 A. Prior to 2011, there were some, I think, 11:05:49 4 Phase 1, 2 studies, mainly performed at Johns 11:06:02 5 Hopkins with DME. I wasn't part of those studies. 11:06:08 6 Q. (BY MR. SUMMERS) Okay. And you don't know, 11:06:10 7 sitting here today, whether they -- the efficacy 11:06:11 8 had been established as of 2011? 11:06:15 9 MS. STRUTHERS: Objection; 11:06:19 10 mischaracterizes the testimony. 11:06:20 11 A. Yeah, the -- the studies, you know, in terms 11:06:21 12 of points in time 12 years ago, I'm not exactly 11:06:22 13 sure when things were presented. 11:06:26 14 Certainly, the data was very positive. I 11:06:27 15 think the trials were called READ, R-E-A-D; Quan 11:06:30 16 Nguyen, Diana Do, authors. 11:06:36 17 But when, exactly, they were presented and 11:06:37 18 were they available? In 2021, I think so, but not 11:06:39 19 real sure. They preceded our VISTA/VIVID Phase 3 11:06:42 20 trials. 11:06:48 21 Q. (BY MR. SUMMERS) And do you recall, did 11:06:48 22 READ establish the efficacy for a route of dosing 11:06:56 23 administration for Eylea for diabetic macular 11:07:01 24 edema? 11:07:05 25 MS. STRUTHERS: Objection to form. 11:07:05 Page 65

17 (Pages 62 - 65)

1 A. I don't recall. I'd have to review those 11:07:05 2 either abstracts, papers, or what came out. I 11:07:18 3 think they're part of 2011, but it could be 11:07:20 4 simultaneous or right about that time. 11:07:24 5 Q. (BY MR. SUMMERS) Does it refresh your 11:07:30 6 recollection, Boyer, et al, referring back to 11:07:40 7 macular edema following CRVO, Boyer, et al? 11:07:43 8 It was -- it was published in 2012. 11:07:45 9 Is that what you were referring to in terms 11:07:48 10 of the publication? 11:07:51 11 A. I don't remember. 11:07:52 12 Q. Okay. And last question, along these same 11:07:52 13 lines, as of November 2011, was there any method of 11:08:01 14 dosing and administering Eylea for diabetic 11:08:04 15 retinopathy that had been established to have 11:08:08 16 efficacy? 11:08:10 17 MS. STRUTHERS: Objection to form. 11:08:11 18 A. Not that I recall. I don't know if READ had 11:08:11 19 diabetic retinopathy criteria in it or not. 11:08:23 20 Probably did, but who knows. 11:08:25 21 Q. (BY MR. SUMMERS) Do you recall, did READ 11:08:27 22 establish the efficacy for diabetic macular edema 11:08:29 23 and diabetic retinopathy? 11:08:32 24 MS. STRUTHERS: Objection to form. 11:08:35 25 A. I -- I'd have to review the data. 11:08:35 Page 66	1 the molecule that plays a critical role in the 11:10:45 2 pathology of angiogenesis and vascular 11:10:48 3 permeability. 11:10:52 4 By 2005, it was recognized by the POSA that 11:10:52 5 treating patients with certain anti-VEGF agents 11:10:55 6 which reduce ocular VEGF levels could reduce the 11:10:59 7 incidents of path -- pathologic angiogenesis and 11:11:04 8 vascular permeability, and prevent loss of vision, 11:11:05 9 and even many cases, improve vision. 11:11:08 10 I go on to talk about the pale fast -- 11:11:10 11 fast -- you know, the past attempts that we failed. 11:11:16 12 But what the POSA would have known is that an 11:11:19 13 effective angiogenic eye disorder, an agent works 11:11:24 14 against all of these disorders. 11:11:28 15 Ranibizumab, bevacizumab were effective 11:11:31 16 against macular edema from vein occlusion, from 11:11:33 17 diabetic macular edema, and from macular 11:11:39 18 degeneration. And there's no reason to think that 11:11:42 19 the POSA wouldn't think that aflibercept would be 11:11:44 20 effective in these same disorders. Obviously, it 11:11:47 21 had to get tested and approved. 11:11:51 22 Q. (BY MR. SUMMERS) So, I'm trying to 11:12:05 23 understand your answer. 11:12:06 24 Is it your view that -- because it's your 11:12:07 25 view that the efficacy of the route for 11:12:12 Page 68
1 Q. (BY MR. SUMMERS) And just to be clear, for 11:08:42 2 the purposes of providing your declaration in this 11:08:48 3 matter, you didn't determine whether it was known 11:08:50 4 that Eylea had efficacy for diabetic macular edema 11:08:55 5 following retinal vein occlusion, diabetic macular 11:09:00 6 edema, and diabetic retinopathy, as of November 11:09:04 7 2011. 11:09:10 8 Is that right? 11:09:10 9 MS. STRUTHERS: Objection; 11:09:11 10 mischaracterizes the testimony. 11:09:12 11 (The witness peruses the document.) 11:09:36 12 A. So I state, in page 7, paragraph 25: 11:09:37 13 Angiogenic eye disorders characterized by 11:10:13 14 pathologic growth of abnormal blood vessels and 11:10:14 15 vascular leakage from damaged blood vessels in the 11:10:19 16 retina presents significant risk to patient's 11:10:21 17 vision, absent treatment. 11:10:24 18 Angiogenic eye disorders or neovascular eye 11:10:25 19 disorders include conditions such as iris 11:10:30 20 neovascularization, retinal vein occlusion, 21 diabetic retinopathy, diabetic macular edema, 22 neovascular glaucoma, wet AMD, and retinopathy of 11:10:37 23 prematurity. 24 A shared feature of angiogenic eye disorders 11:10:40 25 is the presence of elevated ocular levels of VEGF, 11:10:42 Page 67	1 dosing/administering Eylea for wet AMD was 11:12:17 2 established by 2011, that it was reasonable for a 11:12:20 3 POSA to assume that it would also be efficacious 11:12:25 4 for other angiogenic eye disorders? 11:12:30 5 MS. STRUTHERS: Objection to form. 11:12:34 6 A. Repeat the question one more time. 11:12:34 7 Q. (BY MR. SUMMERS) Sure. So, is it your view 11:12:38 8 that because the efficacy of a route of dosing and 11:12:42 9 administering Eylea for wet AMD was established by 11:12:46 10 2011, that it was reasonable for a POSA to assume 11:12:51 11 that it would also be efficacious for other 11:12:54 12 angiogenic eye disorders? 11:13:01 13 MS. STRUTHERS: Same objection. 11:13:03 14 A. Until proven otherwise, correct. 11:13:05 15 Q. (BY MR. SUMMERS) Okay. That -- that was 11:13:16 16 part of your answer I was trying to understand. 11:13:16 17 But there could be some testing or approval or data 11:13:17 18 that would come down the line that might contradict 11:13:20 19 that. But until then, it was reasonable? 11:13:22 20 MS. STRUTHERS: Objection; 11:13:25 21 mischaracterizes the testimony. 11:13:26 22 But you can answer. 11:13:31 23 A. Yeah, to get FDA approval, you certainly had 11:13:32 24 to do studies against things previously treated, 11:13:37 25 and to identify dosing regimens, et cetera, which 11:13:43 Page 69

1 were not established until later. 11:13:48 2 Q. (BY MR. SUMMERS) Okay. Let me refer back 11:13:49 3 now to your declaration again. I think you still 11:13:59 4 have it in front of you. 11:14:02 5 Let's start on paragraph 83, page 41, of 11:14:50 6 your declaration. 11:14:55 7 A. I'm there. 11:15:11 8 Q. So, you see in the second sentence there, 11:15:11 9 you say: Based on review of the clinical trial 11:15:16 10 data in the '681 patent, the POSA would have 11:15:20 11 understood that VEGF Trap-Eye was non-inferior to 11:15:23 12 standard of care Lucentis. 11:15:29 13 And then you go on. I'll stop there. 11:15:31 14 A. I see that. 11:15:38 15 Q. Okay. What do you mean when you refer to 11:15:39 16 standard of care Lucentis, in your declaration? 11:15:41 17 A. I've been involved in research on these 11:15:45 18 disorders for over 25 years. Macular degeneration, 11:16:15 19 in particular, was a blinding disorder. And prior 11:16:22 20 to the Lucentis trials, patients went blind. They 11:16:27 21 just went blind a little bit slower, a little bit 11:16:32 22 less, with either laser photocoagulation or 11:16:34 23 photodynamic therapy. 11:16:39 24 The ranibizumab trials blocking anti-VEGF 11:16:41 25 was a massive paradigm shift. And I may be biased, 11:16:45 Page 70	1 Is it the case that it was the standard of 11:18:09 2 care for Lucentis for wet AMD, in the time frame 11:18:14 3 you're talking about? And maybe we need to get 11:18:21 4 more specific about that for you to answer. 11:18:22 5 But I'm trying to figure out if -- exactly 11:18:24 6 whether -- whether we're talking specific 11:18:26 7 indications or if there's just a general standard 11:18:29 8 of care for all indications, in your mind. 11:18:30 9 A. And we're talking about 2011, the patent 11:18:34 10 date? 11:18:37 11 Q. Yeah, let's talk about 2011, the time of the 11:18:37 12 patent. 11:18:39 13 A. January -- early January 2011. 11:18:40 14 Q. Yeah. 11:18:42 15 MS. STRUTHERS: Yeah, hold on. 11:18:42 16 Objection to form. Was there a question? 11:18:43 17 Q. (BY MR. SUMMERS) Yeah, so let me -- that's 11:18:45 18 fair. 11:18:46 19 MR. SUMMERS: Well taken, Counsel. 11:18:51 20 Q. (BY MR. SUMMERS) So in January 2011, did 11:18:52 21 you view that there was -- the standard of care for 11:18:54 22 Lucentis was -- strike that. 11:18:57 23 Poorly asked. 11:19:04 24 In -- in January of 2011, was it the case 11:19:05 25 that standard of care Lucentis was the standard for 11:19:09 Page 72
1 but the papers in the New England Journal that I 11:16:54 2 authored with Phil Rosenfeld, me as first author of 11:16:58 3 ANCHOR, and him as first author of MARINA, and us 11:17:01 4 being corresponding second authors, established 11:17:04 5 that giving monthly anti-VEGF with ranibizumab not 11:17:06 6 only prevented loss of vision, but on the average, 11:17:11 7 improved vision, maintained and stayed there with 11:17:15 8 consistent treatment. 11:17:17 9 That's what I mean by standard of care 11:17:18 10 Lucentis, which is the best available treatment 11:17:21 11 after that was available. That was approved in 11:17:24 12 2006. 11:17:28 13 I had the benefit of treating patients since 11:17:30 14 2002 with that drug, because I was part of the 11:17:33 15 Phase 2/Phase 3 trials. That's what I mean. Best 11:17:36 16 possible care, which today, it has not been 11:17:39 17 surpassed, improving vision, maintenance of vision, 11:17:46 18 that we saw in MARINE and ANCHOR. 11:17:49 19 Q. Okay. That -- that's helpful. I -- I kind 11:17:53 20 of want to get a little more content on it, just so 11:17:56 21 I understand it. 11:17:59 22 So is it -- is it the case that that was the 11:17:59 23 standard of care -- I want to divide it out a 11:18:04 24 little bit by indication, and then talk about some 11:18:07 25 other things as well. 11:18:08 Page 71	1 all indications for angiogenic eye disorders? 11:19:12 2 MS. STRUTHERS: Objection to form. 11:19:17 3 A. Which specific eye disorders are you 11:19:19 4 questioning? 11:19:28 5 Q. (BY MR. SUMMERS) Sure. So let's -- let's 11:19:28 6 get more specific then. It sounds like we need to. 11:19:29 7 So as of January 2011, is it your opinion 11:19:32 8 that Lucentis was the standard of care for diabetic 11:19:34 9 macular edema? 11:19:40 10 A. January 2011, I'm pretty sure diabetic 11:19:41 11 macular edema was almost approved. We had 11:19:48 12 presented RISE/RIDE. Pretty sure we published 11:19:50 13 RISE/RIDE. And -- and if you had availability to 11:19:55 14 it, the standard of care, at least in my clinic, 11:19:57 15 would have been monthly ranibizumab for diabetic 11:19:58 16 macular edema. 17 THE REPORTER: I'm sorry. Can you 11:20:03 18 repeat that? 11:20:04 19 THE WITNESS: Yes. 11:20:06 20 THE REPORTER: Just that last 11:20:06 21 portion. 11:20:08 22 A. And -- yeah. The standard of care in my 11:20:09 23 clinic, if you could obtain it, would be monthly 11:20:10 24 Lucentis, whether in a clinical trial, or a post 11:20:14 25 pre-approval access programs. 11:20:22 Page 73

1 Q. (BY MR. SUMMERS) You -- you just hit on the 11:20:26 2 question I had for you, which is what -- was -- was 11:20:33 3 Lucentis, in fact, available, as of early 2011, 11:20:35 4 commercially, for treating diabetic macular edema? 11:20:40 5 A. I would have to check the exact dates, but 11:20:45 6 pretty sure it was not available commercially until 11:20:48 7 later that year. 11:20:51 8 Q. Okay. So for other places where it wasn't 11:20:52 9 available commercially, you wouldn't have 11:20:55 10 considered that the standard of care. 11:20:56 11 Is that correct? 11:20:57 12 MS. STRUTHERS: Objection; 11:20:58 13 mischaracterizes the testimony. 11:20:59 14 A. You know, I had patients referred from all 11:20:59 15 over the country. So you could certainly get on a 11:21:07 16 plane and come to me, to try to get in a clinical 11:21:09 17 trial. 11:21:15 18 Bevacizumab was available. Certainly that 11:21:17 19 was an anti-VEGF agent that was available across 11:21:18 20 the United States, Canada, Mexico. The use of 11:21:21 21 consistent bevacizumab, although not proven in DME, 11:21:26 22 was certainly the standard of care for DME, 2011. 11:21:36 23 Q. (BY MR. SUMMERS) Okay. That's helpful. 11:21:38 24 So, you -- you -- for DME, as of 2011, the -- the 11:21:43 25 standard of care included monthly bevacizumab. 11:21:52 Page 74	1 get. 11:23:15 2 Q. (BY MR. SUMMERS) Okay. And that might 11:23:15 3 include Avastin. 11:23:18 4 Is that correct? 11:23:19 5 A. Correct. Bevacizumab is Avastin. I 11:23:19 6 apologize. Bevacizumab, B-E-V-A-C-I-Z-U-M-A-B. 11:23:22 7 In scientific, you can't use trade names, 11:23:29 8 because it's a CME violation. So we're so used to 11:23:31 9 giving generic terms, I apologize. I will try to 11:23:35 10 stick to the trade names. 11:23:38 11 Q. It's okay. Okay. So let's move on to 11:23:42 12 another angiogenic eye disorder, diabetic 11:23:48 13 retinopathy. 11:23:52 14 As of January 2011, was Lucentis the 11:23:52 15 standard of care for diabetic retinopathy? 11:23:54 16 A. In 2011, anti-VEGF therapy was available, 11:23:58 17 bevacizumab, ranibizumab. Diabetic retinopathy is 11:24:07 18 a spectrum from a little intraretinal hemorrhage or 11:24:14 19 microaneurysm in the retina, all the way to 11:24:19 20 blinding proliferative diabetic retinopathy. 11:24:21 21 Standard of care for proliferative diabetic 11:24:24 22 retinopathy, where new blood vessels are created in 11:24:30 23 response to ischemia, was anti-VEGF, followed by 11:24:31 24 panretinal photocoagulation. 25 If you had diabetic macular edema, which is 11:24:40 Page 76
1 Is that correct? 11:22:02 2 A. Standard of care for DME was monthly 11:22:02 3 bevacizumab or ranibizumab, if you could obtain it. 11:22:06 4 Q. Okay. And there would have been patients 11:22:11 5 who couldn't have enrolled in your clinical trials 11:22:13 6 in 2011, because they would have been excluded from 11:22:15 7 those trials for various criteria, correct? 11:22:18 8 A. That's correct. 11:22:21 9 Q. Okay. So for those patients, at least, that 11:22:22 10 wasn't an option, and the standard of care couldn't 11:22:24 11 have been Lucentis. 11:22:26 12 Is that right? 11:22:27 13 MS. STRUTHERS: Objection; 11:22:33 14 mischaracterizes the testimony. 11:22:38 15 A. Due to access to healthcare, other issues, 11:22:39 16 different patients have different access to 11:22:42 17 different levels of healthcare. 11:22:44 18 Standard of care prior to anti-VEGF therapy 11:22:46 19 for diabetic macular edema was focal laser, which 11:22:51 20 didn't improve vision in many cases, but prevented 11:22:56 21 catastrophic loss in a statistical number. 11:22:59 22 If you couldn't get anti-VEGF therapy, many 11:23:01 23 patients still got focal laser in 2011. But if you 11:23:05 24 could obtain it, the highest standard would be 11:23:09 25 monthly anti-VEGF therapy of whatever you could 11:23:13 Page 75	1 part of diabetic retinopathy, certainly the 11:24:42 2 standard of care was anti-VEGF, if you could get 11:24:45 3 it. Most physicians, however, if you're below 11:24:47 4 those thresholds of diabetic macular edema or 11:24:52 5 proliferative diabetic retinopathy, standard of 11:24:58 6 care was observation until you reached those 11:24:59 7 thresholds, and then treatment with anti-VEGF. 11:25:01 8 Q. And I want to get a little more specific, 11:25:03 9 because -- and if you go ahead in your declaration, 11:25:05 10 you go to, for instance, paragraphs 98 and 99, it 11:25:07 11 span across pages 46 and 47. 11:25:11 12 Let me know when you finish reading those 11:25:26 13 two paragraphs. 11:25:28 14 (The witness peruses the document.) 11:25:29 15 A. I've read them. 11:25:36 16 Q. (BY MR. SUMMERS) Okay. So, when you 11:25:37 17 referred to standard of care, and then you say, 11:25:38 18 i.e., Lucentis, in paragraph 99, what I'm trying to 11:25:41 19 get at is where you say: Standard of care is 11:25:45 20 anti-VEGF treatment. 11:25:49 21 But for diabetic retinopathy, was the 11:25:50 22 standard of care Lucentis, or was it bevacizumab, 11:25:55 23 something else, as of January 2011? 11:26:02 24 MS. STRUTHERS: Objection; asked and 11:26:07 25 answered. 11:26:08 Page 77

1 A. In my clinic, standard of care is the best 11:26:08 2 available treatment, which would have been 11:26:15 3 ranibizumab, if available. 11:26:18 4 Q. (BY MR. SUMMERS) Was ranibizumab available 11:26:19 5 for diabetic retinopathy, as of January 2011? 11:26:20 6 A. Not commercially available. 11:26:30 7 Q. Okay. So you would have had to enroll in a 11:26:33 8 clinical trial, or is there any other method? 11:26:40 9 A. There were access programs to get 11:26:42 10 ranibizumab prior to approval. Exactly which 11:26:45 11 indications in January 2011, I don't know. 11:26:48 12 Q. Okay. If a physician who didn't have -- had 11:26:50 13 a patient who didn't have access to the clinical 11:26:56 14 trials, and -- and wasn't eligible for these access 11:26:57 15 programs, prescribed bevacizumab instead, would 11:27:00 16 they have violated the standard of care for 11:27:05 17 diabetic retinopathy? 11:27:09 18 A. A physician can only treat with the best 11:27:10 19 available agents he has available, which is his 11:27:13 20 standard of care. 11:27:15 21 Q. Okay. Let's move on to central retinal vein 11:27:15 22 occlusion. 11:27:29 23 What was the standard of care for central 11:27:30 24 retinal vein occlusion, as of January 2011? 11:27:33 25 A. Ranibizumab was approved for central retinal 11:27:36 Page 78	1 correct? 11:29:38 2 A. Corneal vascularization is new blood vessels 11:29:38 3 in the cornea. I'm not an expert in the cornea, 11:29:43 4 and I honestly don't know. The retina is very 11:29:46 5 specific. I'm a back-of-the-eye retina guy. And 11:29:47 6 if there is a cornea problem, I refer to a cornea 11:29:50 7 specialist. I honestly don't know what they did in 11:29:53 8 2011. 11:29:55 9 Q. Okay. Let me just ask the simpler question. 11:29:56 10 Corneal neo -- neovascularization is an 11:30:01 11 angiogenic eye disorder, correct? 11:30:06 12 A. I would classify it as an angiogenic eye 11:30:12 13 disorder, but again, that's not my level -- area -- 11:30:15 14 area of expertise. 11:30:16 15 Q. Okay. And you don't know what the standard 11:30:17 16 of care was as of January of 20 -- 11:30:19 17 A. I do not. 11:30:21 18 Q. Okay. So do you still have your declaration 11:30:22 19 in front of you? 11:30:36 20 A. I do. 11:30:36 21 Q. Go ahead and -- and turn back to where we 11:30:37 22 were, pages 46 and 47, paragraphs 96 through 100. 11:30:40 23 You give an opinion on claim construction as 11:30:51 24 to the term, a method for treating an angiogenic 11:30:54 25 eye disorder in a patient, there. 11:30:57 Page 80
1 vein occlusion, following the CRUISE study, 11:27:42 2 C-R-U-I-S-E -- I'm the first author -- and after 11:27:44 3 publication and presentation of the RAVE study, 11:27:47 4 which was presented but not published yet. 11:27:50 5 Q. And do you recall the dates of that 11:27:52 6 approval? 11:27:56 7 A. I don't. You can tell me. 2007-ish. 11:27:56 8 Q. Prior -- prior to 2011? 11:28:01 9 A. Correct. 11:28:03 10 Q. And let me move on. Branch retinal vein 11:28:03 11 occlusion, that's another angiogenic eye disorder, 11:28:40 12 correct? 11:28:42 13 A. Correct. 11:28:42 14 Q. And what was the standard of care, as of 11:28:42 15 January 2011, for branch retinal vein occlusion? 11:28:46 16 A. Branch retinal vein occlusion that caused 11:28:50 17 macular edema in the center of the -- in the 11:29:01 18 center -- center-involved macular edema that was 11:29:03 19 persistent to treatment, the standard of care was 11:29:08 20 monthly ranibizumab, after the publication of 11:29:11 21 BRAVO, B-R-A-V-O, which I designed, and again, was 11:29:14 22 first author. 11:29:19 23 Q. Okay. And then the -- let me ask you about 11:29:21 24 corneal neovascularization. 11:29:26 25 That's another angiogenic eye disorder, 11:29:33 Page 79	1 Is that correct? 11:30:58 2 (The witness peruses the document.) 11:31:21 3 A. Yeah, essentially, Dr. Do expounded on this 11:31:26 4 quite a bit. And I say, in 99: I understand that 11:31:30 5 Dr. Do has offered the opinion that the method for 11:31:34 6 treating recited in Claims 1 and 14 of the '681 11:31:37 7 patent requires a high level of efficacy that is on 11:31:41 8 par with the standard of care at the time the 11:31:43 9 patent was filed in 2011. 11:31:45 10 I go on, in 99, to state: I've reviewed 11:31:48 11 Dr. Do's declaration, and agree with her 11:31:51 12 conclusion. The method of treated recited in the 11:31:54 13 challenge claims to the '681 patent requires an 11:31:57 14 effective treatment, and further by 2011, the POSA 11:31:59 15 would have understood an effective treatment was 11:32:02 16 one that was at least on par with standard of care, 11:32:04 17 i.e., Lucentis. 11:32:06 18 Q. (BY MR. SUMMERS) So it's your understanding 11:32:08 19 that the phrase, a method for treating an 11:32:22 20 angiogenic eye disorder in a patient requires an 11:32:24 21 effective treatment, and further, that that 11:32:27 22 effective treatment was one that was at least on 11:32:31 23 par with the standard of care, which in your view, 11:32:33 24 is Lucentis. 11:32:37 25 Is that right? 11:32:37 Page 81

1 MS. STRUTHERS: Objection; document 11:32:39 2 speaks for itself. 11:32:40 3 A. That's exactly what I state -- 11:32:40 4 Q. (BY MR. SUMMERS) Okay. 11:32:43 5 A. -- in 98 and 99. 11:32:44 6 Q. And in forming the opinions in your 11:32:45 7 declaration, did you apply that understanding of 11:32:47 8 the term, a method for treating an angiogenic eye 11:32:51 9 disorder in a patient? 11:32:56 10 A. Excuse me. Repeat the question. 11:32:57 11 Q. Yeah. In forming the opinions in your 11:33:03 12 declaration, did you apply the understanding you 11:33:06 13 give here in paragraph 98, regarding the meaning of 11:33:08 14 a method for treating an angiogenic eye disorder in 11:33:12 15 a patient? 11:33:18 16 A. Yes, I did. 11:33:18 17 Q. Okay. And so, in giving your opinion on, 11:33:19 18 for instance, the reasonable expectation of 11:33:22 19 success, you interpreted the claims to require 11:33:24 20 efficacy, and specifically, an effective treatment 11:33:29 21 that was at least on par with Lucentis. 11:33:34 22 Is that right? 11:33:37 23 A. It's what I state. 11:33:37 24 Q. Okay. Are you aware that the board in, for 11:33:41 25 instance, instituting prior proceedings as to a 11:33:48 Page 82	1 Q. (BY MR. SUMMERS) Okay. And as it follows 11:35:16 2 from that, you didn't apply any construction for a 11:35:17 3 method for treating an angiogenic eye disorder in a 11:35:21 4 patient, other than the one you expressed in 11:35:23 5 paragraphs 98 and 99 here. 11:35:26 6 Is that right? 11:35:29 7 A. I applied my criteria, which is, if I'm 11:35:30 8 going to treat, I'm going to treat with an 11:35:35 9 effective treatment that's the best available, 11:35:37 10 which, according to Dr. Do, and I agree with it, is 11:35:40 11 the best thing you have, which in -- the POSA would 11:35:44 12 have understood would have been at least on par 11:35:47 13 with MARINA/ANCHOR, a treatment that gives 11:35:48 14 improvements in vision, with maintenance, without 11:35:53 15 fluctuation. 11:35:57 16 Q. Okay. And you -- I -- I think this is 11:35:57 17 simple, but for the purposes of your declaration, 11:36:01 18 you -- you did not consider the board's 11:36:05 19 construction for a method of treating an angiogenic 11:36:07 20 eye disorder in a patient that was given in 11:36:09 21 conjunction with the '338 patent proceedings, 11:36:12 22 correct? 11:36:16 23 MS. STRUTHERS: Objection; asked and 11:36:16 24 answered. 11:36:16 25 A. Yeah, I -- I used my own -- my own opinion; 11:36:16 Page 84
1 patent known as the '338 patent has given an 11:33:54 2 opinion on the interpretation of the phrase, a 11:33:57 3 method for treating an angiogenic eye disorder in a 11:33:59 4 patient? 11:34:02 5 A. I was involved in depositions on the '338 11:34:04 6 patent. I reviewed quite a long time ago what the 11:34:19 7 board said, but don't really remember. Sorry. 11:34:24 8 Q. Okay. And you didn't consider, for the 11:34:26 9 purposes of your declaration here, any construction 11:34:29 10 that the board has previously given for a method 11:34:31 11 for treating an angiogenic eye disorder in a 11:34:33 12 patient? 11:34:35 13 A. Repeat the question one more time. 11:34:35 14 Q. Sure. You -- you didn't consider, for the 11:34:43 15 purposes of your declaration here, any construction 11:34:47 16 the board had previously given for a method for 11:34:49 17 treating an angiogenic eye disorder in a patient? 11:34:51 18 MS. STRUTHERS: Objection; 11:34:54 19 mischaracterizes the testimony. 11:34:55 20 A. Yeah, I reviewed the -- I reviewed the -- 11:34:55 21 after depositions in the '338, I remember reviewing 11:35:00 22 the board's decisions, but that was a long time 11:35:04 23 ago. And I did not specifically go back to those 11:35:07 24 board's findings and -- as it pertains to this 11:35:10 25 claim construction. 11:35:16 Page 83	1 that method of treatment requires a high level of 11:36:23 2 efficacy on par with the standard of care at the 11:36:28 3 time the patent was filed. 11:36:30 4 Q. (BY MR. SUMMERS) Okay. Thank you. 11:36:31 5 And if I go down to page 48 of your 11:36:32 6 declaration, here, this is in the section on a 11:36:35 7 reasonable expectation of success. You say, in 11:36:38 8 paragraph 102 there: The claim method of treating 11:36:45 9 in each of the challenged claims requires effective 11:36:51 10 treatment. 11:36:54 11 And you refer to that claim construction 11:36:55 12 section we were just looking at. 11:36:57 13 Do you see that? 11:36:58 14 A. I do. 11:36:59 15 Q. Okay. And then you go on to say: The POSA 11:37:05 16 would have understood that effective treatment at 11:37:07 17 the time of the invention was treatment on par with 11:37:10 18 Lucentis, which was the standard of care at the 11:37:12 19 time. 11:37:14 20 Is that -- do I have that right? 11:37:15 21 A. That's what it states. 11:37:17 22 Q. Okay. So, for the purposes of giving your 11:37:18 23 opinion on reasonable expectation of success, did 11:37:21 24 you believe that it was required to show that any 11:37:28 25 proposed extended dosing regimen would have had 11:37:38 Page 85

1 treatment -- would have provided treatment that was 11:37:43 2 on par with Lucentis? 11:37:45 3 MS. STRUTHERS: Objection to form. 11:37:53 4 A. Repeat the question one more time. 11:37:53 5 Q. (BY MR. SUMMERS) Sure. For the purposes of 11:37:55 6 giving your opinion on reasonable expectation of 11:37:56 7 success in this section, was it your opinion 11:37:59 8 that to show a reasonable expectation of success, 11:38:05 9 it was required to show treatment on par with 11:38:09 10 Lucentis? 11:38:12 11 MS. STRUTHERS: Objection to form. 11:38:18 12 A. So in section -- paragraphs 98 and 99, 11:38:19 13 specifically, regarding whether or not the 11:38:41 14 treatment is in the claim construction, in the 11:38:43 15 reasonable expectations of success, I relied on the 11:38:47 16 CLEAR-IT data, which -- which, in a Phase 2 trial, 11:38:51 17 is a much smaller data set, and you only have the 11:38:58 18 data with which you have. 11:39:05 19 So reasonable explanations -- expectation of 11:39:06 20 success in that was based on the totality of the 11:39:10 21 CLEAR-IT trial. In a Phase 2 trial, I would expect 11:39:13 22 to see anatomic improvements. I would hope to see 11:39:18 23 visual acuity improvements. I wouldn't think that 11:39:22 24 it could prove to me that it was as good as a 11:39:25 25 Phase 3 trial until a Phase 3 trial was completed. 11:39:28 Page 86	1 MS. STRUTHERS: Objection to form; 11:41:15 2 vague. 11:41:17 3 A. So your specific question is? 11:41:17 4 Q. (BY MR. SUMMERS) Yeah, so, you said that -- 11:41:20 5 that's what -- what's required here for reasonable 11:41:24 6 expectation of success is standard of care 11:41:28 7 Lucentis. And my question is, standard of care 11:41:31 8 Lucentis was established via multiple controlled 11:41:36 9 clinical studies, correct, as of 2011? 11:41:41 10 A. Correct. 11:41:43 11 Q. Was it then required to meet that standard 11:41:43 12 of care to show efficacy on par with Lucentis to 11:41:47 13 have multiple controlled clinical studies for any 11:41:50 14 other drug? 11:41:55 15 MS. STRUTHERS: Objection to form; 11:41:58 16 mischaracterizes the testimony. 11:42:00 17 A. On a population basis, it requires multiple 11:42:00 18 well-controlled randomized trials. On an 11:42:02 19 individual patient basis, you have to look at the 11:42:07 20 patient and see how they're responding and take the 11:42:08 21 whole patient into consideration. 11:42:10 22 So, standard of care is -- you know, in a 11:42:11 23 population basis, is one thing. Patient -- 11:42:14 24 standard of care, when you've sent your mom to me, 11:42:18 25 is a different thing. 11:42:21 Page 88
1 Q. (BY MR. SUMMERS) Okay. So Lucentis had 11:39:32 2 been shown to be effective, as of 2011, for at 11:39:45 3 least wet AMD, right? 11:39:50 4 A. By 2011, Lucentis had been shown to be 11:39:52 5 effective in multiple presentations against retinal 11:40:01 6 vein occlusion, central retinal vein occlusion, 11:40:07 7 branch retinal vein occlusion, and diabetic macular 11:40:12 8 edema. Within the diabetic macular edema papers, 11:40:12 9 there are shown improvements in diabetic 11:40:15 10 retinopathy, but was not approved for diabetic 11:40:18 11 macular edema or diabetic retinopathy until later. 11:40:21 12 Q. And what about wet AMD? You left that out. 11:40:23 13 A. Wet AMD was the first indication, approved 11:40:27 14 2006. 11:40:38 15 Q. Okay. Now, at least for wet AMD, that was 11:40:38 16 done, showing was made via multiple controlled 11:40:40 17 clinical studies, correct? 11:40:44 18 A. By 2011, it was shown in multiple controlled 11:40:46 19 clinical trials for branch retinal vein occlusion, 11:40:51 20 central retinal vein occlusion, diabetic macular 11:40:55 21 edema, and age-related macular degeneration. 11:40:57 22 Q. Okay. So to show efficacy on par with 11:41:01 23 Lucentis, as of 2011, was it necessary to show via 11:41:03 24 multiple controlled trials efficacy for -- I'm 11:41:09 25 going to stick to wet AMD. 11:41:13 Page 87	1 Q. (BY MR. SUMMERS) Right. And -- 11:42:22 2 A. Informed, certainly, by the clinical trials, 11:42:22 3 but... 11:42:26 4 Q. Sure. You're putting your finger on the 11:42:26 5 question I have for you, which is, when you talk 11:42:28 6 about standard of care Lucentis and the reasonable 11:42:31 7 expectation of success portion of your opinion, are 11:42:34 8 you talking about it on the population basis or the 11:42:35 9 patient basis? 11:42:38 10 A. Right. Essentially, it's -- it's a patient 11:42:39 11 basis that has to show an improvement in visual 11:42:45 12 acuity, and that is informed by our Phase 3 11:42:49 13 clinical trials that show on a population basis how 11:42:52 14 they would do. 11:42:54 15 Q. Okay. Is there any way, other than a 11:42:55 16 clinical trial, to show efficacy on an individual 11:43:00 17 basis? 11:43:03 18 A. You'd have to look at the exact 11:43:09 19 circumstances of the disease. 11:43:11 20 In other words, there is a lot of things in 11:43:12 21 surgery we don't have a clinical trial for, but 11:43:14 22 we -- you know, surgically, it works and so people 11:43:16 23 adopt that, right. And so not everything has a 11:43:19 24 randomized clinical trial to tell you that it's the 11:43:21 25 right thing for the patient. 11:43:23 Page 89

1 In pharmaceutical trials, they're 11:43:25 2 predominantly our -- our mainstay of scientific 11:43:30 3 evidence is large populations with controlled 11:43:38 4 clinical trials. 11:43:42 5 Q. Okay. Let me give you an example. 11:43:42 6 In the PIER trials, there were individual 11:43:46 7 patients who, in fact, gained greater than 15 11:43:50 8 letters and maintained those gains, correct? 11:43:55 9 A. That's correct. 11:44:00 10 Q. Okay. For those patients, efficacy of the 11:44:00 11 PIER method was established. 11:44:07 12 Is that right? 11:44:09 13 MS. STRUTHERS: Objection; calls for 11:44:11 14 speculation, incomplete hypothetical. 11:44:15 15 A. Yeah, it's really the totality of the 11:44:17 16 patient. You'd have to -- you'd have to examine 11:44:20 17 and get all the data and see all the -- everything 11:44:23 18 about that patient to make that determination. 11:44:23 19 Q. (BY MR. SUMMERS) Okay. So at least for -- 11:44:26 20 and that would have been applied to the entire 11:44:27 21 population, as well, I assume. 11:44:30 22 Is that right? 11:44:31 23 MS. STRUTHERS: Objection to form. 11:44:31 24 A. What would apply? 11:44:31 25 Q. (BY MR. SUMMERS) That you would have to get 11:44:36 Page 90	1 or 25 or 30, if you had treated them monthly. So 11:45:46 2 until you examine the exact patient and everything 11:45:48 3 we have available, you can't really say that they 11:45:50 4 received the maximum effective treatment. 11:45:53 5 Q. (BY MR. SUMMERS) Okay. And is that true 11:45:55 6 across the population, as well? 11:45:57 7 MS. STRUTHERS: Objection to form; 11:45:59 8 asked and answered. 11:45:59 9 A. On an individual patient, it is true. On a 11:45:59 10 population, you'd need to have a randomized trial 11:46:07 11 to prove that your biases aren't -- it's -- 11:46:15 12 population basis requires a randomized trial. 11:46:18 13 Individual patient regards -- trial requires 11:46:21 14 individual examination of the patient and all their 11:46:26 15 indices. 11:46:30 16 Q. (BY MR. SUMMERS) Right. But you don't 11:46:31 17 know, for the population, whether the maximum 11:46:33 18 effect was obtained from that treatment method, 11:46:35 19 correct? 11:46:37 20 MS. STRUTHERS: Objection -- 11:46:37 21 A. Which treatment method? 11:46:38 22 Q. (BY MR. SUMMERS) It -- any. I asked you -- 11:46:39 23 so I asked you, you know, for at least the 11:46:40 24 individuals, taking the criteria of visual acuity 11:46:43 25 gain, in the PIER trial, efficacy was established 11:46:48 Page 92
1 everything about all of those patients and their 11:44:37 2 data to make a determination of efficacy? 11:44:39 3 MS. STRUTHERS: Mischaracterizes the 11:44:44 4 testimony. Objection to form. 11:44:46 5 A. So if you're looking at a population, you 11:44:46 6 take a control trial and take the mean with 11:44:48 7 standard deviations. If you're looking at an 11:44:51 8 individual patient, you have to look at all the 11:44:53 9 indices that are available for you to determine are 11:44:56 10 you doing the most you can for that patient. 11:44:58 11 Q. (BY MR. SUMMERS) Yeah, one -- one of those 11:45:00 12 indices is gain in visual acuity, correct? 11:45:01 13 A. Absolutely. 11:45:09 14 Q. Okay. And in the PIER trial, there were 11:45:09 15 individual patients for whom it was established 11:45:12 16 that they gained and maintained 15 letters through 11:45:18 17 the duration of the trial, correct? 11:45:24 18 A. Correct. 11:45:25 19 Q. So, at least on that entity, efficacy was 11:45:25 20 established for those individual patients, correct? 11:45:34 21 MS. STRUTHERS: Objection; 11:45:35 22 mischaracterizes the testimony, incomplete 11:45:37 23 hypothetical. 11:45:41 24 A. You don't know if maximum efficacy was 11:45:41 25 obtained, right. Some of them might have gained 20 11:45:43 Page 91	1 for certain patients of a gain and maintenance of 11:46:52 2 15 letters. You said you don't know the maximum 11:46:57 3 efficacy. 11:46:59 4 A. In an individual patient -- 11:47:00 5 MS. STRUTHERS: Well, hold on. Hold 11:47:01 6 on. Let him finish his question, please. 11:47:01 7 Q. (BY MR. SUMMERS) Well, so -- so what I'm 11:47:03 8 trying to get at is, do you know the maximum 11:47:04 9 efficacy across the population, that -- that it was 11:47:07 10 reached? 11:47:10 11 MS. STRUTHERS: Objection; calls for 11:47:11 12 speculation, incomplete hypothetical. 11:47:13 13 A. Yeah, you'd have to look at each individual 11:47:15 14 trial and all the data in that trial to determine 11:47:18 15 that. 11:47:21 16 Q. (BY MR. SUMMERS) Okay. You know the PIER 11:47:21 17 trial very well, right? 11:47:22 18 A. I know the PIER trial. 11:47:24 19 Q. Okay. Did you determine whether the PIER 11:47:25 20 trial had the data sufficient to know whether 11:47:26 21 maximum efficacy was obtained for the population? 11:47:29 22 MS. STRUTHERS: Objection to form. 11:47:34 23 (The witness peruses the document.) 11:48:35 24 A. Paragraph 49: I participated as a clinical 11:48:35 25 investigator and was part of the PIER study group 11:48:50 Page 93

1 and was also involved in the presentation and 11:48:53	1 evaluation of that was on a population basis or an 11:51:31
2 publication of the one-year data from PIER. As 11:48:55	2 individual basis. 11:51:35
3 explained below, the PIER study revealed that fixed 11:48:57	3 Am I correct that it's your testimony that 11:51:37
4 quarterly intravitreal injections of ranibizumab 11:49:00	4 you made that evaluation on individual patient 11:51:41
5 over an extended treatment period was not an 11:49:03	5 basis? 11:51:45
6 effective method of treatment. 11:49:05	6 MS. STRUTHERS: Objection to form; 11:51:49
7 As one of the lead clinical investigators on 11:49:06	7 mischaracterizes the testimony. 11:51:50
8 the PIER trial, I received the first readout on the 11:49:09	8 A. Yeah, maybe be a little more specific on 11:51:50
9 one-year data from the study from Genentech in 11:49:12	9 your question. I'm lost. 11:51:53
10 early 2006 and was the first to present this data 11:49:12	10 Q. (BY MR. SUMMERS) Sure. So you give an 11:51:54
11 in -- in May -- early -- end of May -- I think it 11:49:15	11 opinion on reasonable expectation of success, in 11:51:56
12 was the beginning of June 2006. 11:49:20	12 your declaration, correct? I'll be happy to direct 11:51:57
13 The data was highly disappointing, to say 11:49:22	13 you to it. It starts on page 47. 11:52:22
14 the least. While patients saw an initial gain in 11:49:24	14 A. Yep. 11:52:27
15 visual acuity during the three months' loading 11:49:27	15 Q. Okay. 11:52:27
16 doses, these gains were entirely lost once 11:49:29	16 A. Got it, yeah. 11:52:28
17 quarterly dosing began. 11:49:33	17 Q. So you give an opinion on reasonable 11:52:29
18 On average, there was a 4.5-letter decline 11:49:34	18 expectation of success in your declaration, 11:52:33
19 in visual acuity between month 3 and month 12 for 11:49:37	19 correct? 11:52:34
20 both ranibizumab dose groups. 11:49:41	20 A. That's correct. 11:52:35
21 By month 12, the 0.3-milligram study arm saw 11:49:43	21 Q. Okay. In evaluating whether there was a 11:52:35
22 1.6 letter difference from baseline, negative, and 11:49:48	22 reasonable expectation of success, was it necessary 11:52:40
23 the 0.5-milligram group had lost .2 letters from 11:49:51	23 to show, on a population basis, efficacy on par 11:52:47
24 baseline. 11:49:55	24 with Lucentis? 11:52:53
25 OCT also confirmed ranibizumab's failure to 11:49:55	25 MS. STRUTHERS: Again, objection to 11:52:57
Page 94	Page 96
1 main efficacy over the quarterly dosing period. 11:50:01	1 form; calls for speculation. 11:52:58
2 The maximum decrease in foveal center point 11:50:03	2 (The witness peruses the document.) 11:53:10
3 thickness at month 2 and 3, which declined by 11:50:06	3 A. As it pertains to my interpretation of the 11:53:10
4 months 5 and 8. And on average, the foveal center 11:50:10	4 CLEAR-IT 2, and would it lead the POSA to feel that 11:53:16
5 point thickness was greater than months 2 and 3, 11:50:17	5 a Q8 dosing regimen would be successful? Is that 11:53:22
6 and was also greater than at month 12, which 11:50:20	6 what you're asking? 11:53:28
7 followed a ranibizumab dose at month 11. 11:50:22	7 Q. (BY MR. SUMMERS) I -- not just CLEAR-IT 2, 11:53:30
8 It suggested that on average, ranibizumab's 11:50:25	8 because you give more opinions beyond CLEAR-IT 2. 11:53:33
9 therapeutic effectiveness in a patient would wane 11:50:28	9 So, my question is, as it -- in evaluating, 11:53:38
10 between injections with recurrent neovascular 11:50:30	10 for the purposes of the reasonable expectation of 11:53:46
11 activity and associated exudation. 11:50:35	11 success portion of your declaration, did you view 11:53:48
12 So, after examining the totality -- 11:50:37	12 it as necessary to show, on a population basis, 11:53:50
13 totality of the PIER study, you see that they did 11:50:39	13 efficacy on par with Lucentis? 11:53:54
14 not fair near as well as MARINA/ANCHOR, as I go on 11:50:47	14 MS. STRUTHERS: Again, objection to 11:53:59
15 to expound in paragraph 52. 11:50:51	15 form; calls for speculation. 11:54:01
16 So, no, they did not -- were not able to 11:50:54	16 A. Respectfully, I disagree that my reasonable 11:54:01
17 achieve the standard of care MARINA/ANCHOR vision 11:50:55	17 expectation of success deals with much else other 11:54:22
18 gains with maintenance of gains, as was published 11:50:58	18 than CLEAR-IT, and whether the POSA would have a 11:54:24
19 in MARINA and ANCHOR. 11:51:03	19 reasonable expectation of success using the VIEW 11:54:28
20 Q. (BY MR. SUMMERS) So -- so, I want to come 11:51:04	20 regimens to treat wet AMD. 11:54:32
21 back to your opinion on reasonable expectation of 11:51:14	21 I talk about the POSA would not have a 11:54:33
22 success, where we're not just reading from the 11:51:18	22 reasonable expectation of successfully achieving 11:54:35
23 report. 11:51:21	23 the Q8 dosing regimen claimed by the '681 patent 11:54:39
24 We were talking earlier about whether it was 11:51:21	24 until after Regeneron conducted its VIEW 1, VIEW 11:54:40
25 required to meet the standard of care, whether your 11:51:27	25 trials. 11:54:42
Page 95	Page 97

1 As discussed in Section V1.C, the prior art 11:54:43 2 was littered with failed attempts to develop an 11:54:47 3 extended dosing regimen for the treatment of wet 11:54:50 4 AMD. Many of theses failures were only recognized 11:54:52 5 after the trial was completed or upon post hoc 11:54:54 6 analysis, which would have contributed to a general 11:54:58 7 skepticism by the POSA regarding whether a 11:55:02 8 prospective fixed extended dosing regimen would be 11:55:04 9 successful until the results were recognized. 11:55:06 10 In addition here, and I go through for quite 11:55:10 11 a few pages, which we can go over, the Phase 2 11:55:13 12 results of VEGF Trap-Eye in CLEAR-IT 2 would have 11:55:16 13 created uncertainty that VEGF Trap-Eye could be 11:55:20 14 effective if dosed on a Q8 regimen. 11:55:23 15 Q. (BY MR. SUMMERS) Okay. I understand, 11:55:27 16 again, you're reading from your declaration. I'm 11:55:28 17 asking you a question. I'm going to restate it. 11:55:34 18 A. Please. 11:55:42 19 Q. In evaluating whether there was a reasonable 11:55:42 20 expectation of success, was it necessary, in your 11:55:44 21 view, to show, on a population basis, efficacy on 11:55:48 22 par with Lucentis? 11:55:53 23 MS. STRUTHERS: Again, objection to 11:55:55 24 form; calls for speculation. 11:55:58 25 A. As it pertains to CLEAR-IT 2? 11:55:58 Page 98	1 of dosing at eight-week intervals was uncertain, 11:58:00 2 even after the results of CLEAR-IT 2 were reported. 11:58:06 3 He specifically noted data from the Phase 2 11:58:08 4 study of VEGF Trap-Eye were positive, but it will 11:58:11 5 be the results from the non-inferiority Phase 3 11:58:13 6 trials that will establish its efficacy versus 11:58:17 7 ranibizumab. 8 And states a couple of options. One, if its 11:58:22 9 adoption in a clinic practice will depend on the 11:58:25 10 efficacy at four and eight-week intervals, 11:58:28 11 specifically acknowledges the real possibility that 11:58:31 12 VIEW trials would show effectiveness for four-week 11:58:33 13 dosing but not eight-week dosing. 11:58:34 14 He states: If effective at eight-week 11:58:36 15 intervals, VEGF Trap-Eye offers the opportunity to 11:58:38 16 significantly reduce treatment burden on patients 11:58:41 17 and physicians, and would probably find wide -- 11:58:43 18 wide acceptance. 11:58:46 19 But he says: But, if effective at four-week 11:58:47 20 intervals only, VEGF try will be -- Trap-Eye will 11:58:53 21 be adopted into clinical practice, if it offers a 11:58:56 22 competitive price advantage over ranibizumab. 11:59:00 23 So, the results, once we approved, were 11:59:03 24 surprising to us. And I used all the failed trials 11:59:09 25 before, the analysis we have of the Phase 1, and 11:59:15 Page 100
1 Q. (BY MR. SUMMERS) So you, for the purposes 11:56:03 2 of providing your opinion on reasonable expectation 11:56:05 3 of success, you looked only at CLEAR-IT? 11:56:06 4 MS. STRUTHERS: Objection; 11:56:14 5 mischaracterizes the testimony, declaration speaks 11:56:15 6 for itself. 11:56:16 7 A. I mean, as I discuss, I discuss all the 11:56:17 8 failed attempts of extended dosing before. So 11:56:49 9 certainly that was considered. The only real data 11:56:52 10 on how VEGF Trap-Eye would potentially be 11:56:56 11 extendable is from the Phase 1, which didn't have a 11:57:02 12 whole lot of data. Certainly, I'm -- I talk about 11:57:05 13 that as well. It was a single-dose study. 11:57:07 14 But the majority of the data that could lead 11:57:12 15 to a possibility of a reasonable expectation of 11:57:14 16 success is CLEAR-IT 2. And that's where I discuss, 11:57:19 17 looking at the totality of the data, that I 11:57:22 18 concluded the POSA would not have had a reasonable 11:57:26 19 expectation of success that claimed that Q8-week 11:57:29 20 dosing regimen would be effective until we actually 11:57:33 21 conducted the VIEW 1, VIEW 2 trials. 11:57:35 22 I then go on to talk about when we got the 11:57:39 23 data, it was surprising. Jeff Heier -- I quote 11:57:43 24 Jeff Heier. Before we get there, Dixon even 11:57:48 25 said -- Dixon recognized that -- that the efficacy 11:57:54 Page 99	1 predominantly the CLEAR-IT 2 data, to make that 11:59:22 2 determination we're discussing on reasonable 11:59:25 3 expectation of success. 11:59:42 4 MS. STRUTHERS: We've been going a 11:59:42 5 little over an hour, so whenever you're done with 11:59:43 6 this line, we can take a break? 11:59:46 7 MR. SUMMERS: Sure. 11:59:47 8 Q. (BY MR. SUMMERS) You understand that in the 11:59:52 9 prior art, Dixon, for instance, disclosed a dosing 11:59:53 10 administration regimen of three initial loading 12:00:03 11 doses, followed by dosing at eight-week intervals, 12:00:07 12 right? 12:00:13 13 (The witness peruses the document.) 12:01:35 14 A. So I state, in 108, Dr. Chaum, your expert, 12:01:38 15 I think, contends that the POSA would have 12:01:42 16 reasonable expectation of success that the use of 12:01:43 17 the claimed dose regimens disclosed in Dixon in a 12:01:45 18 Phase 3 trial would show efficacy, unquote, because 12:01:48 19 the, quote, less frequent, unquote, regimen tested 12:01:51 20 in CLEAR-IT 2, quote, had already shown efficacy. 12:01:54 21 I disagree with Dr. Chaum that -- that -- 12:01:59 22 that the data presented in Dixon would have led -- 12:02:01 23 that they showed efficacy that would have led the 12:02:04 24 POSA to believe that you could go to Q8-week 12:02:09 25 dosing. Page 101

1 Q. (BY MR. SUMMERS) Right. You -- you 12:02:14 2 understand that Dixon discloses the claimed dosing 12:02:14 3 regimen, right, based on (unintelligible)? 12:02:18 4 THE REPORTER: I'm sorry. Can you 12:02:18 5 repeat that again? 12:02:19 6 Q. (BY MR. SUMMERS) Sure. You understand that 12:02:19 7 Dixon disclose the claimed dosing regimen, correct? 12:02:20 8 A. Can I see Dixon? 12:02:25 9 Q. Yeah. Do you not know, without looking at 12:02:25 10 Dixon, whether it discloses the claimed dosing 12:02:34 11 regimen of the '681 patent? 12:02:40 12 MS. STRUTHERS: Objection. 12:02:40 13 A. Can I see Dixon? 12:02:40 14 Q. (BY MR. SUMMERS) That's -- my ques -- 12:02:41 15 before I give you Dixon, I have a question to you. 12:02:42 16 Do you not know, without looking at Dixon, 12:02:44 17 whether it discloses the claimed dosing regimen of 12:02:46 18 the '681 patent? 12:02:50 19 MS. STRUTHERS: Objection; 12:02:50 20 argumentative. 12:02:50 21 A. I -- I know it discloses it pretty closely. 12:02:51 22 Let's look at it. 12:02:57 23 (The witness peruses the document.) 12:03:12 24 Q. (BY MR. SUMMERS) Let me save you some 12:03:56 25 hunting. Just if you can go to 1576 of Dixon. 12:03:58 Page 102	1 doses, compared to .5 milligram ranibizumab 2 administered every four weeks. So... 12:05:44 3 Q. (BY MR. SUMMERS) Yeah, and you're reading 12:05:45 4 in Dixon there, correct? 12:05:48 5 A. What's that? I read that from Dixon, yeah. 12:05:49 6 Q. You're reading from Dixon. 12:05:50 7 A. Yeah, yeah. That's -- that's very analogous 12:05:51 8 to what we ended up doing. You know, he says 12:05:52 9 we're -- after the first year of patients, we're in 12:05:55 10 our second year of PRN dosing. That's sort of 12:05:58 11 correct. We had a capped PRN dosing. He didn't 12:06:00 12 have that data available to him at that time. 12:06:03 13 Q. Okay. So for the purposes of the claims in 12:06:05 14 the '681 patent, the dosing regimen -- 12:06:09 15 A. Yeah, discloses what we're going to test, 12:06:10 16 correct. 12:06:12 17 Q. Thank you. Okay. 12:06:13 18 So is it your understanding, in providing 12:06:30 19 your opinion on reasonable expectation of success, 12:06:31 20 that that claimed dosing regimen needed to show 12:06:33 21 efficacy on par with Lucentis across an equivalent 12:06:38 22 population in order to provide a reasonable 12:06:43 23 expectation of success? 12:06:48 24 MS. STRUTHERS: Objection to form. 12:06:48 25 A. Repeat the question one more time. I'm 12:06:48 Page 104
1 This is Exhibit 1006. 12:04:03 2 A. What page? 12:04:08 3 Q. Yeah, let me do this properly. So Dixon -- 12:04:09 4 A. 15 -- yeah. 12:04:10 5 Q. One -- one second. 12:04:11 6 Dixon has been introduced. It's 12:04:11 7 Exhibit 1006. 12:04:14 8 If you could turn to page 1576, and go to 12:04:15 9 Section 2.6.3, Phase 3, on the right-hand column. 12:04:19 10 Go ahead and read that paragraph. 12:04:29 11 (The witness peruses the document.) 12:04:30 12 A. Yeah, I see that. 12:05:02 13 Q. (BY MR. SUMMERS) Okay. Does that refresh 12:05:03 14 your recollection about whether Dixon discloses the 12:05:05 15 claimed dosing regimen for the '681 patent? 12:05:08 16 MS. STRUTHERS: Objection; document 12:05:12 17 speaks for itself. 12:05:13 18 A. Yeah, I see that Dixon reports that we're 12:05:13 19 going to do a 1,200 patient trial, with neovascular 12:05:21 20 AMD in the US and Canada. The non-inferiority 12:05:29 21 study will evaluate the safety and efficacy of 12:05:30 22 intravitreal VEGF Trap-Eye at doses of half 12:05:34 23 milligram and 2 milligrams administered at 12:05:35 24 four-week dosing intervals and two-week and 12:05:36 25 eight-week dosing intervals following three monthly 12:05:39 Page 103	1 still confused -- 12:07:09 2 Q. (BY MR. SUMMERS) Sure. Is it your 12:07:09 3 understanding -- 12:07:10 4 A. -- on exactly what I'm supposed to answer. 12:07:11 5 Q. Sure. Is it your understanding that to have 12:07:14 6 a reasonable expectation of success that the Dixon 12:07:16 7 dosing regimen we just reviewed needed to show 12:07:21 8 efficacy on par with Lucentis across an equivalent 12:07:23 9 population, in order to provide a reasonable 12:07:27 10 expectation of success? 11 MS. STRUTHERS: Again, objection to 12:07:31 12 form. 12:07:33 13 (The witness peruses the document.) 12:08:05 14 A. Claim 1 says a method for treating an 12:08:19 15 angiogenic eye disorder in a patient, and said 12:08:23 16 method is, et cetera, et cetera, et cetera. 12:08:25 17 And so, the claims require that it's in a 12:08:26 18 patient with that dosing regimen, and have an 12:08:28 19 effective vision gains that you really -- only way 12:08:30 20 to tell in an individual patient is to examine the 12:08:36 21 totality of the patient in all our tests. 12:08:40 22 The way to get it approved and to get it 12:08:42 23 available to that patient, you have to do 12:08:46 24 randomized clinical trials, as we did in VIEW. 12:08:48 25 And Dixon discloses our proposed dosing 12:08:50 Page 105

27 (Pages 102 - 105)

1 regimens, but in no way gives me a reasonable 12:08:53 2 expectation of success that we would have been 12:08:58 3 successful until we completed the VIEW 1, VIEW 2 12:09:00 4 studies, which were in a population, cohorts of 12:09:05 5 randomized patients. 12:09:08 6 Q. (BY MR. SUMMERS) You -- you said the only 12:09:09 7 way to tell in an individual patient is to examine 12:09:10 8 the totality of the patients in all our tests. 12:09:13 9 What does that mean? 12:09:15 10 A. When an individual patient comes to me for 12:09:16 11 treatment, all I can do is the best care and the 12:09:27 12 best available thing I have. And that is informed 12:09:32 13 based on large Phase 3 clinical trials, such as 12:09:35 14 MARINA/ANCHOR, such as VIEW. 12:09:39 15 You take the patient's history. You see 12:09:42 16 whether they have one eye or two eyes. There are 12:09:46 17 multiple parts of the examination and testing that 12:09:48 18 you need to examine to figure out, are you -- what 12:09:53 19 treatment you should administer and are you -- are 12:09:57 20 you getting the best available treatment for that 12:10:02 21 patient. 12:10:05 22 MS. STRUTHERS: How are we doing on 12:10:16 23 time for a break, Counsel? 12:10:17 24 MR. SUMMERS: Yeah, let's take a 12:10:19 25 break. 12:10:19 Page 106	1 So, if a patient comes to you in time, and 12:45:48 2 you're able to give them frequent anti-VEGF doses, 12:45:51 3 usually Lucentis at that time, it correlated with 12:46:00 4 improved vision, improved OCT, reduction of fluid 12:46:04 5 on exam, reduction of hemorrhage, just like we saw 12:46:10 6 in the patients in ANCHOR/MARINA. 12:46:13 7 And if you see that, you are giving them on 12:46:16 8 par with the standard of care Lucentis. 12:46:20 9 THE REPORTER: Do you want to go 12:46:24 10 off? 12:46:25 11 MR. SUMMERS: Yeah, let me step out 12:46:25 12 there just for one second. Sorry to interrupt. 12:46:29 13 THE REPORTER: We're going off the 12:46:32 14 record. 12:46:33 15 THE VIDEOGRAPHER: Off the record at 12:46:34 16 12:45 p.m. 12:46:35 17 (Break.) 12:47:56 18 THE VIDEOGRAPHER: Back on the 12:47:56 19 record at 12:47 p.m. 12:47:59 20 Q. (BY MR. SUMMERS) And I understood you to 12:48:01 21 list a couple of criteria in that last answer 12:48:05 22 around the standard of care. And they were 12:48:09 23 improved vision, improved OCT, reduction of fluid 12:48:13 24 on the exam, and reduction of hemorrhage. 12:48:19 25 Is that right? 12:48:21 Page 108
1 THE VIDEOGRAPHER: Off the record at 12:10:20 2 12:09 p.m. 12:10:20 3 (Break.) 12:10:21 4 THE VIDEOGRAPHER: Back on the 12:44:13 5 record at 12:43 p.m. 12:44:14 6 Q. (BY MR. SUMMERS) Thank you. Welcome back, 12:44:17 7 Dr. Brown. 12:44:18 8 I want to come back to something we were 12:44:19 9 discussing earlier, which is the meaning of this 12:44:20 10 term that you use, the standard of care Lucentis. 12:44:22 11 How do you determine standard of care 12:44:25 12 Lucentis for an individual patient? 12:44:31 13 A. So, prior to 2002, when we had no 12:44:34 14 anti-VEGFs, up until 2006, when the world had -- 12:45:05 15 the -- the -- the developed world, United States, 12:45:10 16 Canada, et cetera, had ranibizumab and bevacizumab, 12:45:13 17 Lucentis and Avastin, the standards went from 12:45:15 18 diseases that were untreatable, where you just 12:45:21 19 tried to prevent huge vision loss, to treatments 12:45:26 20 that if you gave very intensive treatments, worked 12:45:28 21 pretty well for the most patients, right. 12:45:33 22 If you -- somebody comes in late, you -- the 12:45:37 23 cow may be out of the barn. But in each individual 12:45:41 24 patient, really, the most effective treatments were 12:45:43 25 very intensive treatments. 12:45:47 Page 107	1 A. That's what you'd expect to see. 12:48:21 2 Q. Okay. So, for any individual patient, what 12:48:24 3 was the standard of efficacy that had to be met to 12:48:32 4 meet the standard of care Lucentis? 12:48:37 5 MS. STRUTHERS: Objection to form. 12:48:41 6 A. So, repeat the question. 12:48:41 7 Q. (BY MR. SUMMERS) Sure. For any individual 12:48:56 8 patient, what was the standard of efficacy, as to 12:48:59 9 this criteria, that had to be met to meet the 12:49:03 10 standard of care Lucentis? 12:49:06 11 MS. STRUTHERS: Objection to form. 12:49:07 12 A. Yeah, I -- I don't quite exactly understand 12:49:07 13 what you're getting at. You want to try to do the 12:49:22 14 best for the patient you -- what -- that -- that 12:49:25 15 you can. And you hope to see that the drug is 12:49:27 16 working, both anatomically and functionally. And 12:49:30 17 that's all you can do in an individual patient. 12:49:34 18 Q. (BY MR. SUMMERS) Okay. Right. I'm trying 12:49:36 19 to understand your opinion in this regard. 12:49:52 20 So the standard of care, Lucentis, as to an 12:49:56 21 individual patient is just doing the best you can. 12:50:01 22 Is that right? 12:50:04 23 MS. STRUTHERS: Objection; 12:50:07 24 mischaracterizes the testimony. 12:50:07 25 A. As it pertains to treating an angiogenic eye 12:50:08 Page 109

28 (Pages 106 - 109)

1 disease, the standard of care is to treat with an 12:50:26 2 effective agent, like Lucentis or Eylea, when it 12:50:29 3 became available. And you continue to monitor for 12:50:33 4 effectiveness, anatomically and functionally, while 12:50:41 5 looking for potential adverse events. 12:50:46 6 Q. (BY MR. SUMMERS) And in your view, there's 12:50:50 7 no particular value associated with, for instance, 12:50:56 8 visual acuity that must be achieved with an 12:51:05 9 individual patient in order to meet the standard of 12:51:07 10 care. 12:51:10 11 Is that correct? 12:51:10 12 A. As you'll see in MARINA/ANCHOR, the average 12:51:10 13 patient, if you treat them with monthly Lucentis, 12:51:32 14 gains five to seven or eight letters, and maintains 12:51:36 15 that without loss much. That's what you would 12:51:38 16 expect on average, when you're treating the 12:51:44 17 population. 12:51:48 18 Q. And what about for an individual patient, 12:51:48 19 though? It's not the case that you have in your 12:51:50 20 head that you had to achieve a certain visual 12:51:55 21 acuity, for instance, to meet the standard of care 12:51:58 22 in 2011. 12:52:00 23 Is that right? 12:52:01 24 MS. STRUTHERS: Objection to form. 12:52:03 25 A. Again, every patient is different. They can 12:52:03 Page 110	1 A. Read the question one more time. 12:53:57 2 Q. (BY MR. SUMMERS) Yeah. Is it indicative -- 12:53:59 3 is non -- is nonresponsiveness on OCT indicative of 12:54:00 4 missing the standard of care? 12:54:04 5 MS. STRUTHERS: Again, objection to 12:54:05 6 form. 12:54:10 7 A. If a physician, including me, misses a 12:54:10 8 diagnosis, we hope we correct course and treat the 12:54:27 9 underlying disease to the best standard of care for 12:54:33 10 that disease. For an angiogenic eye disease, it's 12:54:37 11 Lucentis monthly, at the time of 20 -- 2011. 12:54:43 12 Q. (BY MR. SUMMERS) All right. But put more 12:54:45 13 simply, sometimes you meet the standard of care, in 12:54:48 14 your view, but don't get a response across the 12:54:50 15 various indicia of improvement, right? 12:54:54 16 MS. STRUTHERS: Objection; 12:54:57 17 mischaracterizes the testimony. 12:55:00 18 A. When I discuss standard of care in my 12:55:00 19 deposition -- my declaration, as you pointed to me 12:55:27 20 before, I reviewed what Dr. Do had offered the 12:55:30 21 opinion, that method for treating required a high 12:55:34 22 level of efficacy on par with the standard of care. 12:55:37 23 And the standard of care at that time was 12:55:41 24 treatment with monthly Lucentis, which, on average, 12:55:48 25 equaled a vision gain, with maintenance of that 12:55:53 Page 112
1 have concomitant diseases that preclude them from 12:52:10 2 gaining the type of typical visual acuities. 12:52:14 3 If you are improving their anatomy and 12:52:17 4 function and hopefully gaining some vision, which 12:52:23 5 you may not, you're still doing standard of care 12:52:25 6 for that patient. 12:52:27 7 Q. (BY MR. SUMMERS) And does that go for the 12:52:35 8 other indicia, like OCT and hemorrhage, that you're 12:52:37 9 hoping to do your best, but it -- they may not get 12:52:43 10 an improvement, you're still doing the standard of 12:52:47 11 care? 12:52:51 12 MS. STRUTHERS: Objection; 12:52:51 13 mischaracterizes the testimony. 12:52:51 14 A. So anti-VEGF agents block VEGF, vaso 12:52:52 15 endothelial growth factor. VEGF is 50,000 times 12:53:08 16 more potent than histamine at causing vascular 12:53:11 17 leakage. Lucentis, Eylea, very effective at 12:53:16 18 decreasing leakage and decreasing edema. 12:53:20 19 If I didn't see a response on OCT, I'd be 12:53:23 20 concerned that I missed the diagnosis, or, you 12:53:26 21 know -- nonresponsiveness to Lucentis and Eylea is 12:53:31 22 unusual on edema, in particular. 12:53:38 23 Q. (BY MR. SUMMERS) Is it indicative of 12:53:40 24 missing the standard of care, though? 12:53:54 25 MS. STRUTHERS: Objection to form. 12:53:57 Page 111	1 gain, without fluctuation. That same standard of 12:55:55 2 care or efficacy would be an improvement on the 12:56:00 3 OCT, as we showed in RISE/RIDE -- I'm sorry. We 12:56:05 4 showed it in RISE/RIDE as well. But here, we 12:56:08 5 showed it in MARINA/ANCHOR, where the edema or 12:56:11 6 exudation from the wet macular degeneration was 12:56:16 7 controlled and didn't fluctuate. 12:56:19 8 On an individual patient, it's, am I 12:56:33 9 performing the same thing that I would in MARINA 12:56:36 10 and ANCHOR, and seeing activities that are 12:56:39 11 consistent with the positive effects of the agent. 12:56:43 12 If they're not, it may be because of individual 12:56:47 13 factors within that patient. 12:56:56 14 Q. (BY MR. SUMMERS) Let me ask you, why don't 12:56:57 15 you go to page 15 of your declaration? 12:57:19 16 A. Page what? 12:57:22 17 Q. Page 15 of your declaration. 12:57:23 18 A. 1-5. 12:57:24 19 Q. It's Exhibit 2055. 12:57:25 20 And looking at paragraph 40, you say: After 12:57:27 21 Lucentis approval, the POSA would not have viewed 12:57:36 22 loss of less than 15 letters on ETDRS best 12:57:41 23 corrected visual acuity as an effective treatment 12:57:46 24 for an angiogenic eye disorder. 12:57:47 25 You said you also reviewed the '681 patent 12:57:52 Page 113

29 (Pages 110 - 113)

1 in totality? 12:57:57 2 A. I did. 12:57:59 3 Q. Can I draw your attention -- you have it in 12:58:01 4 front of you still? 12:58:04 5 A. I do. 12:58:05 6 Q. That's Exhibit 1001. Can you draw your 12:58:05 7 attention to Column 7 of the '681 patent. It 12:58:11 8 should be on page 7. 12:58:19 9 A. Yep. 12:58:20 10 Q. Okay. And let me call your attention more 12:58:20 11 specifically then to lines -- I'm sorry. Hold up. 12:58:26 12 Here we go. Lines 27 through 33. And I'll read 12:58:48 13 this in. 12:59:00 14 A. Column 7? 12:59:01 15 Q. Yeah, Column 7, lines 27, the sentence 12:59:02 16 starting -- 12:59:05 17 A. Okay. 12:59:05 18 Q. -- in the context of methods for treating 12:59:06 19 angiogenic eye disorders, such as AMD, CRVO, and 12:59:10 20 DME, efficacy means that from the initiation of 12:59:16 21 treatment, the patient exhibits a loss of 15 or 12:59:20 22 fewer letters on their early treatment diabetic 12:59:23 23 retinopathy study, in parens, ETDRS, visual acuity 12:59:28 24 gain chart. 12:59:36 25 A. I see that. 12:59:37 Page 114	1 efficacy means a gain of one or more, e.g., 1, 2, 13:03:29 2 3, 4, 5, 6, 7, 8, 9, 10, 11 or more letters, on the 13:03:32 3 ETDRS chart from the time of initiation of 13:03:37 4 treatment. 13:03:40 5 Also, to the -- Column 1 in the patent, the 13:03:40 6 last sentence of the background, where it said: 13:03:44 7 Nevertheless, there remains a need in the art for 13:03:49 8 new administration regimens for angiogenic eye 13:03:51 9 disorders, especially those which require far less 13:03:54 10 frequent dosing, while maintaining a high level of 13:03:58 11 efficacy. 13:04:02 12 I would contend that the POSA would not 13:04:02 13 consider just -- not losing 15 letters to be a high 13:04:05 14 level of efficacy. I would point you to 13:04:10 15 paragraph 78, where we talked about why we used 15 13:04:17 16 letters. The non-inferiority study seeks to show 13:04:19 17 the amount or margin by which the test drug is 13:04:23 18 inferior or not to the active control. 13:04:26 19 In designing a non-inferiority study, the 13:04:30 20 FDA estimates this margin based on the past 13:04:34 21 performance of the active control, open 13:04:36 22 parentheses, here, Lucentis, close parentheses, and 13:04:38 23 applies a constancy assumption that the 13:04:41 24 non-inferiority study is sufficiently similar in 13:04:45 25 study design, study end points, dose of active 13:04:46 Page 116
1 Q. In your view, is that portion of the 12:59:38 2 specification contrary to your opinion that after 12:59:45 3 2006, a POSA would have viewed a loss of less than 12:59:48 4 15 letters on ETDRS as not an effective treatment? 12:59:52 5 (The witness peruses the document.) 13:00:15 6 A. So repeat the question one more time, and 13:02:20 7 I'm ready to answer it now that I've -- 13:02:22 8 Q. (BY MR. SUMMERS) In your view, is that 13:02:24 9 portion of the specification contrary to your 13:02:26 10 opinion that after 2006, POSA would have viewed a 13:02:28 11 loss of less than 15 letters on ETDRS as not an 13:02:31 12 effective treatment? 13:02:35 13 A. And that was on page 15? Yeah. Yeah. 13:02:36 14 Paragraph 40, I got it. Yeah. 13:02:42 15 Q. Uh-huh. 13:02:44 16 A. And you directed me to Column 7. 13:02:45 17 Q. Uh-huh. 13:02:51 18 A. Repeat that part. 13:02:52 19 Q. Yeah, Column 7, lines 27 to 30, the sentence 13:02:54 20 there. 13:03:02 21 A. Yeah, I -- I, you know, reviewed the 13:03:05 22 totality of the patent. That is one indicator that 13:03:09 23 you have some evidence of effectiveness, loss of 15 13:03:11 24 letters or more. I would implore you to read the 13:03:17 25 next sentence. It also -- in certain embodiments, 13:03:21 Page 115	1 control, characteristics of the patient population 13:04:49 2 of the base studies with the active control. It is 13:04:52 3 appropriate to use the historical studies to 13:04:54 4 estimate the effect of the active control in the 13:04:56 5 non-inferiority study. 13:05:00 6 And we point you to the FDA guidance of 13:05:00 7 that. 13:05:03 8 And I say: Thus, Regeneron's VIEW trials 13:05:04 9 used less than loss of -- loss of less than 15 13:05:10 10 letters on ETDRS visual acuity as a primary 13:05:11 11 endpoint because Genentech's primary endpoint in 13:05:14 12 its pivotal trials of Lucentis, that's what we were 13:05:19 13 required to compare against. 13:05:21 14 I go on in paragraph 83 to state that the 13:05:22 15 results of VIEW are set forth in the patent, and 13:05:27 16 the POSA would have -- based on review of the 13:05:32 17 clinical trial data, the POSA would have understood 13:05:37 18 that the VEGF Trap-Eye was non-inferior to standard 13:05:40 19 of care of Lucentis, based on both the proportion 13:05:44 20 of patients achieving the primary endpoint. But 13:05:46 21 more importantly, by that time, the secondary 13:05:49 22 endpoint data that showed mean visual acuity gains 13:05:51 23 and consistency without losing those gains in the 13:05:55 24 VEGF Trap-Eye dosing in Lucentis arms. 13:06:00 25 The POSA would not have considered the '681 13:06:03 Page 117

30 (Pages 114 - 117)

1 patent specifications to suggest that it was enough 13:06:05 2 for some subjects to achieve the primary endpoint 13:06:07 3 of loss -- of less than 15 letters on ETDRS 13:06:10 4 corrected visual acuity, for its VEGF Trap-Eye to 13:06:15 5 demonstrate that it was non-inferior to standard of 13:06:18 6 care Lucentis. 13:06:22 7 Q. Can you slow down while you're reading for 13:06:22 8 the court reporter? Or are you done? 13:06:24 9 A. I'm not. 13:06:25 10 Q. Okay. 13:06:25 11 A. In addition, by 2011, the average retina 13:06:26 12 specialist would have thought that simply achieving 13:06:30 13 loss of 15 letters in a patient would not be 13:06:32 14 ineffective -- he wouldn't have thought it was 13:06:36 15 effective. 13:06:37 16 If so, PTD, which, in ANCHOR, met that 13:06:37 17 criteria in 60 percent of the patients, wouldn't 13:06:43 18 have gone out of business, essentially. The sham 13:06:44 19 arm of many of our trials had less than 15 letters 13:06:47 20 loss. 13:06:50 21 So, I disagree that -- I -- I agree with my 13:06:51 22 contention in page 15 that the POSA would not view 13:06:55 23 that loss of less than 15 letters best corrected 13:07:02 24 would be an effective treatment. 13:07:06 25 Q. The claims of the '681 patent are in the 13:07:07 Page 118	1 Q. Okay. Do you understand that there are 13:08:25 2 embodiments in the '681 patent? 13:08:29 3 A. I see the wording. 13:08:38 4 Q. Okay. Do you have an opinion, sitting here, 13:08:39 5 about which embodiments -- for which embodiments 13:08:41 6 efficacy means a gain of one or more letters? 13:08:44 7 MS. STRUTHERS: Objection; beyond 13:08:49 8 the scope. 13:08:49 9 A. Yeah, I -- when we're looking at 13:08:49 10 effectiveness of an anti-angiogenic eye disorder, 13:08:56 11 we reset the bar with ANCHOR/MARINA, where we 13:08:58 12 expect vision gains, with maintenance of those 13:09:04 13 gains, without fluctuation. 13:09:07 14 We actually saw that in AMD, DME, with 13:09:08 15 RISE/RIDE and BRAVO/CRUISE, as of the date this 13:09:11 16 patent was effective, or the date that we're 13:09:17 17 supposed to look at. 13:09:22 18 Q. (BY MR. SUMMERS) Right. But which 13:09:23 19 embodiments in the patent -- for which embodiments 13:09:24 20 in the patent is efficacy defined as a gain of one 13:09:27 21 or more letters on the ETDRS chart from the time of 13:09:30 22 initiation of treatment? 13:09:35 23 MS. STRUTHERS: Objection; beyond 13:09:35 24 the scope and mischaracterizes the testimony. 13:09:45 25 A. I'm answering the question in the context of 13:09:46 Page 120
1 context of methods for treating the angiogenic eye 13:07:11 2 disorders, correct? 13:07:14 3 A. One more time. Where are we? The claims? 13:07:17 4 Q. The claims of the '681 patent, they're in 13:07:18 5 the context of treating -- methods of treating 13:07:21 6 angiogenic eye disorders, right? 13:07:28 7 A. That is correct. 13:07:29 8 Q. Okay. And let me -- you referred me there 13:07:29 9 to that sentence, starting in Column 7, lines 31 to 13:07:35 10 34, that says: In certain embodiments, efficacy 13:07:40 11 means a gain of one or more -- and it has a list of 13:07:45 12 letters on the ETDRS chart, from the time of 13:07:48 13 initiation of treatment. 13:07:52 14 Which embodiments in the patent mean a gain 13:07:55 15 of which number of letters on the ETDRS chart from 13:07:59 16 the time of initiation of treatment? 13:08:03 17 MS. STRUTHERS: Objection to form. 13:08:05 18 A. Give me the question one more time. 13:08:05 19 Q. (BY MR. SUMMERS) Yeah, it says: In certain 13:08:10 20 embodiments, efficacy means a gain of one or more, 13:08:11 21 e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or more, 13:08:15 22 letters in the ETDRS chart, from the time of 13:08:20 23 initiation of treatment. 13:08:23 24 Do you see that? 13:08:23 25 A. I see that. 13:08:24 Page 119	1 whether the POSA would have viewed loss of 15 13:09:58 2 letters on ETDRS best corrected visual acuity as an 13:10:01 3 effective treatment. 13:10:05 4 I don't think they would consider that an 13:10:06 5 effective treatment for any angiogenic eye 13:10:08 6 disorder. 13:10:12 7 Q. (BY MR. SUMMERS) No. I'm -- I'm just 13:10:12 8 trying to ask you something much more specific, 13:10:15 9 which is, have you not formed an opinion about 13:10:19 10 which embodiments in the patent require efficacy, a 13:10:22 11 gain of one or more letters, rather than a loss of 13:10:28 12 15? 13:10:32 13 MS. STRUTHERS: Objection; beyond 13:10:33 14 the scope. 13:10:34 15 A. I don't make an opinion on which embodiments 13:10:34 16 in the patent do in my declaration, and I'm not 13:10:38 17 prepared to do so today. 13:10:42 18 Q. (BY MR. SUMMERS) Okay. Efficacy here, in 13:10:48 19 the section of Column 7 that we've been looking at, 13:10:55 20 is defined solely by loss or gain of letters on the 13:10:59 21 ETDRS chart, right? 13:11:04 22 MS. STRUTHERS: Objection; document 13:11:09 23 speaks for itself. 13:11:09 24 A. From the initiation of treatment, the 13:11:10 25 patient exhibits -- yes. 13:11:22 Page 121

31 (Pages 118 - 121)

1 Q. (BY MR. SUMMERS) Okay. When you evaluated 13:11:24 2 efficacy for the reasonable expectation of success, 13:11:25 3 you looked at more than just visual acuity gains 13:11:30 4 and losses, correct? 13:11:33 5 MS. STRUTHERS: Objection to form. 13:11:37 6 A. In reasonable expectations of success, as it 13:11:37 7 regards whether the CLEAR-IT study would inform the 13:11:44 8 Q8-week aflibercept after three loading doses would 13:11:51 9 be successful? Yes, we looked at the entire 13:11:53 10 totality of the CLEAR-IT data, including anatomic 13:11:56 11 and functional end points. 13:12:02 12 Q. (BY MR. SUMMERS) Okay. That includes OCT 13:12:04 13 and hemorrhage? 13:12:06 14 A. Correct. 13:12:06 15 Q. Let me take you to paragraph 46 of your 13:12:07 16 declaration. 13:12:25 17 A. 4-6? 13:12:27 18 Q. 46. It's on page 18. Again, this is 13:12:29 19 exhibit -- 13:12:31 20 A. Okay. 13:12:31 21 Q. -- 2055. 13:12:32 22 And just the last sentence there: However, 13:12:34 23 Dr. Chaum fails to acknowledge that before VIEW 1 13:12:43 24 and VIEW 2, no anti-VEGF clinical trials examining 13:12:47 25 extending dosing regimens demonstrated efficacy on 13:12:52 Page 122	1 Q. (BY MR. SUMMERS) Yeah, yeah. If I took the 13:14:18 2 visual acuity -- the average visual acuity gains 13:14:22 3 for the population in ANCHOR and MARINA and I 13:14:24 4 looked at other anti-VEGF clinical trials, I would 13:14:33 5 see individuals who received, from an extended 13:14:38 6 dosing regimen, efficacy on par with the fixed 13:14:42 7 monthly dosing of ANCHOR and MARINA? 13:14:45 8 MS. STRUTHERS: Objection; calls for 13:14:48 9 speculation, incomplete hypothetical. 13:14:49 10 A. You're going to have to run the trial. So, 13:14:51 11 love running trials. You'd have to run the trial. 13:14:54 12 Q. (BY MR. SUMMERS) Sure. People -- people 13:14:58 13 had run -- and you recount them here -- multiple 13:15:00 14 anti-VEGF clinical trials examining extended 13:15:04 15 dosing, right? 13:15:09 16 A. Correct. 13:15:10 17 Q. And if I looked at the results for those 13:15:10 18 trials, I would see individuals who did, in fact, 13:15:12 19 get efficacy on par with fixed monthly dosing, 13:15:15 20 right? 13:15:18 21 MS. STRUTHERS: Objection; calls for 13:15:19 22 speculation, incomplete hypothetical. 13:15:19 23 A. Which trial do you want to talk about? 13:15:21 24 Q. (BY MR. SUMMERS) Choose one. PRONTO, PIER. 13:15:26 25 MS. STRUTHERS: Is there a question 13:15:34 Page 124
1 par with fixed monthly dosing. 13:12:55 2 When you made that statement, you're talking 13:12:58 3 across the population, correct? 13:13:03 4 MS. STRUTHERS: I'm sorry. It's -- 13:13:05 5 it's hard to hear you when the fan is on. Sorry. 13:13:06 6 MR. SUMMERS: Oh, thanks, Abby. No. 13:13:08 7 That's helpful. 13:13:11 8 Q. (BY MR. SUMMERS) So in that sentence that I 13:13:13 9 just read, you're referring to clinical trials 13:13:15 10 demonstrating efficacy on par with fixed monthly 13:13:17 11 dosing across the population that was studied for 13:13:20 12 those trials, correct? 13:13:22 13 MS. STRUTHERS: Objection to form. 13:13:26 14 A. So clinical trials, by definition, are 13:13:26 15 cohorts of individuals in a population. 13:13:37 16 Q. (BY MR. SUMMERS) If I took the average 13:13:42 17 population gains that you referred to, for 13:13:55 18 instance, in ANCHOR and MARINA, though, I could 13:13:57 19 find individual patients for whom extended dosing 13:14:01 20 regimens did demonstrate efficacy on par with fixed 13:14:04 21 monthly dosing, prior to VIEW 1 and VIEW 2, 13:14:07 22 correct? 13:14:14 23 MS. STRUTHERS: Objection to form. 13:14:15 24 A. One more time. So the population -- repeat 13:14:16 25 the question. I'm sorry. 13:14:18 Page 123	1 pending? 13:15:36 2 MR. SUMMERS: Yeah, he asked which 13:15:36 3 one -- (unintelligible.) 13:15:37 4 A. So in each one of those, PIER, we talked 13:15:38 5 about it before. Sure, there are patients that did 13:15:41 6 okay on quarterly dosing. 13:15:43 7 You know, to tell if they were truly on par, 13:15:46 8 you would have to examine each individual patient, 13:15:50 9 or at least know the data of each individual 13:15:52 10 patient, to see could they have done better with 13:15:54 11 less than -- with more than quarterly dosing. They 13:15:56 12 might have got 15 letters, but could we have done 13:15:59 13 20 or 25. You -- you can't tell. 13:16:01 14 On -- as a -- as a whole, though, as I state 13:16:04 15 multiple times in the declaration -- let me get 13:16:09 16 here. 13:16:15 17 (The witness peruses the document.) 13:16:43 18 A. I'm a graphic kind of guy. And so, go to 13:19:30 19 page 69. It's not reproduced here well, but it's 13:19:33 20 easy to see them if you squint your eyes and can't 13:19:36 21 really read it. That these are the results of the 13:19:38 22 ranibizumab clinical trial results, going from 13:19:44 23 monthly, to PRN, to quarterly. 13:19:45 24 And you see the only things that gain vision 13:19:47 25 and maintain are ANCHOR and MARINA. EXCITE got 13:19:50 Page 125

1 close with a super tight PRN, but starts to fade 13:19:55 2 off at the end. 13:19:59 3 PrONTO got close, with an even tighter PRN, 13:20:01 4 with 24 visits. But every attempt we had before 13:20:04 5 the VIEW trials failed to get the average patient 13:20:10 6 to mimic what we did with MARINA and ANCHOR, with 13:20:15 7 monthly anti-VEGF therapy. 13:20:21 8 As an individual, you can only hope to be 13:20:22 9 equal to the average in one of these trials, where 13:20:26 10 you would have done phenomenally. 13:20:28 11 Are there patients that do better or worse? 13:20:30 12 Sure. Our population is a bell curve. When you 13:20:32 13 treat an individual patient, you inform it based on 13:20:37 14 the results of our clinical trial results, and your 13:20:40 15 clinical examination and judgment of what's best 13:20:45 16 for the patient. 13:20:47 17 THE WITNESS: There's on 13:21:03 18 air-conditioner again. We'll speak up. Or heater, 13:21:05 19 I don't know what it is. 13:21:08 20 Q. (BY MR. SUMMERS) There were individual 13:21:12 21 patients across -- let's take PrONTO, that, at the 13:21:25 22 end of the extended dosing regimen, the trial, 13:21:32 23 gained more than five letters of visual acuity, 13:21:38 24 right? 13:21:41 25 A. Correct. 13:21:42 Page 126	1 However, the PrONTO study in no way 13:23:08 2 decreased the burden of monthly treatment. Rather, 13:23:14 3 it required patients to be seen much more 13:23:16 4 frequently than once a month. The author of the 13:23:18 5 second paper, Alani, says it was designed to 13:23:20 6 minimize the number of re-treatments, but not the 13:23:24 7 number of visits. 13:23:25 8 Even so, patients to visit -- developed 13:23:26 9 vision-threatening complications during PrONTO. 13:23:30 10 Post hoc analysis from PrONTO show that PRN 13:23:35 11 treatment with ranibizumab was not as effective as 13:23:37 12 monthly treatment; and worse yet, led to 13:23:39 13 significant and irreversible vision complications. 13:23:41 14 Quote, when treating patients on an "as 13:23:45 15 needed" basis with either anti-VEGF monotherapy or 13:23:48 16 combination approaches, we observed a subset of 13:23:52 17 patients who experienced recurrent exudation with 13:23:53 18 submacular hemorrhage shortly after a stable eye 13:23:56 19 examine in which the stratus OCT did not detect 13:23:59 20 fluid. 13:24:02 21 It goes on to say, it -- what I'm saying is, 13:24:02 22 in each individual patient, there are patients that 13:24:05 23 did well, but even in the PrONTO manuscripts, they 13:24:08 24 discuss it's not the best way to treat, and they 13:24:12 25 had patients with big complications even after they 13:24:15 Page 128
1 Q. And I believe you report that in the MARINA 13:21:46 2 and ANCHOR trials, that four to five letters is 13:21:52 3 essentially the average across that population for 13:21:56 4 monthly dosing of Lucentis, correct? 13:22:02 5 A. ANCHOR was eight to ten. 13:22:05 6 Q. MARINA was? 13:22:06 7 A. Five-ish. 13:22:09 8 Q. Five-ish. But there were patients cross 13:22:10 9 PrONTO that gained eight to ten letters, at the end 13:22:15 10 of that treatment, correct? 13:22:18 11 MS. STRUTHERS: Objection to form. 13:22:21 12 A. Repeat the question. 13:22:26 13 Q. (BY MR. SUMMERS) There were patients in the 13:22:26 14 PrONTO study that gained eight to ten letters, at 13:22:28 15 the end of the trial, correct? 13:22:33 16 A. Absolutely. PrONTO was a 40-patient, 13:22:41 17 open-label, single center, non-randomized trial. 13:22:44 18 In other words, you don't have a control arm. Very 13:22:48 19 handpicked by my colleague, Phil Rosenfeld, the 13:22:50 20 patients that could come a bunch. 13:22:53 21 They came 24 times, with dilated clinical 13:22:55 22 visits with OCT testing and photography in the 13:22:58 23 first 12 months. And there were patients that had 13:23:01 24 improved visual acuity. On average, most patients 13:23:05 25 did well. 13:23:07 Page 127	1 got gains. 13:24:18 2 Q. And can -- can you just point me to where 13:24:18 3 you were reading from? 13:24:20 4 A. Sorry. That is from page 28, paragraph 64. 13:24:21 5 Q. Thank you. Okay. 13:24:24 6 You said they were -- the patients were 13:24:26 7 handpicked. What do you mean? 13:24:28 8 A. It's not a randomized control trial. It's 13:24:29 9 an investigator-sponsored trial, where, as in 13:24:36 10 having run a lot of investigator-sponsored trials, 13:24:40 11 you're really looking for patients that can be as 13:24:45 12 compliant with your protocol as possible. 13:24:53 13 Very few patients can come 24 times a year 13:24:57 14 for dilated exams. That's what I mean by that. 13:25:00 15 Q. Okay. So those patients were handpicked 13:25:03 16 for -- 13:25:07 17 A. By Dr. Rosenfeld. 13:25:07 18 Q. -- by Dr. Rosenfeld, for -- 13:25:08 19 A. Yeah. 13:25:09 20 Q. -- compliance with the protocol? 13:25:09 21 A. Correct. 13:25:11 22 Q. Okay. 13:25:11 23 A. And they did well, on average, but high 13:25:15 24 treatment burden. 13:25:20 25 Q. Sure. Let me ask you a -- I know I'm 13:25:22 Page 129

1 bouncing around a little bit. Yeah, let me -- let 13:25:34 2 me move on. 13:25:40 3 Let me ask you about the statement you make 13:25:40 4 on page 38 of your declaration. 13:25:43 5 A. I'm sorry. What page? 13:25:48 6 Q. Page 38. Yeah, sorry, that's loud. 13:25:49 7 Paragraph 79, but it's right at the end. 13:25:52 8 And in this paragraph, you're talking about 13:25:54 9 the hierarchal ranking and the conditional sequence 13:25:59 10 of the VIEW 1 and VIEW 2 trials. 13:26:04 11 And then right at the end, you -- you say -- 13:26:07 12 you refer to Regeneron's size and financial 13:26:09 13 condition at the time of the VIEW 1 and VIEW 2 13:26:11 14 trials. 13:26:14 15 Do you see that, in the last sentence? 13:26:14 16 A. Correct. 13:26:16 17 Q. Okay. What do you mean? 13:26:16 18 A. Regeneron was a predominantly neurology 13:26:25 19 company, that had been developing therapies for 13:26:29 20 quite some time. It had, I think, one approved 13:26:34 21 drug for an orphan disease at the time. 13:26:37 22 Phase 3 trials require a lot of money. If 13:26:43 23 you don't have the money to run the trial, you 13:26:46 24 can't prove if your drug works. 13:26:47 25 They had to sell the worldwide rights 13:26:49 Page 130	1 I can quote you to Dixon, which you've referenced 13:29:01 2 multiple times. And in paragraph 113 of my 13:29:03 3 declaration, I state: If VEGF Trap-Eye's adoption 13:29:05 4 in the clinical practice will depend on the 13:29:09 5 efficacy in four and eight-week intervals. 13:29:12 6 And he states: If effective at four-week 13:29:15 7 intervals only, VEGF Trap-Eye will be adopted into 13:29:17 8 clinical practice if it offers a competitive price 13:29:21 9 advantage over ranibizumab. 13:29:25 10 So the drug was worth a lot more, if -- if 13:29:26 11 it was approved. And to get it approved, you had 13:29:29 12 to prove that it was either equal at four weeks or 13:29:31 13 potentially equal at eight weeks. But if you 13:29:37 14 didn't run all four arms, you didn't have both 13:29:39 15 shots on goal. 13:29:42 16 Q. Let me -- well, let me start you here. 13:29:49 17 Let me take you to paragraph, now, 84 of 13:30:01 18 your declaration. It's on page 42. 13:30:06 19 A. 84. I'm there. 13:30:13 20 Q. Okay. At the end of 84, you're referring to 13:30:14 21 the approval of Eylea for the treatment regimen 13:30:18 22 we're discussing. You say: This represented a 13:30:26 23 major breakthrough in the treatment of wet AMD, and 13:30:29 24 the first approved treatment that permitted regular 13:30:32 25 fixed dosing at eight-week intervals. 13:30:35 Page 132
1 outside of the U.S. to Bayer, in order to fund this 13:26:54 2 trial. 13:26:59 3 So you wouldn't give away the worldwide 13:26:59 4 rights to a drug if you could fund it yourself. 13:27:02 5 That's what I mean by that. 13:27:05 6 Q. Okay. I understand you to say in this 13:27:05 7 paragraph that they would have just run the third 13:27:10 8 arm of the trial, if they had confidence that it 13:27:15 9 would work because of their financial condition. 13:27:17 10 Is that right? 13:27:20 11 A. I think that would have been the most 13:27:20 12 financially prudent thing to do. 13:27:25 13 Q. You certainly look at it the other way, 13:27:28 14 right? That they had enough confidence that they 13:27:36 15 thought it was worth selling the worldwide rights 13:27:40 16 so that they could run this portion of the trial? 13:27:43 17 MS. STRUTHERS: Objection to form. 13:27:48 18 A. Repeat the question. 13:27:51 19 Q. (BY MR. SUMMERS) You could certainly look 13:27:53 20 at it the other way, right? That they -- they had 13:27:54 21 enough confidence in the third arm of the VIEW 1 13:27:57 22 and VIEW 2 trials that they thought it was worth 13:28:03 23 selling the worldwide rights to get the funding, 13:28:04 24 right? 13:28:07 25 A. So I'm not an expert on drug economics, but 13:28:58 Page 131	1 Do you see that? 13:30:39 2 Lucentis, when it was approved in 2006, was 13:30:42 3 approved for treatment at regular fixed intervals, 13:30:45 4 but at 12 weeks, correct? 13:30:51 5 MS. STRUTHERS: Objection; form. 13:30:59 6 (The witness peruses the document.) 13:31:09 7 MS. STRUTHERS: Do you want to check 13:31:21 8 your question, Counsel? I'm not sure it's right. 13:31:21 9 Q. (BY MR. SUMMERS) Okay. Let me -- let's do 13:31:23 10 it much more easily, actually. Let me hand you 13:31:25 11 what's been marked as Exhibit 2212. 13:31:29 12 MS. STRUTHERS: Thank you. 13:31:32 13 A. Perfect. 13:31:34 14 Q. (BY MR. SUMMERS) This is what's identified 13:31:34 15 in your report as a Lucentis drug label from 2006. 13:31:36 16 And you can see, under dosage and 13:31:43 17 administration, it says: Although less effective, 13:31:46 18 treatment may be reduced to one injection every 13:31:49 19 three months after the first four injections, if 13:31:51 20 monthly injections are not feasible. 13:31:55 21 Let me know when you see that. 13:31:56 22 A. Where are we? In the label? What page? 13:32:16 23 Q. On -- on Exhibit 2212. 13:32:18 24 A. Yep. 13:32:21 25 Q. On the first page there, under dosage and 13:32:21 Page 133

1 administration, it says: Although less effective, 13:32:25 2 treatment may be reduced to one injection every 13:32:29 3 three months after the first four injections, if 13:32:31 4 monthly injections are not feasible. 13:32:35 5 A. I see that. 13:32:42 6 Q. Okay. So, Lucentis was the first approved 13:32:42 7 treatment that permitted regular fixed dosing at 13:32:46 8 12-week intervals, correct? 13:32:50 9 A. So, in the PIER trial, we actually crossed 13:32:59 10 patients over -- rolled -- rolled patients over to 13:33:05 11 monthly therapy when we found the results of the 13:33:09 12 one-year data, because we thought it was unethical 13:33:11 13 to maintain that dosing interval. 13:33:17 14 I state in paragraph 58: These currents 13:33:19 15 were also reflected in the FDA's label when 13:33:21 16 Lucentis was approved. The label explains, 13:33:24 17 although less effective, treatment may be reduced 13:33:26 18 to one injection every three months during -- after 13:33:28 19 the first four injections, if monthly injections 13:33:30 20 are not feasible. 13:33:33 21 Compared to continued monthly dosing, dosing 13:33:33 22 every five months will lead to an approximate 13:33:37 23 five-letter one line of visual acuity benefit -- 13:33:39 24 loss of visual acuity benefit on average over the 13:33:43 25 following nine months. 13:33:45 Page 134	1 treat a wet AMD patient on a Q12 maintenance dosing 13:35:01 2 regimen of ranibizumab or would view such a dosing 13:35:05 3 regimen as acceptable treatment for an angiogenic 13:35:13 4 eye disorder. 13:35:13 5 Q. Okay. Can you clarify where you were 13:35:13 6 reading from again? 13:35:15 7 A. Sure. That is paragraphs -- paragraphs 58 13:35:15 8 through 60, pages 24 through 26. 13:35:22 9 Q. Okay. Let me repeat my question, because 13:35:26 10 you didn't answer it, which is, Lucentis was 13:35:29 11 approved for the treatment of wet AMD on a regular 13:35:33 12 fixed dosing schedule at 12-week intervals, right? 13:35:40 13 MS. STRUTHERS: Objection; asked and 13:35:46 14 answered. 13:35:51 15 A. Repeat the question. 13:35:51 16 Q. (BY MR. SUMMERS) Lucentis was approved for 13:35:52 17 the treatment of wet AMD on regular fixed dosing at 13:35:57 18 12-week intervals, correct? 13:36:10 19 MS. STRUTHERS: Objection; asked and 13:36:11 20 answered. 13:36:12 21 A. It's in the label with the caveat, if 13:36:22 22 monthly injections are not feasible. 13:36:35 23 Q. (BY MR. SUMMERS) Okay. Stepping back to 13:36:37 24 January of 2011. Did you extend dosing in your 13:36:59 25 practice with your individual patients? 13:37:05 Page 136
1 Patient should be evaluated regularly. 13:33:45 2 I go on in 59: It is my understanding that 13:33:48 3 the FDA would present a comprehensive look at the 13:33:51 4 clinical data submitted when issuing approval 13:33:55 5 guidelines. And indeed, the clinical study section 13:33:59 6 of the Lucentis label plainly shows the drastic 13:34:00 7 disparity between the study results from ANCHOR and 13:34:03 8 MARINA and those of PIER. 13:34:06 9 Figure 1 shows that Lucentis .5 arm had a 13:34:07 10 mean acuity gain of 6.6 letters at 24 months. The 13:34:11 11 .5 arm in Study 2 had an 11.3 mean change at 24 13:34:15 12 months. While Figure 2 shows the Lucentis .5 arm, 13:34:19 13 in Study 3 PIER had a mean loss of visual acuity of 13:34:24 14 0.2 letters at 12 months. 13:34:28 15 The import of these figures should be clear 13:34:30 16 to the POSA. Fixed quarterly dosing of PIER 13:34:33 17 carries a high risk for permanent vision loss. 13:34:38 18 It is my opinion, FDA is reviewing 13:34:40 19 consideration of the PIER results, and this 13:34:42 20 language in the label would not suggest to a person 13:34:44 21 of ordinary skill that quarterly maintenance dose 13:34:48 22 was an effective or acceptable option for a patient 23 with an angiogenic eye disorder, such as wet AMD. 13:34:54 24 Indeed, I am not aware of any doctor who, 13:34:57 25 after the results of PIER were published, would 13:34:59 Page 135	1 A. Repeat the question. And which -- 13:37:08 2 Q. Yes. Stepping back to 2011, let's say 13:37:15 3 January 2011. 13:37:18 4 A. Okay. 13:37:18 5 Q. Time of the patent. 13:37:19 6 Did you practice extended dosing with any of 13:37:20 7 your patients at the time? 13:37:23 8 A. Page 49, paragraph 105 of my declaration: 13:37:25 9 In fact, before 2011 and in 2011, the retina 13:37:46 10 community was hopeful that we could extend dosing 13:37:50 11 of Lucentis and Avastin to every eight weeks, but 13:37:52 12 we found that every eight-week dosing with Lucentis 13:37:55 13 and Avastin was not effective. 13:37:58 14 We observed that most patients needed 13:37:59 15 injections every four to five weeks, in order to 13:38:04 16 maintain a dry retina. It was therefore clear, 13:38:06 17 before 2011 and into 2011, that every eight-week 13:38:09 18 dosing with Lucentis or Avastin did not achieve 13:38:14 19 results that were comparable to those achieved with 13:38:18 20 monthly dosing of Lucentis and Avastin. 13:38:20 21 Q. I'm -- I'm not clear if you answered my 13:38:28 22 question or not. Did -- did you practice extended 13:38:29 23 dosing in your practice in January 2011? 13:38:34 24 THE REPORTER: I'm sorry. I 13:38:34 25 couldn't hear. 13:38:36 Page 137

35 (Pages 134 - 137)

1 Q. (BY MR. SUMMERS) Did you practice, 13:38:37 2 Dr. Brown, extended dosing in your practice as of 13:38:37 3 2011? 13:38:43 4 MS. STRUTHERS: Asked and answered. 13:38:45 5 A. Yeah, I'm part of the retina community. 13:38:47 6 Certainly a leader in the retina community. So 13:38:51 7 same thing. I was hopeful that we could extend 13:38:52 8 dosing of Lucentis and Avastin to every eight 13:38:55 9 weeks. We found that every eight-week dosing of 13:38:58 10 Lucentis and Avastin was ineffective. We observed 13:39:00 11 that most patients needed injections every four to 13:39:04 12 five weeks in order to maintain a dry retina. 13:39:06 13 Q. (BY MR. SUMMERS) Okay. So again, stepping 13:39:08 14 back into 2011, did you always give monthly dosing 13:39:09 15 of Lucentis or Avastin to your patients? 13:39:19 16 A. It depends on individual patients. Every 13:39:22 17 patient started with monthly dosing of anti-VEGF. 13:39:26 18 Q. Okay. Did you practice what's known as 13:39:29 19 treat and extend as of January 2011? 13:39:31 20 A. So myself, like lots of others in the retina 13:39:32 21 community, were looking for ways to determine how 13:39:47 22 frequent patients would need dosing. 13:39:49 23 Treat and extend is a misnomer. It's a way 13:39:51 24 of finding a fixed dose that the patient can 13:39:56 25 tolerate. 13:39:59 Page 138	1 Q. Yeah, I was just going to say, I want, in 13:59:06 2 this case, to take you to page 55. And this is 13:59:08 3 where you discuss more specifically the results of 13:59:18 4 the CLEAR-IT 2 trial. 13:59:24 5 A. Yep. 13:59:25 6 Q. What was the CLEAR-IT 2 trial? 13:59:26 7 A. So, I introduce CLEAR-IT 2 in 73, 13:59:29 8 paragraph 73 on page 34. The CLEAR-IT 2 study was 13:59:48 9 the Phase 2 trial. And it was designed to compare 13:59:52 10 the effects of VEGF Trap-Eye administered in doses 13:59:53 11 of 0.5 milligrams or 2 milligrams every four weeks; 13:59:57 12 in other words, on Day 1 or zero and then week 4, 14:00:05 13 8, 12. So they got four total doses, or a single 14:00:08 14 dose at -- at -- of .5, 2 milligrams, or 14:00:12 15 4 milligrams, given at Day 1, and then it's another 14:00:17 16 dose at week 12. 14:00:20 17 So the primary endpoint of that was the 14:00:22 18 12-week paper, 2011 Brown publication there, 14:00:25 19 Exhibit 2296. And then it extended for a year with 14:00:30 20 PRN dosing, with where you -- it wasn't PRN 14:00:33 21 exactly, like we'd do in the clinic, but was 14:00:36 22 pre-specified criteria. And that continued -- 14:00:39 23 began at week 16, continued through week 52. 14:00:41 24 In Exhibit 2297, Jeff Heier -- I think I'm 14:00:45 25 the second author of that paper. I'm not sure. 14:00:49 Page 140
1 We often had patients that could not have 13:39:59 2 monthly dosing for the rest of their life. As a 13:40:06 3 compromise, we would extend the interval after they 13:40:11 4 were dry, and try to find an interval, fixed dosing 13:40:16 5 interval, with which we could maintain their 13:40:21 6 disease activity to the best of our ability. 13:40:24 7 With -- with Avastin, it was rare that you 13:40:26 8 could go beyond four or five weeks. With Lucentis, 13:40:30 9 it was rare that you could go much beyond that. 13:40:35 10 The average patient, however, with Eylea, 13:40:40 11 was three doses, and then Q8 was the fixed dosing 13:40:43 12 interval which you came upon. 13:40:51 13 MR. SUMMERS: Let me -- we've been 13:40:54 14 going for an hour, and I've lost my connection to 13:40:55 15 realtime. So if we could take a break. 13:41:01 16 THE VIDEOGRAPHER: Off the record at 13:41:03 17 1:40 p.m. 13:41:04 18 (Break.) 13:42:40 19 THE VIDEOGRAPHER: Back on the 13:48:22 20 record at 1:58 p.m. 13:58:44 21 Q. (BY MR. SUMMERS) Dr. Brown, welcome back. 13:58:46 22 You can -- if you can turn again to your 13:58:55 23 reasonable expectation of success opinion. I want, 13:58:59 24 in this case, to -- 13:59:05 25 A. Page what? 13:59:05 Page 139	1 But that's the one-year data of this Phase 2 trial. 14:00:50 2 Q. And what was your role in the CLEAR-IT 2 14:00:53 3 trial? 14:01:21 4 A. Yeah, my role was, one, an investigator, 14:01:21 5 principal investigator, of the Houston site. But 14:01:23 6 also, before we really had a steering committee, 14:01:27 7 but among several doctors who helped interpret the 14:01:30 8 trial, publish the trial, and make comments on the 14:01:36 9 trial. 14:01:42 10 Q. I'm going to hand you -- you referenced 14:01:42 11 Exhibit 2296, so let me start there. 14:02:03 12 A. 2296. 14:02:10 13 Q. This is a document that's been previously 14:02:12 14 marked as Exhibit 2296. 14:02:19 15 A. Yep. Thank you. Sorry about that. I 14:02:21 16 didn't mean to grab you. 14:02:23 17 Q. No. That's all right. And it has the 14:02:24 18 title, Primary Endpoint Results Phase 3 Study of 14:02:26 19 Vascular Endothelial Growth Factor Trap-Eye in Wet 14:02:33 20 Age-Related Macular Degeneration. 14:02:38 21 Are you familiar with this document, 14:02:44 22 Dr. Brown? 14:02:46 23 A. I am. 14:02:46 24 Q. And what is this document? 14:02:46 25 A. I'm sorry? 14:02:56 Page 141

1 Q. And what is this document? 14:02:57 2 A. This document is the publication in what 14:02:58 3 have we call The Blue Journal, which is the Journal 14:03:04 4 of Ophthalmology, the Journal of the American 14:03:07 5 Academy of Ophthalmology, in 2011. 14:03:09 6 And if you look at the footnotes and 14:03:11 7 disclosures, it had been previously presented at 14:03:14 8 Retina Society in 2009, and AAO in 2009, and couple 14:03:19 9 other meetings that year, and in 2010, before we 14:03:23 10 ever got around to publishing it in 2011. So... 14:03:26 11 Q. Okay. And you're the -- if I look on the 14:03:29 12 first page here, you're the first named author? 14:03:33 13 A. That is correct. 14:03:34 14 Q. Okay. Let me turn you, first of all, to 14:03:35 15 page 1095 of this document. 14:03:43 16 A. 1095. I'm there. 14:03:49 17 Q. And go ahead and read the second full 14:03:50 18 paragraph there, starting with, In the Phase 1 14:03:52 19 study, an extended duration of efficacy at 12 weeks 14:03:56 20 is noted in three six patients -- 14:04:00 21 A. I'm sorry. 1095, first para -- 14:04:03 22 Q. The first full paragraph. So -- 14:04:03 23 A. Of the right column or left column? 14:04:05 24 Q. Right column. Thank you. Sorry. 14:04:06 25 A. Okay. 14:04:08 Page 142	1 of this exhibit: Notably, a single 2-mg dose 14:05:31 2 achieved an improvement in visual acuity that was 14:05:37 3 similar to that achieved with a 2-mg dose monthly 14:05:40 4 out to eight weeks, raising the possibility that 14:05:44 5 dosing with 2 mgs every eight weeks may be as 14:05:49 6 effective as monthly dosing. 14:05:52 7 Do you see that? 14:05:54 8 A. I see that. 14:05:55 9 Q. Okay. Why was it that you concluded that a 14:05:55 10 single 2-mg dose achieving an improvement of visual 14:06:02 11 acuity, being similar to that achieved with a 2-mg 14:06:09 12 dose monthly out to eight weeks raised the 14:06:13 13 possibility that dosing with 2 mgs every eight 14:06:17 14 weeks may be as effective as the monthly dose? 14:06:24 15 A. Yeah, that -- that statement is based on 14:06:26 16 Figure 3, bravo, B, where the visual acuity is in a 14:07:47 17 small sample, 32 patients per -- were roughly the 14:07:55 18 same amongst all of them, except for the -- it 14:08:01 19 looked, you know -- it's probably within 14:08:04 20 statistical means, but the .5Q4 was above it, and 14:08:07 21 for whatever reason, the .5Q12 was -- the .5Q12 was 14:08:11 22 below, looking like -- like the .5 was dropping out 14:08:18 23 on visual acuity. But the other arms were pretty 14:08:21 24 close to each other. 14:08:23 25 Q. So you were -- and I just want to be more 14:08:24 Page 144
1 Q. Do you see what I'm -- where I'm referring 14:04:08 2 you in the Phase 1 study and extended duration. 14:04:11 3 A. Yep, yep, yep. 14:04:19 4 Q. Okay. 14:04:20 5 (The witness peruses the document.) 14:04:21 6 A. I see it. 14:04:32 7 Q. (BY MR. SUMMERS) Okay. So in evaluating 14:04:33 8 reasonable expectation of success, you reviewed 14:04:36 9 Exhibit 2296, correct? 14:04:46 10 MS. STRUTHERS: Objection; 14:04:48 11 mischaracterizes the testimony. 14:04:50 12 A. So I reviewed the totality of the data of 14:04:50 13 the VEGF Trap-Eye, which this embodies most of 14:04:58 14 that. 14:05:06 15 Q. (BY MR. SUMMERS) Yeah. And I -- I just 14:05:07 16 sort -- counsel's objections got me off a little 14:05:08 17 bit. 14:05:11 18 But if you look on page 115 of your 14:05:11 19 declaration, you specifically cite Exhibit 2296 as 14:05:16 20 part of your -- 14:05:21 21 A. Yeah, yeah. 14:05:22 22 Q. Okay. 14:05:22 23 -- opinion as to reasonable expectation of 14:05:23 24 success. 14:05:28 25 And you say here, in the final full sentence 14:05:28 Page 143	1 specific. You're looking at Figure 3, you said 14:08:31 2 Figure 3B, as in bravo? 14:08:33 3 A. Yeah. 14:08:35 4 Q. Okay. And Figure 3B is looking at the mean 14:08:35 5 change from baseline BCVA. 14:08:44 6 A. Correct. 14:08:46 7 Q. Okay. Let -- let me ask you a question. 14:08:47 8 A lot of these numbers that get reported on 14:08:49 9 the letters, like 8.8, 8.3, in general, when you're 14:08:51 10 evaluating a patient, do they come up with anything 14:08:57 11 other than multiples of 5 on the ETDRS charts -- 14:09:01 12 A. Not -- 14:09:07 13 MS. STRUTHERS: Well, hold on. Let 14:09:08 14 him finish his question. 14:09:09 15 Q. (BY MR. SUMMERS) Yeah. Go ahead. That -- 14:09:11 16 that's my question. 14:09:12 17 MS. STRUTHERS: Okay. I'm sorry. 14:09:13 18 Could you repeat the question? I got it confused. 14:09:13 19 Q. (BY MR. SUMMERS) Sure. Generally, when 14:09:16 20 you're evaluating a patient on the -- the ETDRS 14:09:18 21 letters chart, do they come up in multiples of 5 14:09:21 22 that they've gained or lost, a line in total? 14:09:26 23 MS. STRUTHERS: Objection to form. 14:09:30 24 A. Yeah, I -- I can answer it. Because the 14:09:31 25 ETDRS eye chart is a unique beast and has five 14:09:38 Page 145

37 (Pages 142 - 145)

1 letters on every line, and they just get bigger as 14:09:41 2 you go up. 14:09:44 3 Q. (BY MR. SUMMERS) Right. And so, it would 14:09:44 4 be unusual for a patient to actually gain eight 14:09:45 5 letters or -- 14:09:49 6 A. They can gain eight letters. It means -- 14:09:50 7 MS. STRUTHERS: Hold on. Just let 14:09:52 8 him finish his question. Thank you. 14:09:53 9 A. Sorry. 14:09:55 10 Q. (BY MR. SUMMERS) That was my question, 14:09:55 11 again. Go -- go ahead. 14:09:56 12 A. So, if you gain eight letters, you gain a 14:09:58 13 whole line, five letters, plus three letters on the 14:10:00 14 next line. 14:10:02 15 Q. Okay. Is it -- I'm just genuinely trying to 14:10:03 16 understand. Is it common for a patient to gain 14:10:07 17 only part of a line on the ETDRS charts? 14:10:08 18 A. In clinical trials or -- sure. You can gain 14:10:14 19 two letters, three letters, 15 letters. 14:10:19 20 Q. Are they the same size on the -- on each 14:10:23 21 line? The five letters on the line are all the 14:10:25 22 same size, though, right? 14:10:27 23 A. Five letters on the line are the same size. 14:10:28 24 Q. Okay. So if I start, you know, at the top 14:10:31 25 line, those letters are all the same, and then the 14:10:33 Page 146	1 the same lenses in front of each patient. What's 14:11:33 2 better? This or this? This or this? 14:11:36 3 Every time you come, so that you're at the 14:11:39 4 best possible. And that's why it's called best 14:11:43 5 refracted ETDRS. That's the name of the eye chart 14:11:47 6 invented for the early treatment for diabetic 14:11:50 7 retinopathy study, vision. 14:11:56 8 And that's one way of remaining constancy 14:11:57 9 between my eye chart in Houston and another 14:12:00 10 investigator is in New Orleans and another 14:12:04 11 investigator is in Minneapolis. We all have the 14:12:05 12 same chart and the same way of checking the vision, 14:12:07 13 with the same illumination measurements, with -- 14:12:11 14 like, they measure the amount of illumination and 14:12:14 15 everything is controlled and checked. 14:12:17 16 And that's one way that you can -- that's 14:12:18 17 one reason in clinical trial, it's so much more 14:12:20 18 regimented than real life. 14:12:23 19 Q. Thank you. Yeah, that's helpful. 14:12:24 20 So, let me bring it back here, then, to my 14:12:33 21 original question. 14:12:35 22 Looking at Exhibit 2296, and I think we're 14:12:36 23 on page 1093, looking at Figure 3B. This is the 14:12:39 24 data that you were looking at when you made the 14:12:45 25 statement over on 1095 that a single 2-mg dose 14:12:48 Page 148
1 next line -- 14:10:36 2 A. (Witness nods head.) 14:10:37 3 Q. Okay. It just seemed -- genuinely, it just 14:10:37 4 seems odd that someone might have an eight-letter 14:10:43 5 gain and stop in the middle of the line, rather 14:10:45 6 than going to the next line. 14:10:47 7 A. It means that -- 14:10:48 8 Q. That's why I'm asking. 14:10:48 9 Yeah, go ahead. 14:10:50 10 MS. STRUTHERS: Go ahead. 14:10:51 11 A. When you go to the eye doctor and they give 14:10:52 12 you a line, and you tell them five things, you -- 14:10:54 13 it means you missed two, right. It doesn't mean 14:10:58 14 that you got the first three and not the last two, 14:11:00 15 it means of the five, you were wrong on two of 14:11:03 16 them. 14:11:05 17 Q. (BY MR. SUMMERS) I see. So, in general, 14:11:05 18 it's sort of reflects where it's getting to the 14:11:07 19 border of their visual acuity. 14:11:11 20 Is that right? 14:11:12 21 A. So in a clinical trial, you do what's called 14:11:13 22 a protocol refraction, which is very artificial. 14:11:18 23 But you have a refractionist who has no idea, 14:11:24 24 typically, what trial you're in, typically whether 14:11:28 25 you're control arm or treatment arm, that's putting 14:11:30 Page 147	1 achieved an improvement in visual acuity that was 14:12:54 2 similar to the 2-mg dose monthly out to eight 14:12:57 3 weeks? 14:13:02 4 A. What the sentence reads is more what I felt. 14:13:02 5 It raised the possibility that dosing with 14:13:07 6 2 milligrams every eight weeks may be as effective. 14:13:10 7 That's a pretty doggy, possibly raising the 14:13:12 8 possibility may be as effective. 14:13:15 9 Q. Okay. 14:13:16 10 A. So... 14:13:17 11 Q. But you were -- when you made the statement, 14:13:17 12 you were specifically looking at data from the 14:13:19 13 trial and -- 14:13:21 14 A. Correct. 14:13:22 15 Q. -- specifically 3B. 14:13:23 16 Okay. And that's not an unreasonable thing 14:13:26 17 for you to have done, I presume, or you wouldn't 14:13:28 18 have put it here to have looked at 3B, and then -- 14:13:32 19 and then made this statement. 14:13:34 20 MS. STRUTHERS: Objection to form. 14:13:35 21 Is there a question pending, 14:14:40 22 Counsel? 14:14:42 23 A. Oh, I'm sorry. Is there a question? 14:14:42 24 Q. (BY MR. SUMMERS) Oh, I thought -- 14:14:43 25 A. I got a little lost. 14:14:44 Page 149

1 Q. That's all right. That's okay. Let's move 14:14:45 2 on. 14:14:46 3 A. If there was a question, I'm happy to answer 14:14:48 4 it. I just didn't -- I missed it. 14:14:50 5 Q. There -- there was. My -- my question, I 14:14:52 6 think, was really straightforward, which is you 14:14:54 7 didn't view it as unreasonable at the time to make 14:14:58 8 the statement that you did in Exhibit 2297 based on 14:15:01 9 Figure 3B, correct? 14:15:05 10 MS. STRUTHERS: Objection to form. 14:15:08 11 A. Yeah, so, in a Phase 2 trial, or especially 14:15:08 12 a Phase 1 trial, but in a Phase 2 trial, such as 14:16:01 13 CLEAR-IT like we're discussing, the -- we really 14:16:06 14 pay more attention to the anatomic end points, in 14:16:10 15 other words, the OCT, than the visual acuity, 14:16:14 16 because it's really easy in the smaller trial for 14:16:17 17 the mean visual acuity to be affected by one or two 14:16:19 18 patients that do really good or really poorly, 14:16:22 19 right. 14:16:24 20 The mean OCT, or the individual OCTs, are 14:16:25 21 more of an indication of is your drug achieving a 14:16:30 22 therapeutic effect and when does it wear off. 14:16:33 23 So as I state in 116: The results from 14:16:37 24 CLEAR-IT 2 show that the therapeutic effect of VEGF 14:16:42 25 Trap-Eye had begun to wear off between week 4 and 14:16:45 Page 150	1 where it's easier to see, Figure 2, in 14:18:03 2 Exhibit 2296, there's reaccumulation of fluid 14:18:06 3 between week 4 and week 8 in the quarterly dosing 14:18:10 4 arms, curves for arms 0.5Q2, 2Q12, and 4Q12, trend 14:18:13 5 upwards, which continues through week 12. 14:18:22 6 In fact, the only treatment arms that were 14:18:24 7 successful at sustaining effective treatment were 14:18:27 8 the monthly dosing arms, that is, 0.5Q4 and 14:18:29 9 2-milligrams Q4. 14:18:35 10 In addition, the CR2 data at week 16 shows 14:18:36 11 that the study subjects who received monthly 14:18:41 12 loading doses continue to experience reductions in 14:18:42 13 CRT, with the fourth monthly loading dose 14:18:46 14 corresponding to further drying of the retina. 14:18:49 15 So... 14:18:51 16 Q. Where you were reading from there? 14:18:51 17 A. I'm reading from page 56 and 57, 14:18:52 18 paragraphs 116 -- paragraph 116. 14:18:59 19 Q. In your declaration, correct? 14:19:02 20 A. Yes, declaration. Yeah. 14:19:04 21 Q. Let me bring you back to figures -- the 14:19:05 22 Figures 2 and 3 in Exhibit 2296. 14:19:09 23 A. Okay. 14:19:14 24 Q. Is it the case -- I think this is something 14:19:14 25 you're saying, that -- that OCT outcomes in 14:19:18 Page 152
1 week 8. 14:16:50 2 And I direct you to the table -- the figure 14:16:51 3 right next to it, Figure 2, where you see that 14:16:53 4 the -- it starts at zero, and minus 50, minus 100. 14:16:55 5 This is Figure 2 in the Brown, et al, Exhibit 2296. 14:16:58 6 Q. Yeah. 14:17:03 7 A. You see that with every dose, the OCT 14:17:04 8 improves, the -- the retina gets thinner, because 14:17:08 9 you're getting rid of edema. And then by week 8, 14:17:12 10 it continues to get thinner in both the arms that 14:17:17 11 you give another dose at week 4. 14:17:20 12 But all the other arms tip up. In other 14:17:21 13 words, they bounce up with resolution of edema, 14:17:25 14 meaning that the average patient was not controlled 14:17:29 15 and was not continuing to improve on monthly 14:17:36 16 therapy. 14:17:39 17 So I go on to say: A decrease in central 14:17:39 18 retinal thickness corresponds to drying of the 14:17:43 19 macula and the fluid that is created by the 14:17:46 20 angiogenic process of wet AMD. In contrast, an 14:17:47 21 increase in CRT, central retinal thickness, 14:17:49 22 corresponds to fluid reaccumulation on the retina 14:17:56 23 and indicates a need for retreatment. 14:17:57 24 As shown in the slide below and in the -- 14:18:00 25 probably better shown in the figure right there, 14:18:02 Page 151	1 Figure 2, they don't correlate directly with the 14:19:23 2 mean change from baseline BCVA in Figure 3, 14:19:29 3 correct? 14:19:37 4 In other words, you -- you see, to your 14:19:37 5 point, that you lose some of the thinning, in some 14:19:41 6 of these groups, but that's not necessarily 14:19:47 7 reflected in the change in visual -- visual acuity 14:19:51 8 in Figure 3, correct? 14:19:52 9 MS. STRUTHERS: Objection to form. 14:19:53 10 A. Visual acuity is a lagging indicator. In 14:20:07 11 other words, you have to improve the anatomy before 14:20:10 12 you can get better function or visual acuity. 14:20:14 13 Once you get better vision or function and 14:20:17 14 you start to get recurrent edema, you often don't 14:20:22 15 lose vision immediately, but you -- if that is 14:20:27 16 maintained, then you lose visual acuity. 14:20:30 17 So, that's one of the reasons in a Phase 2 14:20:33 18 or smaller study, we really look more at the 14:20:36 19 anatomic to see if a drug works, as opposed to the 14:20:41 20 visual acuity. The visual acuity is confirmatory 14:20:44 21 that you're doing something right, but the OCT 14:20:47 22 findings often precede visual acuity changes. 14:20:54 23 Q. (BY MR. SUMMERS) Okay. Looking at 14:20:58 24 Figure 2, let's -- let's take Figure 2, where you 14:21:00 25 said you saw the loss of that thinning between the 14:21:03 Page 153

1 initial dose. 14:21:10	1 of Exhibit 2297, and specifically Figure 3B. Let 14:24:09
2 So let me just -- to be clear on how we're 14:21:11	2 me know when -- when you're there. 14:24:18
3 looking at the figure together here, for the 2Q12 14:21:13	3 A. Yep. 14:24:19
4 group, for instance, there's a dose at zero, 14:21:20	4 Q. This chart is essentially a continuation of 14:24:25
5 correct? 14:21:26	5 the chart 2B that we were just looking at in 14:24:28
6 A. Correct. 14:21:26	6 Exhibit 2296, correct? 14:24:31
7 Q. And then another dose at 12. 14:21:26	7 MS. STRUTHERS: Objection to form. 14:24:33
8 Is that right? 14:21:30	8 A. So Figure 3B is what happened to the cohort 14:24:33
9 A. That's correct. 14:21:30	9 of patients described in Figure 2B, in Brown, et 14:24:51
10 Q. Okay. And in between, there is not a dose 14:21:34	10 al, after they were switched to a different dosing 14:24:57
11 for that group at weeks 4 or 8 or anywhere else in 14:21:39	11 regimen where they had to have some visual -- they 14:25:01
12 between. 14:21:42	12 had to have criteria for retreatment. 14:25:05
13 A. That's correct. 14:21:43	13 In other words, they weren't given fixed 14:25:10
14 Q. Okay. And thinking back to the dosing 14:21:48	14 dosing. They were -- had -- had mandated criteria, 14:25:13
15 regimen that we looked at in Dixon, with three 14:21:50	15 which you gave a dose if you met that criteria. 14:25:15
16 initial loading doses, for comparison, you would 14:21:53	16 Q. (BY MR. SUMMERS) Okay. And that's that PRN 14:25:17
17 have there a dose at 0, 4, and 8, but then the next 14:21:57	17 dosing that you referred to, with certain objective 14:25:18
18 dose would come at week 16, right? 14:22:06	18 criteria that distinguished it from normal, kind of 14:25:22
19 A. That is correct. 14:22:09	19 in your practice PRN dosing, right? 14:25:25
20 Q. Okay. Let's flip over to Exhibit 2297, if 14:22:14	20 A. Yep, PRN therapy. But it's PRN, not just at 14:25:27
21 you still have that. 14:22:32	21 the physician's whim, but page 1100 tells you the 14:25:35
22 A. Which one is that? 14:22:33	22 retreatment criteria during the fixed dosing phase, 14:25:55
23 Q. Did I give that to you yet? 14:22:34	23 end of first column. 14:25:59
24 MS. STRUTHERS: I don't think so. 14:22:36	24 Retreatment criteria, during the fixed 14:26:00
25 A. It's that Heier paper? 14:22:38	25 dosing phase, one eye was designated as the study 14:26:04
Page 154	Page 156
1 Q. (BY MR. SUMMERS) I didn't. Thank you. Let 14:22:39	1 eye. Beginning at week 16, patients were evaluated 14:26:06
2 me give that to you. 14:22:41	2 every four weeks to determine the need for 14:26:08
3 It is -- this is the Heier paper you 14:22:42	3 continued dosing. The study eye was reinjected 14:26:10
4 referred to earlier. This is Exhibit 2297. 14:22:48	4 with VEGF Trap-Eye. If any of following changes 14:26:14
5 MS. STRUTHERS: Thank you.	5 were observed, an increase in central retinal 14:26:18
6 Q. (BY MR. SUMMERS) I know the heater just 14:23:07	6 CR/LT -- greater than a hundred microns, as 14:26:23
7 kicked on. 14:23:08	7 measured by OCT; a loss of -- greater than or equal 14:26:25
8 The title is The One-Year Results of 14:23:08	8 to 5 letters on conjunction with recurrent fluid; 14:26:29
9 CLEAR-IT 2, a Phase 2 Study of Vascular Endothelial 14:23:14	9 or persistent fluid, as indicated by OCT, new onset 14:26:35
10 Growth Factor Trap-Eye Dosed As Needed After 14:23:19	10 classic neovascularization; new or persistent leak 14:26:42
11 12-Week Fixed Dosing. 14:23:22	11 on fluorescein angiography or new macular image. 14:26:45
12 Do I have that right? 14:23:25	12 Those were the retreatment criteria mandated PRN. 14:26:48
13 A. Yes. 14:23:27	13 Q. Uh-huh. So, I want to refer you now to 14:26:55
14 Q. Okay. And you're listed as an author here. 14:23:27	14 page 1104, which has a portion of the discussion 14:27:00
15 In this case, you're the -- the last listed author. 14:23:30	15 section of Exhibit 2297. Let me know when you're 14:27:06
16 A. Yep. 14:23:32	16 there. 14:27:10
17 Q. Okay. What is this doc -- what is this 14:23:32	17 A. I'm here. 14:27:10
18 document, Dr. Brown? 14:23:37	18 Q. Okay. So in the -- in the first paragraph 14:27:12
19 A. This is the one-year results after -- or the 14:23:38	19 here, it's reported that for all groups combined, 14:27:19
20 secondary end point results after the primary end 14:23:48	20 there is a clinically significant improvement in 14:27:23
21 points, which were in the first paper, Brown, et 14:23:52	21 visual acuity at 12 weeks, that was maintained to 14:27:26
22 al, of the exact same study, which was published 14:23:54	22 52 weeks, correct? 14:27:29
23 sequentially with this study in -- in the Blue 14:23:57	23 MS. STRUTHERS: Objection; document 14:27:32
24 Journal in Ophthalmology in 2011. 14:24:01	24 speaks for itself. 14:27:33
25 Q. Okay. And if I go to Figure 3 on page 1101, 14:24:05	25 A. One more time. Where are we in this -- 14:27:34
Page 155	Page 157

40 (Pages 154 - 157)

1 Q. (BY MR. SUMMERS) Yeah. In the discussion 14:27:37 2 section, just the second -- second sentence there. 14:27:38 3 A. Second sentence of the discussion. Here we 14:27:40 4 go. 5 (Witness reads document to self.) 14:27:43 6 A. Okay. I see. 14:27:52 7 Q. (BY MR. SUMMERS) So this is reporting, at 14:27:53 8 least for all groups combined, there was both a 14:27:54 9 clinically significant improvement at 12 weeks and 14:27:57 10 that was maintained out to 52 weeks during the 14:28:02 11 duration of the PRN dosing portion of the treatment 14:28:07 12 regimen, right? 14:28:12 13 MS. STRUTHERS: Objection; the 14:28:13 14 document speaks for itself. 14:28:13 15 A. That's what it says. 14:28:14 16 Q. (BY MR. SUMMERS) Okay. And then it goes 14:28:16 17 on, on the rightmost column, in the first full 14:28:18 18 paragraph there, to discuss what the 52-week 14:28:21 19 results of CLEAR-IT 2 study suggests, correct? 14:28:25 20 A. Where is that? 14:28:30 21 Q. Rightmost column, on page 1104 -- 14:28:31 22 A. Okay. Yeah, yeah. 14:28:35 23 Q. -- the first full paragraph. Let's start 14:28:36 24 there. And go ahead and read that. 14:28:39 25 (The witness peruses the document.) 14:28:49 Page 158	1 which - which you're a coauthor, correct? 14:30:37 2 A. Correct. 14:30:38 3 Q. Okay. And it goes on, in fact, to say, 14:30:39 4 based on the binding affinity and estimated half 14:30:42 5 life in humans, that it's predicted that it will 14:30:44 6 maintain its biological activity for 10 to 12 14:30:49 7 weeks, whereas ranibizumab would maintain such 14:30:53 8 activity for 30 days, right? 14:30:57 9 MS. STRUTHERS: Objection; document 14:30:59 10 speaks for itself. 14:30:59 11 A. That's what it says. 14:31:00 12 Q. (BY MR. SUMMERS) Okay. And just to be 14:31:02 13 clear, you reported this data as part of your 14:31:09 14 discussion around CLEAR-IT 2. 14:31:12 15 What was the reason for including it here? 14:31:17 16 MS. STRUTHERS: Objection; beyond 14:31:19 17 the scope, and objection to form. 14:31:26 18 A. So, discussions are exactly that, 14:31:34 19 discussions. They're hypothesizing why something 14:31:36 20 may be occurring or why it may be reasonable to 14:31:38 21 test this molecule in further trials. 14:31:47 22 It doesn't change the fact that, in your 14:31:50 23 fixed dosing -- or not your fixed dosing, in your 14:31:59 24 interval in that -- the only time we really tested 14:32:01 25 it head to head -- in PRN, everybody is getting 14:32:03 Page 160
1 A. Okay. I read it. 14:28:50 2 Q. (BY MR. SUMMERS) Okay. And this discusses 14:29:07 3 some particular characteristics of the affinity and 14:29:10 4 half-life of VEGF Trap-Eye, correct? 14:29:14 5 MS. STRUTHERS: Objection; document 14:29:18 6 speaks for itself. 14:29:19 7 A. Yep, talks about binding affinity of VEGF 14:29:21 8 Trap-Eye. 14:29:28 9 Q. (BY MR. SUMMERS) And what was known about 14:29:28 10 the binding affinity of VEGF Trap-Eye, as of 2011? 14:29:29 11 MS. STRUTHERS: Objection; beyond 14:29:35 12 the scope. 14:29:39 13 A. Very little, if anything, was known about 14:29:39 14 the intravitreal half-life in humans. 14:30:01 15 The binding affinity data came from the 14:30:05 16 manufacturer, and every drug company thinks their 14:30:10 17 drug has the greatest binding affinity, and the 14:30:13 18 longest half-life. 14:30:15 19 Part of that is you can test it at different 14:30:18 20 temperatures or pH's. And so, comparative binding 14:30:22 21 ability, I'm not sure we exactly knew. Certainly 14:30:26 22 Regeneron reported that it had a higher binding 14:30:31 23 affinity. 14:30:34 24 Q. (BY MR. SUMMERS) Okay. And -- and that 14:30:34 25 was, in fact, then repeated in this document, in 14:30:34 Page 159	1 different doses at different times. You don't know 14:32:06 2 when they're getting a dose. And you can't see 14:32:09 3 that from this paper. 14:32:11 4 But the only time that doses were mandated 14:32:11 5 was that first 12 weeks. And again, I take more 14:32:14 6 credence, as do most clinician scientists, looking 14:32:18 7 at this, at that OCT data, which is where -- where, 14:32:23 8 when discussing with Regeneron, and then in my 14:32:30 9 declaration, I didn't think that Q8-week dosing had 14:32:32 10 a high probability of success. I was skeptical 14:32:41 11 that it would be successful in a comparative head 14:32:45 12 to head with ranibizumab monthly dosing. 14:32:49 13 Q. (BY MR. SUMMERS) Okay. But in your paper, 14:32:53 14 in 2011 -- and we can go back to Exhibit 2296 -- 14:32:55 15 where you're the lead author, you looked at that 14:33:03 16 same OCT data and, in fact, suggested that it 14:33:06 17 raised the possibility that dosing with 2-mgs every 14:33:11 18 eight weeks may be as effective as monthly dosing, 14:33:17 19 right? 20 MS. STRUTHERS: Objection; 14:33:19 21 mischaracterizes the testimony, document speaks for 14:33:20 22 itself. 14:33:21 23 A. Yeah, I said -- I didn't say that at all. I 14:33:22 24 said that the visual acuity data, not the OCT data, 14:33:24 25 raised the possibility that it may be as effective. 14:33:30 Page 161

41 (Pages 158 - 161)

1 Again, I said it from the visual acuity 14:33:59 2 data, which is a lagging indicator. I did not 14:34:02 3 comment on the change in OCT in this discussion. 14:34:04 4 Q. (BY MR. SUMMERS) Right. But the visual 14:34:09 5 acuity is a lagging indicator of the anatomical 14:34:10 6 indicators, correct? 14:34:14 7 A. That's what I said, correct. 14:34:15 8 Q. Okay. So, to the extent the visual acuity 14:34:16 9 indicator here gave you a basis to believe that 14:34:19 10 eight-week dosing would be as effective as monthly 14:34:26 11 dosing -- 14:34:29 12 MS. STRUTHERS: Objection. 14:34:29 13 Q. (BY MR. SUMMERS) -- it would have to -- 14:34:30 14 MS. STRUTHERS: Sorry. 14:34:31 15 A. Raise the possibility that it might be as -- 14:34:34 16 may be effective, is all I can say, till we ran the 14:34:37 17 trial. 14:34:41 18 Q. (BY MR. SUMMERS) Okay. And that's what you 14:34:41 19 said in 2011, before you submitted this 14:34:41 20 declaration. And let's look a little bit more 14:34:44 21 about what -- what you said here in 2011, looking 14:34:47 22 at this data. 14:34:50 23 So, at the bottom of the second full 14:34:51 24 paragraph here, in -- and I'm going to refer you 14:34:54 25 back to Exhibit 2297, there's a discussion of the 14:34:56 Page 162	1 then they really drift when you go to PRN therapy. 14:37:47 2 You didn't see quite as much drift in the other 14:37:51 3 groups, but you started at a low -- a lot lower 14:37:53 4 bar. 14:37:56 5 So, you know, PRN, I think, which has been 14:37:56 6 abandoned by most of us by 2011, is not effective 14:38:01 7 therapy. Certainly hurt, like the 2Q -- the 2Q12 14:38:04 8 went down a bit. They had a dose right -- who 14:38:10 9 knows when the dosing was. 14:38:12 10 So, it's -- in any Phase 2, where you're 14:38:14 11 changing things, and have no control arm, it's 14:38:18 12 really tough to make a comparison. But I agree the 14:38:21 13 paragraph says what it says on page 1104. 14:38:25 14 Q. (BY MR. SUMMERS) And let's -- let's -- I 14:38:34 15 don't know how long we've been going, by the way. 14:38:37 16 If we're getting to a break, and I want to dive 14:38:38 17 into this a little bit more. So just let me know. 14:38:42 18 A. We can keep going. You probably need to 14:38:44 19 leave by 5:20, if you've got a 7:40. Houston 14:38:47 20 traffic 5:00 to 6:00 is a -- not pleasant. 21 Q. We'll figure that out. 22 A. On I-45 or 59. 14:38:53 23 Q. So -- okay. So let's look at this a little 14:38:53 24 more specifically, this conclusion in this 14:38:57 25 paragraph. 14:38:59 Page 164
1 significant improvement in visual acuity from 14:35:08 2 baseline that was maintained to week 52. 14:35:09 3 A. So we're on 2297. Which column? 14:35:12 4 Q. The rightmost column, thank you, second full 14:35:14 5 paragraph. 14:35:18 6 A. Second full paragraph. Okay. 14:35:18 7 Q. Go ahead. I -- I didn't give you an 14:35:20 8 opportunity read that again. So please go ahead 14:35:21 9 and read that. 14:35:23 10 (The witness peruses the document.) 14:35:30 11 A. Okay. I've read it. 14:35:48 12 Q. (BY MR. SUMMERS) So looking at that visual 14:35:49 13 acuity data, the conclusion here was that what was 14:35:51 14 missing from the quarterly injections was 14:35:54 15 potentially initial sequential monthly doses, which 14:35:59 16 could be then followed by less frequent dosing, 14:36:04 17 right? 14:36:07 18 MS. STRUTHERS: Objection; document 14:36:08 19 speaks for itself. 14:36:09 20 (The witness peruses the document.) 14:37:22 21 A. Well, it says that it's a bit of a challenge 14:37:27 22 to interpret, because you sort of changed treatment 14:37:34 23 modalities. 14:37:38 24 If you look at Figure 5B, yes, your 14:37:38 25 monthlies ended up with a higher level at 12, but 14:37:43 Page 163	1 So, it says: Patients randomized to monthly 14:38:59 2 injections had a trend towards improved visual 14:39:03 3 acuity outcomes at 52 weeks, compared to those 14:39:06 4 randomized to quarterly injections. 14:39:09 5 And again, you referred here to Figure 5B, 14:39:11 6 for the data that's being discussed. 14:39:14 7 The point here being that the patients who 14:39:16 8 received fixed initial monthly doses up to week 12 14:39:20 9 had improved visual acuity outcomes at the end of 14:39:30 10 52 weeks, compared to those that just got it 14:39:33 11 quarterly. 14:39:36 12 Is that right? 14:39:36 13 MS. STRUTHERS: Objection; document 14:39:37 14 speaks for itself. 14:39:38 15 A. Again, small numbers, change in treatments, 14:39:49 16 you know, when -- don't know when they got treated, 14:39:51 17 but the .5Q4 marginally above -- 5.4 letters 14:39:53 18 marginally above the 5.2. Certainly no statistical 14:39:59 19 significance. 14:40:02 20 Q. (BY MR. SUMMERS) The -- 14:40:03 21 A. Trend. That's why it says trend. 14:40:04 22 Q. Right. The -- the -- the suggestion being, 14:40:05 23 though, that you could potentially close the gap 14:40:09 24 here, by using fixed monthly doses, at least for 14:40:11 25 those first three doses, as was done for that group 14:40:17 Page 165

42 (Pages 162 - 165)

1 that had the better visual acuity outcome, right? 14:40:21	1 document are you in now? 14:43:45
2 MS. STRUTHERS: Objection; 14:40:24	2 MR. SUMMERS: Still in 2297. 14:43:46
3 mischaracterizes the document, mischaracterizes the 14:40:25	3 MS. STRUTHERS: Okay. And -- and 14:43:48
4 testimony. 14:40:27	4 which paragraph? 14:43:49
5 A. It's one interpretation of the data. 14:40:27	5 Q. (BY MR. SUMMERS) Looking -- looking at the 14:43:50
6 Certainly, we have good experience from a very 14:40:37	6 discussion that we've been looking at, regarding 14:43:51
7 large anti-VEGF trial, PIER, again, with the 14:40:42	7 whether less frequent dosing was possible, based on 14:43:54
8 different agent. But three monthly doses didn't 14:40:47	8 the results, there's no discussion of the OCT data 14:43:58
9 seem to be the secret sauce. 14:40:50	9 in Figure 3 B, right? 14:44:03
10 Q. (BY MR. SUMMERS) Just to be clear, though, 14:40:52	10 MS. STRUTHERS: Are you referring to 14:44:08
11 it's the interpretation of the data that you 14:41:10	11 page 1104? 14:44:09
12 offered in 2011. 14:41:11	12 Q. (BY MR. SUMMERS) Referring to page 1104, 14:44:13
13 MS. STRUTHERS: Objection; 14:41:15	13 there's a discussion here regarding, in the words 14:44:14
14 mischaracterizes the testimony, mischaracterizes 14:41:16	14 of the document, the concept of less frequent 14:44:23
15 the document. 14:41:18	15 dosing, and whether it's possible. 14:44:25
16 A. Yes. Anytime you use the word trend, that 14:41:18	16 And there's no reference to the OCT data 14:44:27
17 means it's not statistically significant. 14:41:45	17 that's reproduced in Figure 3B, correct? 14:44:34
18 This trial, as is all Phase 2 trials, are 14:41:48	18 MS. STRUTHERS: I'm sorry. Which 14:44:37
19 not powered to be statistically significant to 14:41:52	19 para -- you're -- 14:44:38
20 prove concepts. 14:41:55	20 MR. SUMMERS: Let the witness 14:44:38
21 It certainly makes statements based on the 14:41:57	21 testify. I -- 14:44:40
22 trend, but nothing that would change my opinion on 14:42:02	22 MS. STRUTHERS: I'm just -- I just 14:44:40
23 the reasonable expectation that aflibercept dosed 14:42:16	23 want to follow along. So which paragraph are you 14:44:41
24 Q8 after three doses would be non-inferior to 14:42:24	24 on? 14:44:43
25 ranibizumab dosed monthly. 14:42:30	25 MR. SUMMERS: I'm -- I'm looking at 14:44:43
Page 166	Page 168
1 This trial had four doses before it went to 14:42:30	1 the discussion that we've been looking at on 14:44:45
2 PRN therapy. The PRN therapy is nowhere -- no 14:42:34	2 page 1104. 14:44:48
3 what -- in no way, shape, or form what anyone would 14:42:40	3 MS. STRUTHERS: Third paragraph 14:44:52
4 do clinically. 14:42:44	4 down? 14:44:54
5 You know, it's a small study. It showed 14:42:46	5 MR. SUMMERS: The entire discussion 14:44:55
6 promise, and that's why Regeneron was able to move 14:42:52	6 here of whether less frequent dosing is possible. 14:44:56
7 forward with Phase 3 trials. But it is what it is. 14:42:56	7 A. I don't see where there was discussion of 14:45:12
8 Q. (BY MR. SUMMERS) Okay. And -- 14:43:05	8 the OCT. You can see at the conclusion: After the 14:45:14
9 MS. STRUTHERS: I'm sorry. Go 14:43:05	9 first year of treatment, patients in the VIEW 1 and 14:45:17
10 ahead.	10 VIEW studies will be evaluated monthly and treated 14:45:22
11 MR. SUMMERS: What were you going to	11 on a PRN basis to prevent undertreatment. The PRN 14:45:24
12 say?	12 dosing scheduled in the second year does allow the 14:45:26
13 MS. STRUTHERS: I was just going to 14:43:06	13 patients to remain untreated for greater than 12 14:45:28
14 say it would be a good time for a break when -- 14:43:08	14 weeks. So many patients in CLEAR-IT 2 study did 14:45:31
15 when you're ready. 14:43:11	15 maintain initial visual acuity gains. Design of 14:45:35
16 MR. SUMMERS: Let me -- let me do 14:43:12	16 Phase 3 programs meant to optimize visual acuity 14:45:36
17 just a little bit more. I'm not going to leave the 14:43:13	17 pretty much for all patients by using this capped 14:45:39
18 document, but I'll take a break. 14:43:14	18 PRN. These studies should provide further 14:45:41
19 Q. (BY MR. SUMMERS) Looking back to the OCT 14:43:17	19 information on the duration and extent of the 14:45:45
20 data that's reproduced in Figure 3B, in the 14:43:19	20 clinical benefit of VEGF Trap-Eye. 14:45:49
21 discussion that we've been looking at, on the 14:43:30	21 So, certainly the Phase 2 CLEAR-IT provided 14:45:51
22 interpretation of this data, as to whether less 14:43:34	22 information for the design and -- and ongoing 14:45:55
23 frequent dosing is possible, there's no discussion 14:43:38	23 Phase 3 trial. But in no way did it make me feel 14:45:58
24 of this OCT data, right? 14:43:39	24 that -- that there was a reasonable certainty that 14:46:07
25 MS. STRUTHERS: Sorry. Which 14:43:44	25 Q8-week dosing after three monthly doses, which 14:46:14
Page 167	Page 169

43 (Pages 166 - 169)

1 were not done at all in CLEAR-IT 2 or CLEAR-IT 1, 14:46:16 2 would be successful. 14:46:20 3 With the OCT data, particularly in that 14:46:22 4 first three months being particularly concerning 14:46:25 5 for the ability of the agent to be maintaining 14:46:31 6 effectiveness out to eight weeks. 14:46:34 7 Q. (BY MR. SUMMERS) Yeah, you agree, though -- 14:46:36 8 that's -- that's great, actually. Let's look at 14:46:37 9 the -- the third full paragraph down here, on 14:46:39 10 Exhibit 2297, page 1104, on the right-hand side, it 14:46:44 11 refers to the VIEW 1 and VIEW 2 studies, right? 14:46:50 12 A. Correct. 14:46:54 13 Q. And it discusses, as I think you just made 14:46:55 14 reference to, the rationale for using extended 14:47:00 15 eight-week dosing, correct? 14:47:04 16 MS. STRUTHERS: Objection; document 14:47:09 17 speaks for itself. 14:47:13 18 A. I read it, yeah. 14:47:13 19 Q. (BY MR. SUMMERS) And in your declaration, 14:47:14 20 you make quite a lot of this OCT data that's over 14:47:15 21 in Figure 3B on page 1101. But there's no 14:47:19 22 suggestion here that that data raised a doubt as to 14:47:24 23 the success of that Phase 3 study that was ongoing, 14:47:30 24 in VIEW 2 trial, right? 14:47:33 25 MS. STRUTHERS: Objection; document 14:47:35 Page 170	1 of Exhibit 2296, and in Figure 5, bravo, and 14:49:20 2 Exhibit 2297, there is re-accumulation of fluid 14:49:31 3 between week 4 and week 8 in any of the quarterly 14:49:35 4 dosing arms; in fact, the only treatment arms that 14:49:41 5 were successful in the monthly dosing arms, and in 14:49:44 6 sustaining effective OCT dryness. 14:49:47 7 And then you see the patients who achieved 14:49:53 8 monthly loading continued to experience reductions 14:49:56 9 in center retinal thickness with the fourth monthly 14:50:00 10 dose. 14:50:03 11 And based on that, I state the POSA would 14:50:03 12 have understood that fluid -- fluid re-accumulation 14:50:06 13 between week 4 and 8, on CRT, would strongly 14:50:08 14 suggest the VEGF Trap-Eye would not be effective on 14:50:12 15 an eight-week dosing interval. 14:50:15 16 Similarly understood the visual acuity 14:50:16 17 decrease at week 8 in some of the arms suggest it 14:50:19 18 may wane. Although, like I've talked about before, 14:50:22 19 the POSAs would look at the totality of the data 14:50:26 20 and wouldn't just read the discussion. They would 14:50:28 21 look at the OCT graphs that were published and 14:50:29 22 presented multiple times. 14:50:33 23 Q. Great. But contemporaneously, you and your 14:50:34 24 co-authors didn't think it was worth commenting on 14:50:37 25 the OCT data that you say strongly suggests that 14:50:40 Page 172
1 speaks for itself. 14:47:37 2 A. Repeat the question. 14:47:37 3 Q. (BY MR. SUMMERS) There's no suggestion in 14:47:38 4 this paragraph discussing VIEW 1 and VIEW 2, that 14:47:40 5 the OCT data from CLEAR-IT 2 raised some doubt 14:47:43 6 whether eight-week extended dosing would work? 14:47:49 7 MS. STRUTHERS: Same objection; 14:47:52 8 document speaks for itself. 14:47:53 9 A. I agree it's not discussed. 14:47:55 10 Q. (BY MR. SUMMERS) Okay. And that's a 14:47:59 11 primary point of discussion in your declaration 14:48:00 12 now, however, right? 14:48:03 13 A. Correct. Paragraph 116, the results on 14:48:06 14 CLEAR-IT 2 show that therapeutic effect on VEGF 14:48:49 15 Trap-Eye began to wear off between week 4 and 14:48:51 16 week 8. 14:48:54 17 The slide below is what we've been talking 14:48:55 18 about. The central retinal thickness, a decrease 14:48:56 19 in central retinal thickness, corresponds with 14:48:59 20 drying of the macula. The fluids created by the 14:49:02 21 angiogenic process for wet AMD, and contrast and 14:49:08 22 increase in the CRT responds to fluid 14:49:09 23 re-accumulation on the retina and indicates a need 14:49:12 24 for retreatment. 14:49:12 25 As shown in the slide below and in Figure 2 14:49:13 Page 171	1 VEGF Trap-Eye would not be effective on an 14:50:44 2 eight-week dosing interval here, in Exhibit 227 -- 14:50:47 3 2297? 14:50:51 4 MS. STRUTHERS: Objection to form; 14:50:51 5 mischaracterizes the document. 14:50:56 6 A. When I'm the first author on a publication, 14:50:57 7 I draft every word of the introduction and 14:51:28 8 discussion. In the paper I first authored, I 14:51:30 9 tempered the note to say that achieved -- raised 14:51:35 10 the possibility that maybe is effective. 14:51:39 11 The OCT findings didn't have space or we 14:51:42 12 didn't put it in. But it doesn't alter the fact 14:51:46 13 that the POSA would have seen the OCT findings, and 14:51:50 14 known that if you don't -- if you -- if you're not 14:51:54 15 giving a dose and you have an increase in the CRT, 14:51:59 16 the drug is waning and wearing off. 14:52:02 17 Q. (BY MR. SUMMERS) Right. That's right. And 14:52:04 18 in the publication in which you're the first named 14:52:06 19 author, Exhibit 2296, you also didn't comment on 14:52:08 20 the OCT data. 14:52:12 21 You did comment on the fact that the visual 14:52:13 22 acuity data raises the possibility that dosing with 14:52:16 23 2 mgs every eight weeks may be as effective as 14:52:20 24 monthly dosing, right? 14:52:25 25 MS. STRUTHERS: Objection; the 14:52:26 Page 173

44 (Pages 170 - 173)

1 document speaks for itself. 14:52:26 2 A. That's correct. 14:52:27 3 Q. (BY MR. SUMMERS) Okay. And that's -- even 14:52:28 4 though it's now your position that POSAs think the 14:52:29 5 OCT data is the most important data, more important 14:52:32 6 than visual acuity, right? 14:52:37 7 A. That's correct. 14:52:38 8 Q. But you didn't comment on it. 14:52:38 9 MS. STRUTHERS: Objection; asked and 14:52:40 10 answered, document speaks for itself. 14:52:40 11 A. It wasn't commented on in the discussion. 14:52:41 12 Q. (BY MR. SUMMERS) Why was that? 14:52:45 13 MS. STRUTHERS: Objection; document 14:52:51 14 speaks for itself. 14:52:53 15 A. It -- I don't exactly recall. It may be 14:52:53 16 that we had limitations to length. It's also, if 14:53:00 17 you're trying to get some -- a paper published, you 14:53:04 18 try not to diminish the potential impact. 14:53:07 19 Not that that's the only reason to -- not 14:53:16 20 that we would hide side effects. Certainly those 14:53:19 21 discussions were more, after really looking at the 14:53:25 22 data, trying to determine which arms that we could 14:53:29 23 design view with. 14:53:32 24 And that's -- that's more of the thought 14:53:34 25 process around that OCT data than when we published 14:53:40 Page 174	1 MS. STRUTHERS: Objection; 14:54:43 2 argumentative, document speaks for itself. 14:54:44 3 A. They would find it more important than 14:54:45 4 dosing interval. Then would be visual acuity. 14:54:50 5 Q. (BY MR. SUMMERS) But yet, your discussion 14:54:54 6 in both papers left out OCT and did discuss visual 14:54:56 7 acuity, didn't it? 14:55:00 8 MS. STRUTHERS: Objection; asked and 14:55:02 9 answered, documents speaks for themselves. 14:55:03 10 A. Most important thing for the patient is 14:55:05 11 visual acuity. Most important thing for 14:55:13 12 determining dosing intervals in a Phase 2 is 14:55:19 13 anatomical effectiveness and duration. 14:55:25 14 Q. (BY MR. SUMMERS) In both of these papers, 14:55:27 15 you suggested that the visual acuity gains that you 14:55:29 16 saw from CLEAR-IT 2, in fact, suggested or raised 14:55:31 17 the possibility that dosing with 2 mgs every eight 14:55:35 18 weeks may be as effective as monthly dosing, right? 14:55:39 19 MS. STRUTHERS: Objection; 14:55:42 20 mischaracterizes the testimony, mischaracterizes 14:55:43 21 the documents, and the documents speak for 14:55:45 22 themselves. 14:56:55 23 (The witness peruses the document.) 14:56:55 24 A. It was certainly very encouraging that we 14:56:55 25 got visual acuity gains in the first 12 weeks with 14:57:04 Page 176
1 this data. 14:53:42 2 Q. (BY MR. SUMMERS) So it's your testimony 14:53:43 3 that you may have had length considerations and so 14:53:44 4 you left in discussion of a less important variable 14:53:48 5 in favor of taking out the OCT data, that you now, 14:53:54 6 in 2023, say undercuts the idea that eight-week 14:53:58 7 extending dosing would work? 14:54:04 8 MS. STRUTHERS: Objection; 14:54:06 9 mischaracterizes the testimony. The witness -- go 14:54:07 10 ahead. 14:54:08 11 A. Yeah -- sorry. 14:54:08 12 MS. STRUTHERS: No. Go ahead. 14:54:09 13 A. To the patient, visual acuity is the most 14:54:09 14 important variable. Pharmacologically, if you're 14:54:12 15 trying to figure out how long a drug lasts, OCT is 14:54:15 16 a better indicator. But for us, just like 14:54:20 17 oncologists, the outcome is life and death. For 14:54:23 18 us, it's vision. 14:54:26 19 Q. (BY MR. SUMMERS) And your audience here 14:54:26 20 isn't the patient, though, right? 14:54:27 21 A. Our audience is other retinal specialists 14:54:29 22 who treat patients. 14:54:36 23 Q. Who you've testified would find the OCT data 14:54:36 24 to be more important than the visual acuity data, 14:54:39 25 right? 14:54:42 Page 175	1 CLEAR-IT, and that they were still visual acuity 14:57:08 2 gains at the end, incredibly positive. 14:57:11 3 Incredibly positive, we saw OCT improvements 14:57:13 4 that were robust. All those things are positive to 14:57:17 5 move forward to a Phase 3 trial. 14:57:21 6 The lack of catastrophic side events -- side 14:57:24 7 effects, like killed later drugs, such as 14:57:27 8 bevacizumab -- I'm sorry, such as brolicizumab, 14:57:32 9 the -- the Allergan DARPIn drug -- you know, did 14:57:36 10 not blow up eyeballs, in other words -- did not 14:57:39 11 have terrible side effects with positive visual 14:57:42 12 acuity in OCT, is what you want to see in a 14:57:47 13 Phase 2. 14:57:48 14 What you're looking for is -- is how to 14:57:49 15 design that Phase 2 to get the drug approved. And 14:57:51 16 as -- as I state in my declaration, and stand to 14:57:55 17 it, the POSA would have understood that fluid 14:57:58 18 re-accumulation between week 4 and 8, on CRT, would 14:58:01 19 strongly suggest that VEGF Trap-Eye would not be 14:58:04 20 effective on an eight-week dosing interval. 14:58:07 21 They would have understood that visual 14:58:10 22 acuity is important, that the gains were there. 14:58:11 23 But certainly in a smaller trial, you can't hang 14:58:14 24 your hat on little visual acuity gains. 14:58:17 25 Why the discussion didn't fully merit that 14:58:20 Page 177

1 in our 2011 ophthalmology papers, I can only say 14:58:25 2 what's in the papers. So... 14:58:30 3 Q. (BY MR. SUMMERS) The -- the dosing regimen 14:58:31 4 that's disclosed in Dixon would provide for an 14:58:33 5 injection at weeks 4 and 8, when you say that fluid 14:58:38 6 re-accumulation would cause concern in the OCT 14:58:44 7 data, correct? 14:58:48 8 MS. STRUTHERS: Objection; 14:58:50 9 mischaracterizes the testimony. 14:58:51 10 A. In the treatment of angiogenic eye 14:58:57 11 disorders, treatment with an anti-VEGF is repeated 14:59:03 12 at consistent intervals. Patients routinely 14:59:09 13 re-leak at those persistent intervals. 14:59:13 14 It's not like curing your staph infection, 14:59:17 15 where three doses and you're done. It's a 14:59:23 16 recurring chronic disease. 14:59:26 17 So if the dose -- if giving the doses -- and 14:59:28 18 you'll see that in -- in -- in PIER. You know, we 14:59:30 19 gave three doses, but people recurred with fluid, 14:59:34 20 even though we gave those three doses. It would 14:59:38 21 have been the expectation of me, and the POSA, that 14:59:41 22 three doses alone wouldn't have solved the problem. 14:59:45 23 Q. (BY MR. SUMMERS) You didn't see that in 14:59:47 24 CLEAR-IT 2, though, right? The conclusion that you 14:59:49 25 actually provide on page 10 -- 1104 is that, 14:59:50 Page 178	1 monthly ranibizumab. 15:00:59 2 Q. (BY MR. SUMMERS) Okay. That's not what you 15:01:01 3 said in 2011, though, right? You said initial 15:01:02 4 sequential monthly loading doses seem to provide 15:01:05 5 better control of neovascular leakage. 15:01:06 6 MS. STRUTHERS: Objection; document 15:01:09 7 speaks for itself. 15:01:10 8 A. Any document with ten authors has a lot of 15:01:10 9 compromises. 15:01:28 10 Q. (BY MR. SUMMERS) Do you have any evidence 15:01:28 11 that you stood up and said, guys, we shouldn't say 15:01:29 12 this? 15:01:33 13 A. I didn't say we shouldn't say it. It would 15:01:33 14 have been nice to have more discussion of OCT, but 15:01:37 15 I don't think it changes the importance of -- of 15:01:40 16 the Phase 2 and informing the Phase 3 results. 15:01:43 17 Q. As the lead author of Exhibit 2296, did you 15:01:46 18 have final say over the text? 15:01:51 19 A. I did. 15:01:52 20 MR. SUMMERS: Okay. Let's take a 15:02:01 21 break. 15:02:01 22 MS. STRUTHERS: Okay. 15:02:02 23 THE VIDEOGRAPHER: Off the record at 15:02:03 24 3:01 p.m. 15:02:05 25 (Break.) 15:02:06 Page 180
1 initial sequential loading doses seem to provide 14:59:54 2 better control of neovascular leakage and lead to 14:59:57 3 superior gains in visual acuity, and can then 15:00:00 4 subsequently be maintained with less frequent 15:00:02 5 dosing. 15:00:05 6 So as to VEGF Trap-Eye, which is being 15:00:05 7 studied here, your conclusion was initial 15:00:07 8 sequential monthly dosing would actually help you 15:00:11 9 get control of neovascular leakage, right? 15:00:12 10 MS. STRUTHERS: Objection; 15:00:15 11 mischaracterizes the document, document speaks for 15:00:15 12 itself. 15:00:17 13 A. Yeah, I mean, I -- I think that -- that that 15:00:17 14 sentence is very optimistic. And if you look at 15:00:20 15 the actual data of the vision, the monthly 15:00:23 16 .5-milligram arm actually gains to about nine 15:00:27 17 letters and ends up 5.4. So it lost half its gains 15:00:31 18 with that PRN, after that fixed dosing of three. 15:00:35 19 If you look at the 2-milligram, it -- you 15:00:37 20 know, the 2-milligram, it gets up to 10. It 15:00:41 21 waffles around. It gets as low as below 8. They 15:00:45 22 probably -- a bunch of them got a dose then, and it 15:00:48 23 got up to 9. 15:00:50 24 But that is not the consistent maintained 15:00:51 25 vision you see with standard of care MARINA/ANCHOR 15:00:54 Page 179	1 THE VIDEOGRAPHER: Back on the 15:17:28 2 record at 3:18 p.m. 15:19:04 3 Q. (BY MR. SUMMERS) Welcome back, Dr. Brown. 15:19:05 4 I'm going to keep us on Exhibit 2297. 15:19:09 5 Actually, before I do that, we've taken a 15:19:12 6 number of breaks today. 15:19:16 7 Have you discussed the substance of your 15:19:17 8 testimony with your counsel today, during any of 15:19:20 9 the breaks? 15:19:22 10 A. No. 15:19:22 11 Q. No. Have you reviewed any of your testimony 15:19:23 12 during the breaks? 15:19:27 13 A. I haven't. 15:19:28 14 Q. Okay. Counsel just took realtime with her. 15:19:29 15 You didn't review any of your testimony during this 15:19:34 16 last break? 15:19:36 17 A. She was doing her thing, and I was cookie. 15:19:37 18 Q. Thank you, sir. Okay. Appreciate that. 15:19:39 19 A. Checking my texts for babies and child -- 15:19:43 20 et cetera. 15:19:47 21 Q. Yes, appreciate that. 15:19:48 22 So let me refer you back again to page 1104, 15:19:50 23 on Exhibit 2297. 15:19:53 24 And I want to come back again to that 15:19:56 25 paragraph on the right-hand column, third full 15:20:02 Page 181

46 (Pages 178 - 181)

1 paragraph down, that starts, ongoing Phase 3 15:20:06 2 studies, and it refers to VIEW 1 and VIEW 2. 15:20:10 3 Just let me know when I've got you in the 15:20:13 4 right place. 15:20:16 5 A. Okay. 15:20:16 6 Q. So, it says there, in the second full 15:20:17 7 sentence: The rationale for the 2-mg Q8-week dose 15:20:21 8 was based on an observation from the fixed dosing 15:20:26 9 phase of CLEAR-IT 2. 15:20:30 10 Do you see that? 15:20:32 11 A. I do. 15:20:33 12 Q. Okay. And then it goes on, it says: At 15:20:33 13 eight weeks, the improvement in BCVA, after a 15:20:36 14 single 8-mg dose, was similar to that obtained with 15:20:40 15 2-mg dose monthly to eight weeks, and that the 15:20:44 16 effect in visual acuity gain for the single dose 15:20:48 17 groups began to wane by week 12. 15:20:52 18 Do you see that? 15:20:54 19 A. I see that. 15:20:54 20 Q. So this is explaining that the rationale for 15:20:59 21 using three initial monthly loading doses, followed 15:21:03 22 by eight-week dosing, was based on the observation 15:21:07 23 that you got similar visual acuity gains to eight 15:21:12 24 weeks, but then they began to wane by week 12, in 15:21:18 25 CLEAR-IT 2, correct? 15:21:21 Page 182	1 Q. (BY MR. SUMMERS) Okay. 15:31:41 2 A. I would expound, though, that it says the 15:31:42 3 effect wanes by week 12, is probably an 15:31:46 4 understatement. 15:31:48 5 The 4-milligram group, which should be the 15:31:49 6 strongest, tanked to 2.5 letters, which would 15:31:53 7 concern me. Otherwise, I agree with what it says. 15:31:56 8 Q. (BY MR. SUMMERS) That's a strong reason to 15:31:58 9 intervene every 8 weeks, instead of every 12, 15:32:02 10 right? 15:32:05 11 MS. STRUTHERS: Objection; document 15:32:08 12 speaks for itself, and mischaracterizes the 15:32:14 13 testimony. 15:32:15 14 A. I agree with what it says. 15:32:15 15 Q. (BY MR. SUMMERS) Okay. In paragraph 117 of 15:33:03 16 your declaration, again referring to the OCT data, 15:33:09 17 you say, this would strongly suggest that VEGF 15:33:14 18 Trap-Eye would not be effective on an Q8-week 15:33:19 19 dosing interval. 15:33:24 20 Did you ever, prior to providing 15:33:25 21 declarations for Regeneron for use in litigation, 15:33:27 22 go on record regarding the CLEAR-IT 2 OCT data 15:33:32 23 strongly suggesting that VEGF Trap-Eye would not be 15:33:39 24 effective in an Q8-week dosing interval? 15:33:43 25 A. Paragraph 121, I state: In fact, I recall 15:33:47 Page 184
1 MS. STRUTHERS: Objection; document 15:21:23 2 speaks for itself. 15:21:24 3 A. That's what it says. 15:21:24 4 Q. (BY MR. SUMMERS) Okay. And you don't 15:21:27 5 disagree with the observation that's made here in 15:21:32 6 Exhibit 2297, regarding visual acuity gains to 15:21:37 7 eight weeks? 15:21:43 8 MS. STRUTHERS: Again, objection, 15:21:45 9 document speaks for itself. 15:21:46 10 (The witness peruses the document.) 15:22:18 11 A. I'm sorry. What was the question? You got 15:31:01 12 a question? 15:31:06 13 Q. (BY MR. SUMMERS) Yeah, I do. 15:31:07 14 A. Okay. 15 Q. That was a seven-minute break you took. 15:31:09 16 I'll -- make sure you time the next here, so 15:31:12 17 if you've forgotten the question, please ask it a 15:31:16 18 little earlier. 15:31:19 19 You don't disagree with the observation 15:31:20 20 that's made in Exhibit 2297 that we've been 15:31:22 21 discussing, regarding visual acuity gains at eight 15:31:27 22 weeks, right? 15:31:33 23 MS. STRUTHERS: Objection; document 15:31:34 24 speaks for itself. 15:31:35 25 A. I don't disagree. 15:31:35 Page 183	1 discussing at the time Regeneron's Phase 3 VIEW 15:34:31 2 trials with co-investigator Jeff Heier before the 15:34:35 3 initiation of the VIEW trials. At that time, we 15:34:37 4 had only preliminary Phase 2 data from CLEAR-IT 2, 15:34:39 5 and I recall that, looking at the rise in mean 15:34:42 6 central retinal thickness, we both thought that the 15:34:45 7 VEGF Trap-Eye might last six weeks, but had great 15:34:48 8 skepticism that it would be non-inferior to 9 Lucentis on an eight-week fixed dosing regimen. 15:34:53 10 While we thought monthly dosing of VEGF 15:34:54 11 Trap-Eye would likely work (i.e., be non-inferior 15:34:58 12 to Lucentis monthly dosing), we viewed the Q8 arm 15:35:00 13 as a long shot. Indeed, as discussed above, when 15:35:05 14 Regeneron ranked its dosing regimens for 15:35:05 15 statistical reporting, it ranked the 2Q8 arm below 15:35:08 16 both the 2Q4 arm and the .5Q4 dosing arms, 15:35:13 17 indicating that Regeneron believed both Q4 dosing 15:35:16 18 arms were more likely than the Q8 arm to hit their 15:35:18 19 primary endpoints. 15:35:23 20 I state here I discussed it with Jeff Heier, 15:35:23 21 but also discussed with multiple other key opinion 15:35:25 22 leaders, including Peter Kaiser, including 15:35:28 23 Regeneron, potentially at ad boards that were 15:35:33 24 recorded. Never on the court-reported record. And 15:35:36 25 not that I know in a publication, although I'm 15:35:39 Page 185

47 (Pages 182 - 185)

1 widely cited. If you found some, let me know. 15:35:41 2 Q. Okay. So, Jeff Heier is a co-author on both 15:35:43 3 Exhibit 2296 and 2297, correct? 15:35:48 4 A. Correct. 15:35:53 5 Q. In fact, he's the lead author of 15:35:54 6 Exhibit 2297, while you're the lead author of 15:35:57 7 Exhibit 2296, correct? 15:36:00 8 A. Correct. 15:36:04 9 Q. Okay. And it's -- is there any 15:36:05 10 documentation of this alleged conversation you had 15:36:09 11 with Jeff Heier, that you recount in paragraph 121? 15:36:12 12 MS. STRUTHERS: Objection; 15:36:17 13 argumentative. 15:36:20 14 A. I'm under oath. 15:36:20 15 Q. (BY MR. SUMMERS) Okay. But is there a 15:36:22 16 documentation of it? 15:36:24 17 MS. STRUTHERS: Same -- 15:36:27 18 A. In Texas, a word is as good as his bond. 15:36:28 19 And so if you're saying that I didn't say it, 15:36:30 20 you're -- you're impugning my integrity, which I 15:36:33 21 disagree with. 15:36:36 22 Q. (BY MR. SUMMERS) I'm not actually 15:36:36 23 suggesting -- and I'm asking you, is there a record 15:36:37 24 of that conversation. 15:36:43 25 MS. STRUTHERS: Objection; asked and 15:36:44 Page 186	1 MS. STRUTHERS: Objection; asked and 15:37:54 2 answered. 15:37:54 3 A. So these discussions with Jeff would have 15:37:54 4 been between 2017 and 2010. While we're -- and 15:38:02 5 probably before that. They're probably before we 15:38:06 6 ever started the VIEW trials, trying to figure out 15:38:08 7 on how to design that trial. 15:38:16 8 So those discussions would be 2007, 2008, as 15:38:17 9 Regeneron was trying to design that trial with us. 15:38:21 10 We designed -- Jeff and I were both on the 15:38:23 11 steering committee for VIEW. The discussions would 15:38:25 12 have been at the VIEW steering committee, which 15:38:29 13 were under confidentiality agreements. 15:38:32 14 So, no, there's probably no reported record 15:38:34 15 of that, other than potentially internal Regeneron 15:38:37 16 notes. 15:38:39 17 I do not know if I said it at ad boards. I 15:38:40 18 wouldn't have been shy. I don't necessarily -- I'm 15:38:45 19 not shy about speaking my opinion on interpretation 15:38:51 20 of scientific data. 15:38:54 21 Q. (BY MR. SUMMERS) All right. But beyond 15:38:55 22 what you pointed to here in paragraph 121, are you 15:39:00 23 aware of any record evidence that shows that you 15:39:03 24 expressed, prior to being retained by Regeneron, as 15:39:08 25 an expert in this litigation, that a POSA would 15:39:13 Page 188
1 answered. 15:36:44 2 A. I don't know. 15:36:44 3 Q. (BY MR. SUMMERS) Sitting here today, you -- 15:36:47 4 you don't know of a record of that conversation. 15:36:51 5 Is that right? 15:36:55 6 MS. STRUTHERS: Objection; asked and 15:36:55 7 answered. 15:36:56 8 A. Correct. 15:36:56 9 Q. (BY MR. SUMMERS) Okay. And I asked you 15:37:00 10 before -- when you pointed me to this paragraph, I 15:37:01 11 asked you, before providing declarations for 15:37:05 12 Regeneron as used in litigation, if there was any 15:37:09 13 record that you -- you would -- recorded that you 15:37:13 14 had strongly -- strike that. 15:37:21 15 The original question was, before providing 15:37:21 16 your declaration to Regeneron for use in patent 15:37:26 17 proceedings, whether you were aware of any record 15:37:29 18 showing that you expressed that the CLEAR-IT 2 data 15:37:32 19 strongly suggested that eight-week dosing intervals 15:37:37 20 wouldn't work. And you pointed me here. 15:37:39 21 Is there anything else, that you're aware 15:37:42 22 of? 15:37:44 23 MS. STRUTHERS: Objection to form. 15:37:44 24 Where -- can you clarify what you mean by, here? 15:37:46 25 MR. SUMMERS: Paragraph 121. 15:37:50 Page 187	1 have understood, that the CLEAR-IT 2 data strongly 15:39:14 2 suggests that VEGF Trap-Eye would not be effective 15:39:19 3 on an eight-week dosing interval? 15:39:21 4 MS. STRUTHERS: Objection; asked and 15:39:26 5 answered. 15:39:29 6 A. I don't know when the litigation started, 15:39:29 7 but those conversations would have been 12, 13 15:39:36 8 years before Samsung and/or Mylan instituted 15:39:38 9 litigation against Regeneron. 15:39:45 10 Q. (BY MR. SUMMERS) Sure. And I just want to 15:39:46 11 be very clear, though. My question isn't just as 15:39:47 12 to this conversation. 15:39:52 13 I want to know if you're aware of anywhere, 15:39:53 14 any paper, publication, any piece of evidence, that 15:39:56 15 shows that you expressed, prior to being retained 15:40:03 16 as an expert by Regeneron, that CLEAR-IT 2 data 15:40:06 17 strongly suggested that VEGF Trap-Eye would not be 15:40:10 18 effective on an eight-week dosing interval? 15:40:12 19 MS. STRUTHERS: Objection; asked and 15:40:15 20 answered several times now. 15:40:16 21 A. Yeah, other than my sworn oath that I'm 15:40:17 22 telling the truth. So... 15:40:20 23 Q. (BY MR. SUMMERS) Okay. Thank you. 15:40:21 24 In paragraph 121, you just referred to this 15:40:24 25 actually, you said you viewed the Q8 arm as a long 15:40:26 Page 189

48 (Pages 186 - 189)

1 shot. 15:40:33	1 hypothetical. 15:43:31
2 Do you see that? 15:40:33	2 A. It depends on the individual trial. I was 15:43:31
3 A. Yes. 15:40:33	3 okay randomizing patients to aflibercept, 15:43:38
4 Q. Okay. Is it ethical, in a clinical trial, 15:40:33	4 2-milligram Q8, following three monthly loading 15:43:40
5 to subject patients to a long shot? 15:40:36	5 doses, in this trial. 15:43:45
6 MS. STRUTHERS: Objection; 15:40:38	6 Q. (BY MR. SUMMERS) So I'm going to hand you 15:44:14
7 mischaracterizes the testimony. 15:40:39	7 what's previously marked for the purposes of this 15:45:16
8 You can answer. 15:40:41	8 proceeding, as Exhibit 2131. 15:45:18
9 (The witness peruses the document.) 15:40:41	9 A. 2131. 15:45:24
10 A. So, in designing clinical trials, for 15:41:22	10 MS. STRUTHERS: Thank you. 15:45:26
11 example, VIEW 1 and VIEW 2, paragraph 75: 15:41:25	11 Q. (BY MR. SUMMERS) All right. This is a 15:45:27
12 Regeneron, conducted two Phase 3 studies designed 15:41:30	12 document entitled, Randomized, Double-Masked, 15:45:30
13 to test the use of VEGF Trap-Eye compared to 15:41:32	13 Sham-Controlled Trial of Ranibizumab for 15:45:36
14 ranibizumab. VIEW trials compared three different 15:41:36	14 Neovascular Age-Related Macular Degeneration: PIER 15:45:40
15 dosing arms of aflibercept to monthly 15:41:40	15 Study 1. 15:45:47
16 administration of 0.5-milligram ranibizumab. 15:41:41	16 Do you recognize this document, Dr. Brown? 15:45:47
17 At the conclusion of study enrollment, 15:41:43	17 A. I do. 15:45:49
18 patients were randomized in a 1 to 1 to 1 to 1 15:41:46	18 Q. And what is this document? 15:45:50
19 ratio to the following four dosing regimens: 15:41:49	19 (The witness peruses the document.) 15:46:03
20 2-milligram aflibercept every four weeks; 15:41:50	20 A. This is the one-year end point of the PIER 15:46:04
21 half-milligram aflibercept every four weeks; 15:41:53	21 study, published in the American Journal of 15:46:24
22 2-milligram aflibercept every eight weeks, after 15:41:56	22 Ophthalmology in 2008. 15:46:28
23 three injections; and -- and -- and ranibizumab 0.5 15:41:57	23 Q. (BY MR. SUMMERS) Okay. And you're the 15:46:31
24 milligrams monthly. Sham injections were given at 15:42:07	24 second-listed author on this paper, correct? 15:46:32
25 interim four-week visits to match the ranibizumab 15:42:08	25 A. That's correct. 15:46:35
Page 190	Page 192
1 dosing. 15:42:11	1 Q. Okay. And I want to direct your attention 15:46:36
2 The primary endpoint was non-inferiority of 15:42:11	2 to page 247 of this document. It's page 9 of 15 in 15:47:05
3 the intravitreal aflibercept injections. 15:42:15	3 the document, the discussion section. 15:47:11
4 If you design a clinical trial, what you 15:42:18	4 A. Okay. 15:47:14
5 need to have is equipoise. Equipoise is defined as 15:42:21	5 Q. Let me know when you're there. 15:47:14
6 you're okay randomizing to one group versus 15:42:25	6 A. I'm here. 15:47:16
7 another. 15:42:29	7 Q. Okay. The first sentence here reads: 15:47:17
8 I was okay randomizing to any of these four 15:42:29	8 Results of the PIER study indicate that ranibizumab 15:47:23
9 groups. 15:42:32	9 administered on a schedule of monthly dosing for 15:47:27
10 Q. My question is, is it ethical, in a clinical 15:42:35	10 three months, followed by quarterly dosing, 15:47:31
11 trial, to subject patients to a long shot? 15:42:41	11 provides significant visual acuity benefit to 15:47:34
12 MS. STRUTHERS: Objection to form, 15:42:45	12 patients with all angiograph subtypes, CNV, and 15:47:38
13 calls for speculation, incomplete hypothetical. 15:42:46	13 then parens, i.e., minimally or predominantly 15:47:43
14 A. You would have to know the exact trial and 15:42:48	14 classic or occult with no classic component, end 15:47:49
15 what you're treating, whether you're treating 15:42:57	15 paren, with a low incidence of serious ocular and 15:47:53
16 cancer, whether you're treating AMD, what the other 15:42:59	16 non-ocular adverse events and an acceptable rate 15:48:02
17 concomitant available options are. 15:43:01	17 of nonserious adverse events. 15:48:02
18 And I don't participate in what I consider 15:43:04	18 Do you see that? 15:48:05
19 unethical trials, and I was the lead recruiter in 15:43:07	19 A. I see that. 15:48:05
20 view. So I did not consider it unethical. 15:43:10	20 Q. And then in the next sentence, it explains 15:48:06
21 Q. (BY MR. SUMMERS) So are you okay, in a 15:43:12	21 that both of the ranibizumab dose groups exhibited 15:48:08
22 clinical trial, randomizing patients to a long 15:43:23	22 a clinically meaningful, at least three-line, 15:48:16
23 shot? 15:43:28	23 benefit, relative to the sham-injected control 15:48:18
24 MS. STRUTHERS: Objection; asked and 15:43:28	24 group. 15:48:22
25 answered, calls for speculation, incomplete 15:43:29	25 Do you see that? 15:48:22
Page 191	Page 193

49 (Pages 190 - 193)

1 A. I see that. 15:48:22 2 Q. And so, as an author of this study, you 15:48:23 3 characterized the results from PIER as providing a 15:48:28 4 significant visual acuity benefit to patients, 15:48:32 5 correct? 15:48:36 6 MS. STRUTHERS: Objection; document 15:48:37 7 speaks for itself. 15:48:38 8 A. Compared to the sham injected control group, 15:48:38 9 correct. 15:48:45 10 Q. (BY MR. SUMMERS) And in the first sentence, 15:48:46 11 at least, you don't say that. You say, provides a 15:48:48 12 significant visual acuity benefit to patients, 15:48:52 13 across all angiographic subtypes, right? 15:48:55 14 MS. STRUTHERS: Again, the document 15:49:03 15 speaks for itself. 15:49:33 16 (The witness peruses the document.) 15:49:33 17 A. So, I discussed here in my declaration, 15:49:33 18 2004, which would be prior to approval of any 15:49:43 19 Lucentis Genentech initiated PIER, which ran from 15:49:46 20 August 2004 to March 2007, designed to compare 15:49:52 21 three monthly loading doses, followed by fixed 15:49:55 22 quarterly dosing of .3-milligram and .5-milligram 15:49:58 23 Lucentis against sham control over 24 months. 15:50:03 24 I participated as a clinical investigator, 15:50:05 25 was part of the PIER study group, and was also 15:50:07 Page 194	1 in your declaration? 15:51:22 2 A. As I stated, page 19 and 20, starting at 15:51:23 3 paragraphs 47 and ending on 50. 15:51:26 4 Q. Okay. You -- you give a comparison between 15:51:29 5 the visual acuity benefits in PIER and MARINA and 15:51:35 6 ANCHOR in -- contemporaneously in Exhibit 2131. 15:51:40 7 And I want to direct you there. 15:51:45 8 So, on 247, the document says: In 15:51:47 9 conclusion, ranibizumab, administered monthly for 15:51:52 10 three months, and then the quarterly, provided VA 15:51:56 11 benefit to patients with neovascular AMD, is well 15:51:58 12 tolerated. However, observations from the MARINA 15:52:04 13 and ANCHOR trial suggest that the PIER regimen of 15:52:07 14 dosing every three months -- for three monthly 15:52:10 15 doses provides less benefit in VA on average than 15:52:12 16 continued monthly dosing. 15:52:16 17 And you conclude with: Monthly dosing may 15:52:17 18 be necessary in some patients to achieve maximal 15:52:20 19 treatment benefit from ranibizumab. 15:52:25 20 Do you see that? 15:52:26 21 A. I see that. 15:52:26 22 Q. Okay. That was your conclusion at the time 15:52:27 23 that Exhibit 2131 was published, correct? 15:52:31 24 MS. STRUTHERS: Objection; 15:52:39 25 mischaracterizes the document. 15:52:40 Page 196
1 involved in the presentation and publication of the 15:50:11 2 year-one data. As explained below, the PIER study 15:50:12 3 revealed that fixed quarterly intravitreal 15:50:15 4 injections was not an effective method of 15:50:19 5 treatment, particularly when compared to 15:50:21 6 MARINA/ANCHOR, when you saw visual acuity gains 15:50:23 7 that are maintained and persistent. 15:50:27 8 I go on to state, it's paragraph 50 on 15:50:29 9 page 19: As one of the lead clinical investigators 15:50:33 10 on the PIER trial, I received the first readout of 15:50:36 11 the one-year data, the study from Genentech, and 15:50:39 12 was the first to present the data. 15:50:41 13 The data was highly disappointing, to say 15:50:43 14 the least. I think most of us, investigators, were 15:50:45 15 expecting quarterly dosing would work. 15:50:48 16 The data we saw in MARINA and ANCHOR were 15:50:51 17 amazing. While patients saw an initial gain in 15:50:54 18 visual acuity during the three-month loading doses, 15:50:57 19 these gains were entirely lost once quarterly 15:51:00 20 dosing began. 15:51:05 21 By month 12, the .3-milligram arm saw a 15:51:05 22 1.6-letter loss from baseline, and the 15:51:09 23 half-milligram study arm saw a 0.2-letter 15:51:11 24 difference loss from baseline. 15:51:14 25 Q. Dr. Brown, where have you been reading from 15:51:17 Page 195	1 A. Yeah, you -- you talked about ethics 15:52:41 2 earlier. As you see, in paragraph 52, page 21, on 15:53:15 3 my declaration: Over the course of the study, the 15:53:22 4 study sponsor implemented two key protocol 15:53:29 5 amendments. Once we saw that the results of MARINA 15:53:31 6 and ANCHOR, the protocol was amended to provide 15:53:37 7 sham injection patients the opportunity to cross 15:53:40 8 over to receive ranibizumab, .5 milligrams. 15:53:44 9 And then the 12-month data -- as explained 15:53:48 10 above, the 12-month data from MARINA and ANCHOR 15:53:53 11 established to the retina community it would be in 12 the best interest of subjects in the sham cohorts 15:53:57 13 to receive ranibizumab, rather than be put at 15:53:59 14 further risk for severe irreversible vision loss. 15:54:02 15 And the second protocol amendment was after 15:54:06 16 we saw the results of PIER. Once we saw the 15:54:08 17 results of PIER, we basically took everybody out of 15:54:11 18 the trial and gave them monthly ranibizumab. 15:54:13 19 So, that was partially based on 15:54:16 20 recommendations of the data and safety monitoring 15:54:19 21 committee, but also all the members of the trial. 15:54:23 22 And if you look at Exhibit 2131, you see 15:54:25 23 that in Figure 4, page 245, you see that 15:54:32 24 catastrophic vision loss that occurs prior to 15:54:41 25 anti-VEGF therapy was just sham. You saw patients 15:54:45 Page 197

50 (Pages 194 - 197)

1 that -- sorry. That's mean thickness. There was 15:54:49 2 visual acuity. Sorry. Wrong graph. 15:54:53 3 Here you go. You see Figure 1. You see -- 15:54:57 4 Q. You're on -- and let me just help the record 15:55:00 5 here. And you're on page 243. 15:55:03 6 Is that correct? 15:55:05 7 A. I'm on page 243, correct. 15:55:06 8 Q. Okay. 15:55:10 9 A. You see with PIER, you get gain of vision 15:55:10 10 with those first three doses, like you saw in 15:55:15 11 MARINA and ANCHOR. You see loss of five letters by 15:55:18 12 one month, loss of seven letters by two months, 15:55:20 13 loss of almost ten letters by three months. 12 or 15:55:25 14 13 by 5 months. 15:55:26 15 And you see we -- we crossed some people 15:55:27 16 over, so there's a little uptick at the end. But 15:55:30 17 it -- this -- the treatment methods in sham needed 15:55:33 18 the -- you know, we -- they were crossed over 15:55:41 19 whenever we found out that MARINA and ANCHOR was 15:55:44 20 successful. 15:55:47 21 Q. So, you talked about pulling people out and 15:55:48 22 crossing them over or rolling them over. 15:55:58 23 That wasn't done at the time you had 15:56:00 24 published Exhibit 2131, correct? 15:56:03 25 A. The one year -- the protocol amendments of 15:56:10 Page 198	1 speaks for itself. 15:57:23 2 A. I see that, and I agree. 15:57:23 3 Q. (BY MR. SUMMERS) Okay. Compared to the 15:57:26 4 treatment protocol in PIER, VIEW 1 and VIEW 2 study 15:57:48 5 protocol provided for more doses in the first 52 15:57:59 6 weeks of the study, correct? 15:58:04 7 MS. STRUTHERS: Objection to form. 15:58:12 8 A. Repeat the question. 15:58:12 9 Q. (BY MR. SUMMERS) Yeah. Compared to 15:58:13 10 treatment protocol in PIER, VIEW 1 and VIEW 2 study 15:58:14 11 protocol provided more doses in the first 52 weeks 15:58:20 12 of the study, correct? 15:58:23 13 MS. STRUTHERS: Objection to form. 15:58:24 14 A. The monthly arm said on average 12. 3Q8 15:58:24 15 had, on average, more than PIER. 15:58:44 16 Q. (BY MR. SUMMERS) Yeah. And let's -- let's 15:58:47 17 focus on the 3Q8. So for 3Q8, patients enrolled in 15:58:50 18 that arm had, on average, more injections than were 15:58:59 19 given to the PIER study groups, correct? 15:59:03 20 A. That is correct. 15:59:06 21 Q. Okay. And similarly, compared to the study 15:59:10 22 groups in the CLEAR-IT 2 trial, the patients in the 15:59:17 23 3Q8 arm of VIEW 1 and VIEW 2 received, on average, 15:59:22 24 more injections than were given to the CLEAR-IT 2 15:59:29 25 participants, correct? 15:59:35 Page 200
1 rollover and crossover, the crossover happened on 15:56:17 2 February 27, 2006. This was published in 2007 -- 15:56:24 3 2008. I'm sorry. 15:56:33 4 The -- that's in my declaration, page 21, 15:56:34 5 paragraph 52, the protocol was amended on 15:56:39 6 February 27, 2006, to provide sham injections in 15:56:42 7 patients to crossover after they completed the 15:56:46 8 12-month visit. 15:56:49 9 So, yes, it would be after this data is 15:56:50 10 presented, but before this -- after -- certainly 15:56:52 11 before it was published. 15:56:55 12 Q. It happened -- the -- the actual crossover 15:56:56 13 and rollover -- 15:56:58 14 A. Right. 15:56:59 15 Q. -- though, happened in the second year of 15:56:59 16 the trial, correct? 15:57:00 17 A. Correct. 15:57:02 18 Q. Okay. And it -- after the first year of the 15:57:03 19 trial, which was what this publication reflects, 15:57:05 20 you gave the conclusion I referred to earlier, 15:57:08 21 which -- which ends: Monthly dosing may be 15:57:12 22 necessary in some patients to achieve maximal 15:57:15 23 treatment benefit from ranibizumab. 15:57:18 24 Right? 15:57:21 25 MS. STRUTHERS: Objection; document 15:57:21 Page 199	1 MS. STRUTHERS: Objection to form. 15:59:36 2 A. So what's the question? I'm sorry. 15:59:36 3 Q. (BY MR. SUMMERS) Yeah. Compared to the 16:00:09 4 study groups in CLEAR-IT 2 trial, the patients in 16:00:13 5 the 3Q8 arm of VIEW 1 and VIEW 2 received, on 16:00:16 6 average, more injections, correct? 16:00:21 7 A. So the CLEAR-IT 2 arms received PRN 16:00:40 8 injections requiring them to have -- we were 16:00:45 9 required to have -- they had monthly examinations, 16:01:56 10 with injections, if the central retinal thickness 16:02:05 11 was over -- or greater than 100 microns; a loss 16:02:09 12 of -- or greater than five letters, ETDRS letters; 16:02:13 13 persistent fluid on OCT; new onset classic 16:02:18 14 neovascularization; new or persistent leak; or 16:02:23 15 newer macular hemorrhage. 16:02:25 16 From Exhibit 2297, the mean number of 16:02:27 17 retreatments in each criteria were two -- were -- 16:02:36 18 you got to add four to some of these, because the 16:02:40 19 monthlies. So the -- the Q4s had a mean of 5.55. 16:02:43 20 The .5 monthlies had a mean of 6.52. The others 16:02:52 21 had less. And the 2Q8 arms should have gotten 16:03:01 22 eight doses, if dosed according to protocol. 16:03:07 23 Q. The 2Q8 arms of the VIEW 1 and VIEW 2, 16:03:10 24 right? 16:03:21 25 A. The VIEW 1 and VIEW 2, correct. Sorry. 16:03:21 Page 201

51 (Pages 198 - 201)

1 Q. So, yeah, to simplify this -- and I didn't 16:03:22 2 mean to make it so complex. I apologize. 16:03:24 3 The 2Q8 arms in VIEW 1 and VIEW 2 protocol 16:03:27 4 got eight doses, while those in CLEAR-IT 2 got 16:03:32 5 somewhere between, on average, five and six and a 16:03:36 6 half. 16:03:39 7 Is that right? 16:03:39 8 A. That's correct. 16:03:39 9 Q. Okay. Did you have any financial interest 16:03:42 10 in Regeneron prior to 2011? 16:04:06 11 A. In terms of stock or equity, I did not. 16:04:08 12 Q. Okay. What about after 2011? 16:04:13 13 A. I did not. 16:04:15 14 Q. You don't have any financial interest in 16:04:16 15 them now, either, right? 16:04:18 16 A. I have no stock or equity in Regeneron. 16:04:19 17 Q. Okay. Were you compensated in any way for 16:04:21 18 any of the papers that you authored relating to 16:04:24 19 clinical trials for aflibercept? 16:04:29 20 A. Yeah. Never compensated for work on a 16:04:32 21 paper. Compensated for consulting, designing 16:04:35 22 trials, and that kind of thing. But the papers 16:04:38 23 themselves were not compensated for. 16:04:42 24 Q. And you were compensated previously by 16:04:43 25 Genentech for the design of those trials in which 16:04:48 Page 202	1 one thing or another. And I don't know exactly. 16:06:07 2 Q. (BY MR. SUMMERS) Fair. You're -- yeah, 16:06:09 3 let's -- let's clarify that. 16:06:13 4 Your compensation, relating to your 16:06:15 5 testimony today and in your declaration, is in no 16:06:17 6 way contingent on the outcome of the matter, right? 16:06:21 7 A. Correct. 16:06:25 8 Q. And your compensation relating to your 16:06:25 9 testimony and your declaration is no way contingent 16:06:27 10 on the substance of what you say, either. 16:06:31 11 Is that correct? 16:06:33 12 A. Correct. 16:06:33 13 Q. Okay. You say you don't know exactly. Do 16:06:34 14 you have a sense of how -- generally, of how much 16:06:37 15 you've been compensated by Regeneron for your work 16:06:40 16 on the patent portfolio? 16:06:42 17 A. I -- I don't. 16:06:46 18 Q. Is it -- 19 A. Probably less than your law firm, but -- I 16:06:46 20 would think. 16:06:49 21 Q. Is it more than a hundred thousand dollars? 16:06:49 22 MS. STRUTHERS: Objection; asked and 16:06:54 23 answered. 16:06:55 24 A. I don't think so. 16:06:55 25 Q. (BY MR. SUMMERS) Okay. What is your hourly 16:06:59 Page 204
1 you participated, as well, right? 16:04:51 2 A. Compensated as a consultant to help design 16:04:52 3 trials, but when I'm writing a paper, I'm not 16:04:55 4 compensated. That's felt to be unethical by most 16:04:57 5 journals. Myself. 16:05:00 6 Q. And glad those interests align. 16:05:02 7 A. Yeah. 16:05:09 8 Q. The -- the -- when were you first retained 16:05:09 9 as a consultant by Regeneron, relating to its 16:05:18 10 patent portfolio? 16:05:24 11 MS. STRUTHERS: I'm sorry. Could 16:05:26 12 you repeat the question? The fan just kicked on. 16:05:26 13 Q. (BY MR. SUMMERS) Sorry. I should have 16:05:28 14 noted that. The heat's just kicked on. 16:05:31 15 When were you first retained as a consultant 16:05:33 16 by Regeneron, relating to its patent portfolio? 16:05:35 17 A. I don't recall exactly. Probably a couple 16:05:38 18 years ago. 16:05:41 19 Q. Okay. And do you have a sense, sitting here 16:05:41 20 today, of how much Regeneron has compensated you as 16:05:47 21 a consultant for work relating to its patent 16:05:49 22 portfolio? 16:05:54 23 MS. STRUTHERS: Objection to form. 16:05:55 24 A. I'm paid for my experience and time, not for 16:05:55 25 what I say, in terms of, I can't be bought to say 16:06:03 Page 203	1 rate for your consulting work relating to this 16:07:02 2 matter? 16:07:07 3 A. I'm not sure exactly. For most scientific 16:07:07 4 consulting, and most legal, I'm around a thousand 16:07:16 5 an hour. I usually charge investment banks double 16:07:18 6 that, because they're sharks. But... 16:07:22 7 You can strike that probably. That's 16:07:26 8 probably not... 16:07:27 9 Q. Have you ever testified for anyone other 16:07:30 10 than Regeneron, as regards a patent litigation? 16:07:35 11 A. I have. 16:07:40 12 Q. You have. And who have you testified on 16:07:40 13 behalf of? 16:07:42 14 A. That's a good question. Some surgical -- I 16:07:43 15 think it was Alcon and -- and some patents 16:07:53 16 involving OCT imaging. 16:07:57 17 Q. Okay. Any -- anyone else? 16:08:02 18 A. I don't think so. 16:08:03 19 Q. Okay. Were you on the patentee side in that 16:08:05 20 matter for Alcon? 16:08:11 21 A. I wasn't on the outcome patent. I was on 16:08:12 22 the -- I was on an imaging patent for Optos. 16:08:14 23 Q. Okay. What's the -- what's the spelling on 16:08:24 24 that? 16:08:28 25 A. O-P-T-O-S. 16:08:28 Page 205

1 Q. Oh, I see. 16:08:31 2 So, I want to turn now back to your 16:08:46 3 understanding of the claims here. 16:08:50 4 Do you have an understanding -- actually, 16:08:51 5 let me ask you outside of the claims, because we 16:08:57 6 tried that already. 16:08:59 7 Outside of the context of the patent, do you 16:09:00 8 have an opinion on what an exclusion criteria is? 16:09:04 9 MS. STRUTHERS: Objection; beyond 16:09:09 10 the scope. 16:09:09 11 A. What's the question? 16:09:09 12 Q. (BY MR. SUMMERS) All right. Do you have -- 16:09:10 13 outside of the context of the patent, do you have 16:09:12 14 an understanding of exclusion criteria is? 16:09:15 15 MS. STRUTHERS: Objection; beyond 16:09:20 16 the scope. 16:09:20 17 A. Exclusion criteria. I don't offer an 16:09:20 18 opinion on exclusion criteria within the context of 16:09:24 19 the patent, or outside -- inside or outside. And 16:09:26 20 not prepared to do so yet. 16:09:29 21 Q. (BY MR. SUMMERS) Do you have an 16:09:31 22 understanding, inside or outside of the patent, of 16:09:45 23 what an exclusion criteria is? 16:09:50 24 MS. STRUTHERS: Objection; beyond 16:09:52 25 the scope, asked and answered. 16:09:54 Page 206	1 So I'm going to try one more time. 16:11:10 2 I'm not asking for an opinion about them. 16:11:12 3 I'm asking for your understanding. 16:11:16 4 Do you have an opinion that you are willing 16:11:18 5 to share with me today about what an exclusion 16:11:24 6 criteria is, inside or outside the patent? 16:11:28 7 MS. STRUTHERS: Objection; beyond 16:11:31 8 the scope, asked and answered. 16:11:32 9 A. No idea what context. I don't offer an 16:11:33 10 opinion, as it pertains to this matter on 16:11:48 11 exclusions, in the patent or outside the patent, 16:11:51 12 and I'm not prepared to do so today. 16:11:54 13 Q. (BY MR. SUMMERS) Okay. So, if you do have 16:11:56 14 an understanding of what an exclusion criteria is, 16:12:01 15 you will not share that with me today. 16:12:04 16 Is that right? 16:12:06 17 MS. STRUTHERS: Objection; 16:12:07 18 mischaracterizes his testimony, beyond the scope, 16:12:08 19 asked and answered. 16:12:10 20 A. I don't offer an opinion on exclusions, 16:12:10 21 inside the patent or outside, and I don't -- I'm 16:12:22 22 not prepared to offer one today. 16:12:25 23 MR. SUMMERS: Counsel, I'm entitled 16:12:51 24 to an answer here. So I don't know if you want to 16:12:52 25 take a break and rethink this, or if you would like 16:12:54 Page 208
1 A. Again, I don't discuss that in my 16:09:54 2 declaration, and not prepared to do so today. 16:09:59 3 Q. (BY MR. SUMMERS) Okay. But my question is 16:10:01 4 more specific. 16:10:02 5 Do you have an understanding, inside or 16:10:03 6 outside of the patent, of what an exclusion 16:10:04 7 criteria is? 16:10:06 8 MS. STRUTHERS: Objection; beyond 16:10:07 9 the scope, asked and answered. 16:10:09 10 A. That's -- as before, I don't offer an 16:10:09 11 opinion, and I'm not prepared to do so today. 16:10:21 12 Q. (BY MR. SUMMERS) My question isn't whether 16:10:23 13 you're prepared to offer an opinion. My question 16:10:29 14 is more specific. So I'm going to ask again. 16:10:32 15 Do you have an understanding, inside or 16:10:36 16 outside of the patent, on what an exclusion 16:10:38 17 criteria is? 16:10:40 18 MS. STRUTHERS: Objection; beyond 16:10:42 19 the scope, asked and answered. 16:10:42 20 A. I don't offer an opinion, inside the patent 16:10:49 21 or outside, and not prepared to do so today. 16:10:50 22 Q. (BY MR. SUMMERS) Yeah. I -- I'm plainly 16:10:53 23 entitled to this information. You've given 16:10:57 24 multiple opinions dependent on the scope of the 16:11:03 25 claims here, which include the exclusion criteria. 16:11:07 Page 207	1 to continue on. 16:12:58 2 MS. STRUTHERS: Have you run out of 16:12:59 3 questions on his declaration opinions? Because if 16:13:00 4 you have, we can -- we can end the deposition. You 16:13:03 5 can end your questioning and I may have some 16:13:05 6 redirect. I haven't considered that yet. 16:13:07 7 But if you're done with questions on 16:13:08 8 his declaration, perhaps you're done. 16:13:10 9 MR. SUMMERS: Okay. So I'm not. I 16:13:12 10 want to know if you want to take a break and 16:13:15 11 rethink your position on whether he can give me his 16:13:18 12 understanding of exclusion criteria. 16:13:21 13 MS. STRUTHERS: No break is 16:13:24 14 necessary. If you have questions on his 16:13:25 15 declaration, you should ask them. If you're out of 16:13:27 16 questions on his declaration, you should turn over 16:13:29 17 the questioning. 16:13:32 18 MR. SUMMERS: Okay. 16:13:32 19 Q. (BY MR. SUMMERS) Dr. Brown, let's come back 16:13:33 20 to your declaration here. So I want to talk to you 16:13:38 21 about your role as it relates to -- let's take the 16:14:28 22 CLEAR-IT 2 trial. 16:14:38 23 You said you acted as a consultant for 16:14:40 24 Regeneron as to the CLEAR-IT 2 trial. 16:14:43 25 Is that correct? 16:14:45 Page 209

1 A. For the CLEAR-IT 2 trial? 16:14:46 2 Q. Uh-huh. 16:14:53 3 A. I did. 16:14:53 4 Q. Okay. Did you have any other role as it 16:14:55 5 relates to the CLEAR-IT 2 trial? 16:14:58 6 A. I was the principal investigator in the 16:14:59 7 Houston site, which means I made sure that the 16:15:02 8 study was performed in a manner that was -- 16:15:12 9 protected human subjects, protected the data 16:15:21 10 integrity. 16:15:24 11 I was a mask examiner, which means that I 16:15:26 12 would examine the patients and wouldn't know if 16:15:36 13 they were getting a treatment at any interval, 16:15:38 14 looking for clinical findings, to -- for the data. 16:15:41 15 Additionally, with CLEAR-IT 2, I was -- I 16:15:48 16 was a coauthor on some of the presentations. I'm 16:15:54 17 not the primary author of the presentations, but 16:15:56 18 the primary author of the -- of the -- the primary 16:15:59 19 manuscript, and a secondary author, with Jeff 16:16:05 20 Heier, on the one-year manuscript. 16:16:09 21 Q. You said you were responsible for human 16:16:10 22 safety. 16:16:12 23 What do you mean by that? 16:16:13 24 A. In other words, in human subjects, the 16:16:13 25 principal investigator is really responsible. And 16:16:20 Page 210	1 interested in working with them. 16:17:31 2 Q. In terms of making sure the protocol is 16:17:34 3 followed, what does that involve? 16:17:37 4 MS. STRUTHERS: Objection; beyond 16:17:38 5 the scope. 16:17:39 6 A. So there's a -- a protocol in -- in -- when 16:17:49 7 you're supposed to see patients, et cetera. You 16:17:53 8 know, I don't get into my deposition exactly how we 16:17:56 9 run every trial. And -- and we certainly can -- we 16:17:59 10 could talk hours about how different trials are 16:18:04 11 ran. And I'm not prepared to do that today. 16:18:06 12 Q. (BY MR. SUMMERS) Okay. In terms of making 16:18:08 13 sure the protocol is followed, is one of the things 16:18:15 14 you do, make sure that the exclusion criteria that 16:18:17 15 are specified in the protocol are followed? 16:18:20 16 MS. STRUTHERS: Objection; beyond 16:18:23 17 the scope. 16:18:24 18 A. Yeah. And again, I'm not going to talk 16:18:24 19 about exactly how we decide which patients are in 16:18:30 20 which trials, and not going to offer an opinion 16:18:32 21 today. 16:18:38 22 Q. (BY MR. SUMMERS) What was your role as it 16:18:38 23 relates to the PIER trial? 16:18:39 24 A. PIER trial, I was more of a consultant for 16:18:41 25 Genentech, after working with them quite a while 16:18:52 Page 212
1 the primary responsibility, in my mind, the first 16:16:23 2 step is to make sure people have an informed 16:16:25 3 consent of what they're getting into; you know, 16:16:28 4 what potential risks, what potential benefits, how 16:16:30 5 many visits they're going to have to come, how long 16:16:33 6 it's going to take. 16:16:35 7 That's -- one of the most important things 16:16:40 8 is the informed consent. And then, beyond that, 16:16:42 9 making sure that the study is performed like the 16:16:44 10 protocol, without deviations or deviating from the 16:16:50 11 way the protocol is. 16:16:56 12 Q. Okay. Do you have input on setting the 16:16:57 13 protocol -- let me make it more specific. 16:16:59 14 Do you have -- did you have input on setting 16:17:01 15 the protocol for CLEAR-IT 2? 16:17:03 16 A. I honestly don't remember. I mean, this 16:17:05 17 would have been an early trial with Regeneron. I 16:17:07 18 was mainly doing -- really busy with all the 16:17:09 19 Genentech RISE/RIDE, you know, all the big 16:17:12 20 Phase 3's with Genentech. 16:17:17 21 Regeneron was a secondary player, and 16:17:21 22 it's -- I certainly worked with them. But I don't 16:17:22 23 remember if I did much consulting at all on 16:17:24 24 CLEAR-IT 2 until I got involved and saw that the 16:17:26 25 molecule was actually working some, and got more 16:17:29 Page 211	1 with MARINA ANCHOR, RISE/RIDE -- actually, 16:18:54 2 RISE/RIDE wasn't even there yet. It was just 16:18:58 3 MARINA ANCHOR. 16:19:02 4 I was also a principal investigator in 16:19:02 5 Houston, mask examiner. 16:19:04 6 Q. Okay. And so, as a principal investigator 16:19:06 7 in Houston, was one of your jobs to ensure that 16:19:16 8 protocol was followed? 16:19:22 9 MS. STRUTHERS: Objection; beyond 16:19:25 10 the scope. 16:19:28 11 A. Yeah, again, we can talk about every trial 16:19:28 12 I've done, which is -- you've seen my CV. It's 16:19:31 13 literally hundreds of trials. And every one, we 16:19:34 14 make sure the protocol is followed. 16:19:40 15 Q. (BY MR. SUMMERS) Okay. So, for the PIER 16:19:41 16 study, were you responsible for making sure that 16:19:46 17 the exclusion criteria were followed? 16:19:48 18 MS. STRUTHERS: Objection; beyond 16:19:52 19 the scope. 16:19:53 20 A. Again, we don't talk about how I run 16:19:53 21 clinical trials in my declaration, other than the 16:20:08 22 fact we do it ethically. And I'm not going to 16:20:12 23 offer testimony today on how exactly we do clinical 16:20:16 24 trials. 16:20:20 25 Q. (BY MR. SUMMERS) Okay. So you won't tell 16:20:20 Page 213

1 me whether it's part of your role in the PIER 16:20:27 2 study, you were responsible for making sure 16:20:30 3 exclusion criteria were followed? 16:20:35 4 MS. STRUTHERS: Objection; 16:20:38 5 mischaracterizes the testimony, beyond the scope. 16:20:39 6 A. At the end of the day, the principal 16:20:40 7 investigator is responsible for the entire clinical 16:20:58 8 trial site. 16:21:01 9 But what you're referring to, rarely those 16:21:01 10 patients get to the study. So I'm not going to 16:21:08 11 talk about all the nuances and how we run trials. 16:21:11 12 Like I said, ran hundreds of trials. Didn't offer 16:21:15 13 an opinion and not going -- not prepared to do so 16:21:20 14 today. 16:21:21 15 MS. STRUTHERS: We've been going for 16:21:37 16 a little over an hour. Should we take a break? 16:21:38 17 MR. SUMMERS: Sure. 16:21:41 18 THE VIDEOGRAPHER: Off the record at 16:21:42 19 4:21 p.m. 16:21:43 20 (Break.) 16:21:44 21 THE VIDEOGRAPHER: Back on the 16:33:43 22 record at 4:33 p.m. 16:33:43 23 Q. (BY MR. SUMMERS) Welcome back, Dr. Brown. 16:33:45 24 A. Good to be back. 16:33:48 25 Q. So, I want to refer you back to exhibit -- 16:33:49 Page 214	1 A. I haven't looked at it in probably 14 years, 16:34:55 2 so... 16:35:06 3 Q. (BY MR. SUMMERS) Okay. But do you 16:35:07 4 recognize it? 16:35:09 5 MS. STRUTHERS: Same. 16:35:13 6 A. I recognize it, but don't offer an opinion 16:35:13 7 on it in my testimony. 16:35:16 8 Q. (BY MR. SUMMERS) Okay. Thank you. 16:35:17 9 And if you go down -- I'm going to struggle 16:35:29 10 to direct you there, but it's about, let's say, 16:35:32 11 three-fifths of the way down the page. 16:35:37 12 One of the eligibility criteria listed for 16:35:39 13 the PIER study is active intraocular inflammation, 16:35:41 14 and in parens, grade tracer above in the study eye. 16:35:45 15 Do you see that? 16:35:49 16 MS. STRUTHERS: Objection. Counsel, 16:35:51 17 this is beyond the scope of the witness' 16:35:51 18 declaration. You've spent a lot of time today 16:35:53 19 asking beyond the scope questions. 16:35:56 20 If you are out of questions about 16:35:57 21 his opinions in his declaration, you should turn 16:35:59 22 over the questioning. 16:36:04 23 MR. SUMMERS: I'm not going to turn 16:36:04 24 over the questioning. There's a pending question. 16:36:05 25 Q. (BY MR. SUMMERS) So, do you see where I'm 16:36:07 Page 216
1 what's been marked for this proceeding as 16:33:55 2 Exhibit 2131. That's the PIER Study Year 1. 16:33:58 3 A. Okay. 16:34:02 4 Q. Let me know when you've got that exhibit 16:34:03 5 back. 16:34:13 6 A. I've got it. Regillo, et al. 16:34:14 7 Q. Okay. And -- that's right. And you -- 16:34:17 8 again, you're the second named author on this 16:34:18 9 publication, right? 16:34:20 10 A. That's correct. 16:34:21 11 Q. And you see if you will turn to -- it's the 16:34:21 12 13th page of the document. It's page 24E (sic). 16:34:26 13 A. One more time. 16:34:34 14 Q. It's the 13th page of the document. It's 16:34:35 15 24 -- or 248 -- 16:34:38 16 A. Yeah, that Supplemental Table A, right? 16:34:42 17 Q. Yeah, you see that. 16:34:44 18 A. Okay. 19 Q. And it's got eligibility criteria for PIER 16:34:46 20 study. 16:34:49 21 A. Okay. 16:34:49 22 Q. Are you familiar with Supplemental Table A 16:34:49 23 here? 16:34:53 24 MS. STRUTHERS: Objection; beyond 16:34:54 25 the scope. 16:34:55 Page 215	1 referring? 16:36:08 2 MS. STRUTHERS: Objection; beyond 16:36:08 3 the scope. 16:36:08 4 A. I didn't offer an opinion on Supplemental 16:36:08 5 Table A, and I'm not prepared to do so today. 16:36:12 6 Q. (BY MR. SUMMERS) Okay. Do you have an 16:36:14 7 understanding, sitting here today, of what active 16:36:15 8 intraocular inflammation is? 16:36:20 9 MS. STRUTHERS: Objection; beyond 16:36:21 10 the scope. 16:36:22 11 A. I don't offer an opinion on that, and not 16:36:22 12 prepared to do so today. 16:36:37 13 Q. (BY MR. SUMMERS) Okay. And do you see, 16:36:38 14 further down, it refers to infective 16:36:40 15 conjunctivitis, keratitis, scleritis, or 16:36:45 16 endophthalmitis, in either eye? 16:36:49 17 A. I see that. 16:36:50 18 Q. Okay. And do you have an understanding of 16:36:55 19 what that entry in the eligibility criteria 16:36:58 20 (unintelligible) -- 16:37:02 21 THE REPORTER: Can you repeat that? 16:37:02 22 I'm sorry. 16:37:02 23 Q. (BY MR. SUMMERS) Do you have an 16:37:03 24 understanding of what that entry in the eligibility 16:37:04 25 criteria means? 16:37:08 Page 217

55 (Pages 214 - 217)

1 A. Understanding what? I'm sorry. 16:37:08 2 MS. STRUTHERS: Object. 16:37:11 3 Q. (BY MR. SUMMERS) Do you have an 16:37:11 4 understanding of what that entry in the eligibility 16:37:12 5 criteria means, the one referring to infective 16:37:16 6 conjunctivitis, et cetera? 16:37:21 7 MS. STRUTHERS: Objection; beyond 16:37:23 8 the scope. 16:37:24 9 A. Yeah. I don't offer an opinion on how it 16:37:24 10 pertains to our proceedings, and I'm not prepared 16:37:26 11 to do so today. 16:37:28 12 MS. STRUTHERS: And, again, Counsel, 16:37:28 13 if you're going to ask questions that are beyond 16:37:29 14 the scope, it's time to end the deposition. 16:37:32 15 MR. SUMMERS: Okay. I'm going to 16:37:34 16 continue the deposition, Counsel. 16:37:35 17 Q. (BY MR. SUMMERS) Let me now turn you to the 16:37:36 18 '681 patent again. Again, that's Exhibit 1001. 16:37:40 19 A. Okay. 16:37:48 20 Q. And earlier today, you remember, you 16:37:48 21 referred me to Example 4. And specifically, I 16:37:51 22 believe to the portion of Example 4 that recites a 16:38:00 23 number of exclusion criteria. It starts on -- 16:38:06 24 well, let me -- let me -- let me take a step back. 16:38:10 25 Earlier today you referred me to Example 4. 16:38:12 Page 218	1 related to the opinions in his declaration? 16:41:36 2 MR. SUMMERS: I do, including these. 16:41:38 3 MS. STRUTHERS: These are not to do 16:41:43 4 with his declaration. 16:41:48 5 MR. SUMMERS: Counsel, there is a 16:41:48 6 question pending, so why don't you hold your 16:41:49 7 comments. I'm happy to go off the record and have 16:41:53 8 that discussion, if you want, but not while there's 16:41:56 9 a question pending. 16:41:57 10 (The witness peruses the document.) 16:41:59 11 MS. STRUTHERS: Could you repeat the 16:42:01 12 question, please? 16:42:03 13 Q. (BY MR. SUMMERS) Dr. Brown, do you 16:42:04 14 understand the question? 16:42:07 15 A. Yeah, repeat -- repeat the question. 16:42:07 16 Q. I -- 17 A. I -- I read through this entire laundry list 16:42:09 18 of exclusion criteria, and don't believe I talk 16:42:12 19 about any of them in my -- in my declaration. 16:42:14 20 Q. That's fine. 16:42:16 21 A. And I'm not prepared to do so today. 16:42:17 22 Q. That's all right. And if you come over to 16:42:18 23 Claim 1 of the '681 patent. 16:42:20 24 A. Go where, Claim 1? 16:42:22 25 Q. Claim 1 of the '681 patent? 16:42:25 Page 220
1 Do you remember that? 16:38:15 2 A. I see Example 4, yeah. I remember that, 16:38:15 3 yes. 16:38:20 4 Q. Okay. And you see, starting at column 10, 16:38:21 5 line 58 -- let me know when you're there. 16:38:25 6 (The witness peruses the document.) 16:38:41 7 Q. (BY MR. SUMMERS) Are you there, column 10, 16:38:59 8 line 58? 16:39:00 9 A. I'm reading Example 4 so I can understand 16:39:01 10 the context. 16:39:04 11 Q. Okay. 16:39:04 12 (The witness peruses the document.) 16:39:10 13 A. Okay. I see it, yeah. 16:40:40 14 Q. (BY MR. SUMMERS) Okay. So you see 16:40:41 15 there's -- from column 10 over to column 12, 16:40:42 16 there's a list of 37 exclusion criteria that you 16:40:45 17 looked at earlier, when you reviewed the entire 16:40:51 18 patent, right? 16:40:54 19 MS. STRUTHERS: Objection, beyond 16:40:55 20 the scope. 21 Again, Counsel, if all you have to 16:41:10 22 talk about is exclusion criteria, and nothing 16:41:12 23 further related to his declaration, it's time to 16:41:14 24 end the deposition. 16:41:16 25 Do you have any further questions 16:41:34 Page 219	1 A. Okay. 16:42:28 2 Q. Of that laundry list, there is only three 16:42:29 3 exclusion criteria listed. 16:42:32 4 Do you see that? 16:42:33 5 MS. STRUTHERS: Objection; beyond 16:42:34 6 the scope. 16:42:34 7 A. Yeah. I don't discuss exclusion criteria, 16:42:40 8 or its importance to the -- to the -- in the 16:42:42 9 declaration, and I'm not prepared to do so today. 16:42:48 10 Q. (BY MR. SUMMERS) Okay. This is a simple 16:42:50 11 question. 16:42:52 12 Do you see there's only 3 of the 37 from 16:42:53 13 that laundry list of exclusion criteria there 16:42:56 14 listed in Claim 1? Do you see that? 16:42:58 15 MS. STRUTHERS: Objection; beyond 16:43:00 16 the scope, document speaks for itself. 16:43:01 17 A. I see the text, but again, don't offer an 16:43:02 18 opinion in the declaration to its importance or 16:43:10 19 significance, and don't -- aren't prepared to do so 16:43:14 20 today. 16:43:18 21 Q. (BY MR. SUMMERS) Okay. One of the things 16:43:18 22 that you testified to regarding the PrONTO study 16:43:19 23 was that, in your view, the patients were 16:43:24 24 handpicked, right? 16:43:26 25 A. It's what I said. 16:43:27 Page 221

56 (Pages 218 - 221)

1 Q. Okay. And in other words, investigators can 16:43:31 2 use the criteria by which they populate their 16:43:37 3 studies to, in your view, increase the likelihood 16:43:42 4 of success, right? 16:43:45 5 MS. STRUTHERS: Objection; 16:43:47 6 mischaracterizes the testimony. 16:43:48 7 A. I disagree with that. They were handpicked 16:43:48 8 and they weren't randomized. It wasn't a 16:43:51 9 randomized study. 16:43:54 10 A randomization, you randomize to one group 16:43:56 11 or the other. In a non-randomized study, they're 16:43:58 12 picked to be in the study, and everybody gets the 16:44:01 13 same treatment. 16:44:03 14 Q. (BY MR. SUMMERS) Right. But earlier, you 16:44:03 15 told me with the PrOnto study, that in your view, 16:44:04 16 they were selected by the investigator for -- to be 16:44:08 17 likely to comply with the study protocol, right? 16:44:12 18 A. Correct. You only pick patients for any 16:44:14 19 study that you think can come to the visits. 16:44:19 20 Q. Right. And that's -- that's one of the 16:44:21 21 reasons why you argue that the PrOnto results 16:44:23 22 should be discounted, right? 16:44:27 23 MS. STRUTHERS: Objection; 16:44:30 24 mischaracterizes his testimony. 16:44:30 25 A. I'm just saying, you can't -- and without a 16:44:35 Page 222	1 Although, we are very cognizant that if we enroll 16:45:59 2 patients in studies, we want them to complete. So 16:46:09 3 we often, as part of our informed consent process, 16:46:11 4 really spend a lot of time letting them know what 16:46:13 5 those time commitments are. 16:46:16 6 Q. (BY MR. SUMMERS) I'm trying to get to the 16:46:19 7 basis of this criticism you make in the PrOnto 16:46:22 8 study. 16:46:25 9 Which is, in your view, in populating the 16:46:25 10 study, Dr. Rosenfeld specifically tried to pick 16:46:36 11 patients who would comply, right? 16:46:43 12 MS. STRUTHERS: Objection; asked and 16:46:46 13 answered. 16:46:47 14 A. That's correct. 16:46:47 15 Q. (BY MR. SUMMERS) And the reason that's a 16:46:54 16 problem, in your view, is that increased the 16:46:55 17 likelihood of success for that study to meet the 16:46:59 18 endpoints, right? 16:47:04 19 MS. STRUTHERS: Objection; 16:47:05 20 mischaracterizes his testimony. 16:47:08 21 A. I don't know that it increases likelihood 16:47:09 22 for success. It's probably just a different 16:47:11 23 population pool than what we saw in some of our 16:47:13 24 other randomized trials. 16:47:17 25 Q. (BY MR. SUMMERS) Can the way you select 16:47:19 Page 224
1 randomized study, you can't give it the same 16:44:37 2 credence as you would a well-controlled, 16:44:42 3 randomized, double-blinded study. 16:44:45 4 Q. (BY MR. SUMMERS) Why is that? 16:44:46 5 A. You know, we're not going to go over exactly 16:44:48 6 how to do studies, but I will tell you that when 16:44:59 7 you have a non-randomized study, you can have all 16:45:03 8 kinds of biases, and that the patients know they're 16:45:06 9 getting an active drug, the refractionists know 16:45:10 10 they're getting the active drug, patients are 16:45:12 11 trying harder, et cetera. Often, non-randomized 16:45:15 12 studies do better randomized, because of those 16:45:19 13 inherent biases. 16:45:22 14 Q. Right. But you didn't necessarily refer to 16:45:23 15 randomization earlier. You referred to handpicking 16:45:27 16 to increase compliance of the population in that 16:45:29 17 study, right? 16:45:32 18 MS. STRUTHERS: Objection; 16:45:34 19 mischaracterizes the testimony. 16:45:35 20 A. Dr. Rosenfeld had a very hard study protocol 16:45:35 21 with which they had to come back often, multiple 16:45:48 22 days in a row. And sure, he picked patients he 16:45:51 23 thought could do that. 16:45:53 24 Is that a different population that would be 16:45:54 25 in the study that could be monthly, potentially? 16:45:57 Page 223	1 your population pool for a study affect the 16:47:20 2 likelihood that you'll meet the clinical endpoints? 16:47:23 3 MS. STRUTHERS: Objection; beyond 16:47:27 4 the scope. 16:47:32 5 A. Repeat the question one more time. 16:47:32 6 Q. (BY MR. SUMMERS) Yeah. Can the way you 16:47:33 7 select your population pool for a clinical study 16:47:34 8 affect the likelihood that you'll meet the 16:47:39 9 endpoints? 16:47:41 10 MS. STRUTHERS: Objection; beyond 16:47:42 11 the scope. 16:47:43 12 A. You know, we could talk a lot about how to 16:47:43 13 design clinical trials. And I don't go into that 16:47:46 14 and am not prepared to do so today. 16:47:47 15 Q. (BY MR. SUMMERS) So you don't have an 16:47:50 16 opinion about whether or not the way you select 16:47:51 17 your population pool for a clinical study can 16:47:55 18 affect the likelihood you'll meet your endpoints? 16:48:00 19 MS. STRUTHERS: Objection; beyond 16:48:02 20 the scope. 16:48:02 21 A. I don't offer an opinion in this 16:48:02 22 declaration. Nope. 16:48:04 23 Q. (BY MR. SUMMERS) Okay. But you do offer an 16:48:04 24 opinion in this declaration about reasonable 16:48:06 25 expectation of success, as it relates to the VIEW 1 16:48:09 Page 225

1 and VIEW 2 dosing arm disclosed in Dixon, right? 16:48:17 2 A. Certainly. In paragraph 101, I state: The 16:48:20 3 POSA would not have had a reasonable expectation of 16:48:40 4 successfully achieving the Q8 dosing regimen 16:48:43 5 claimed by the '681 patent until after Regeneron 16:48:48 6 conducted its VIEW 1, VIEW 2 trials. As discussed 16:48:50 7 in Section V1.C, the prior art was littered with 16:48:53 8 failed attempts to develop and extended dosing 16:48:57 9 regimen for the treatments of wet AMD. Many of 16:48:59 10 these failures are only recognized after the trial 16:49:01 11 was completed, or upon post hoc analysis, which 16:49:03 12 would have contributed to a general skepticism by 16:49:07 13 the POSA regarding whether a prospective fixed 16:49:09 14 extended dosing regimen would be successful until 16:49:13 15 the results were recognized. 16:49:16 16 In addition here, the Phase 2 results of 16:49:18 17 VEGF Trap-Eye and CLEAR-IT 2 would have created 16:49:22 18 uncertainty that VEGF Trap-Eye would be effective 16:49:25 19 if dosed on a Q8 regimen. That skepticism is 16:49:27 20 reflected in Regeneron's design of its Phase 3 16:49:31 21 study design, on the hierarchal ranking, et cetera. 16:49:33 22 So I do offer that opinion, yes. 16:49:39 23 Q. And as part of offering that opinion, you 16:49:42 24 considered the CLEAR-IT 2 trial, right? 16:49:50 25 A. I beg your pardon? 16:49:53 Page 226	1 Q. -- 1006? 16:51:28 2 A. I've got Dixon. 16:51:32 3 Q. Okay. I want to now refer you to page 1577, 16:51:40 4 in Dixon, right above, expert opinion. Let me know 16:51:46 5 when you're on that page, and I'll point you -- 16:52:02 6 A. So page 1577? 16:52:03 7 Q. Uh-huh. 16:52:04 8 A. Okay. 16:52:06 9 Q. Do you see, on the first full -- second full 16:52:06 10 sentence there, rather, it -- again, on the 16:52:11 11 left-hand column, it begins: VEGF Trap-Eye differs 16:52:13 12 from established anti-VEGF therapies, and it's 16:52:16 13 higher binding affinity for VEGF A, and its 16:52:20 14 blockage of placental growth factors 1 and 2. 16:52:26 15 Do you see that? 16:52:31 16 A. I see that. 16:52:31 17 Q. So, placental growth factors 1 and 2 are 16:52:32 18 sometimes abbreviated P1G1, and P1G2. 16:52:36 19 Is that right? 16:52:42 20 A. I'm not sure about that. 16:52:43 21 Q. Okay. 16:52:43 22 A. Maybe. 16:52:44 23 Q. Have you -- you don't recall seeing that? 16:52:44 24 A. I -- it's not a common -- it's -- it's -- 16:52:46 25 yes, I agree with this, that VEGF Trap-Eye is 16:52:53 Page 228
1 Q. As part of offering that opinion, you 16:49:59 2 considered the CLEAR-IT 2 trial? 16:50:01 3 A. Yeah. We call it the CLEAR-IT trial. 16:50:04 4 Q. CLEAR-IT 2 trial. 16:50:06 5 A. CLEAR-IT 2 trial, yeah. I don't know why 16:50:09 6 they called it CLEAR-IT, but... 16:50:09 7 Q. So, in doing that, did you consider the 16:50:12 8 patient population that was studied in the clear -- 16:50:16 9 in the CLEAR-IT -- sorry. I'm going to speak much 16:50:20 10 more loudly. So let me start that again, given the 16:50:22 11 heater's on. 16:50:25 12 As part of opining on the CLEAR-IT 2 trial, 16:50:25 13 did you consider the patient population that was 16:50:29 14 studied? 16:50:33 15 MS. STRUTHERS: Objection; beyond 16:50:34 16 the scope. 16:50:34 17 A. Yeah. I certainly don't discuss the 16:50:39 18 differences in populations. However, the CLEAR-IT 16:50:41 19 population, as was the VIEW population, was really 16:50:48 20 not different than our previous A and B studies. 16:50:53 21 It's mainly composing of older white patients with 16:50:59 22 wet age-related macular degeneration. 16:51:04 23 Q. (BY MR. SUMMERS) Do you have Dixon in front 16:51:08 24 of you now, exhibit -- 16:51:23 25 A. I can scare it up. 16:51:25 Page 227	1 supposed to block it. But it's not commonly 16:52:57 2 impugned in the pathophysiology of macular 16:53:01 3 degeneration. 16:53:04 4 Q. You -- you just hit on something I want to 16:53:04 5 ask you about. 16:53:05 6 As of 2011, was there a belief that 16:53:05 7 placental growth factors 1 and 2 were involved in 16:53:10 8 the pathogenesis of macular degeneration? 16:53:15 9 MS. STRUTHERS: Objection; beyond 16:53:19 10 the scope. 16:53:20 11 A. Yeah, we certainly don't talk about all the 16:53:20 12 different cytokines that could potentially affect. 16:53:31 13 But placental growth factors have never been high 16:53:39 14 on the list of targets for blockade. 16:53:42 15 Q. (BY MR. SUMMERS) Okay. I just want to talk 16:53:44 16 about as of 2011, because it's discussed in Dixon 16:53:46 17 here. 16:53:50 18 Was there a belief that, in fact, VEGF 16:53:50 19 Trap-Eye might have a higher likelihood of success 16:53:54 20 over, for instance, Lucentis, because it not only 16:53:58 21 found VEGF, but also would block placental growth 16:54:02 22 factors 1 and 2? 16:54:10 23 MS. STRUTHERS: Objection; beyond 16:54:12 24 the scope. 16:54:13 25 A. Yeah, we certainly don't talk about it in 16:54:13 Page 229

1 the declaration. It's -- it -- there wasn't a 16:54:16 2 whole lot of discussion around that, that I 16:54:24 3 remember. 16:54:26 4 Q. (BY MR. SUMMERS) Okay. So that's not 16:54:26 5 something in forming your opinion on reasonable 16:54:27 6 expectation of success that you considered? 09:34:28 7 A. I don't discuss that that's informing my 16:54:31 8 reasonable expectation of success. My reasonable 16:54:39 9 expectation of success was predominantly paragraph 16:54:43 10 116, page 56: The results of the CLEAR-IT 2 show 16:54:58 11 the therapeutic effect of VEGF Trap-Eye began to 16:55:03 12 wear off between week 4 and week 8. The slide 16:55:05 13 below shows central retinal lesion thickness. A 16:55:08 14 decrease in central retinal thickness corresponds 16:55:12 15 to drying of the macula and the fluid that is 16:55:13 16 created by the angiogenic process of wet macular 16:55:17 17 degeneration. In contrast, an increase in CRT 16:55:21 18 corresponds to fluid re-accumulation on the retina 16:55:23 19 and indicates a need for retreatment. 16:55:26 20 As shown in the slide below, there's 16:55:29 21 re-accumulation of fluid between week 4 and week 8, 16:55:32 22 in the quarterly dosing arms (curves for arms 16:55:37 23 0.5Q1, 2Q12, and 4Q12 trend upwards) which 16:55:40 24 continues through week 12. In fact, only the 16:55:44 25 treatment arms were successful in sustaining 16:55:46 Page 230	1 it's because this is part of the discussions around 16:57:17 2 whether or not extended dosing would be possible 16:57:24 3 with VEGF Trap-Eye? 16:57:30 4 MS. STRUTHERS: Objection to form, 16:57:32 5 and the same -- same objection, calls for 16:57:33 6 speculation. 16:57:35 7 A. Yeah, I don't know. 16:57:35 8 Q. (BY MR. SUMMERS) Okay. It says -- 9 A. I would have to speculate. 16:57:45 10 Q. It says right before it, right, the most 16:57:46 11 effective dosing regimen is a monitoring program 16:57:48 12 for anti-VEGF therapy and has yet to be firmly 16:57:52 13 established, but new treatments are aimed at 16:57:54 14 extending and improving on the efficacy of 16:57:55 15 ranibizumab. 16:58:01 16 Do you see that? 16:58:02 17 MS. STRUTHERS: Objection; document 16:58:03 18 speaks for itself. 16:58:04 19 A. I see that. 16:58:04 20 Q. (BY MR. SUMMERS) Okay. And then in the 16:58:10 21 very next sentence, it says that VEGF Trap-Eye has 16:58:11 22 both a higher binding affinity for VEGF and blocks 16:58:15 23 placental growth factors 1 and 2, right? 16:58:22 24 MS. STRUTHERS: Same objection; 16:58:26 25 document speaks for itself. 16:58:26 Page 232
1 effective treatment were the monthly dosing arms; 16:55:50 2 i.e., 0.5Q4, and 2Q4. 16:55:51 3 Q. Okay. So in forming your opinions under 16:55:57 4 reasonable expectation of success, you -- you 16:56:02 5 didn't consider -- I was trying make this in 16:56:04 6 one shot. So strike that. 16:56:16 7 You didn't consider whether there was, among 16:56:29 8 POSAs, a belief that VEGF Trap-Eye was more likely 16:56:34 9 to succeed because of its characteristics for 16:56:39 10 blocking placental growth factors 1 and 2. 16:56:44 11 Is that right? 16:56:49 12 A. So POSA, at the time, would have presumably 16:56:49 13 the same information I had, that -- that there was 16:56:52 14 very little evidence that placental growth factor 16:56:53 15 was influenced with age-related macular 16:56:57 16 degeneration. 16:57:00 17 Q. What's your understanding of why it's 16:57:00 18 discussed here in Dixon, then? 16:57:02 19 A. Repeat the question. 16:57:03 20 Q. What's your understanding of why placental 16:57:06 21 growth factors 1 and 2 are discussed here in Dixon? 16:57:10 22 MS. STRUTHERS: Objection; calls for 16:57:13 23 speculation. 16:57:14 24 A. No idea. 16:57:14 25 Q. (BY MR. SUMMERS) Okay. You don't think 16:57:15 Page 231	1 A. I see that. 16:58:26 2 Q. (BY MR. SUMMERS) Okay. But you don't think 16:58:27 3 that would have been relevant to a POSA's 16:58:28 4 consideration of the likelihood of the extended 16:58:31 5 dosing schedule of the VIEW 1 and 2 trials 16:58:34 6 succeeding, right? 16:58:41 7 A. I do not. 16:58:42 8 Q. Okay. All right. Who is Jeffrey Heier? 16:58:43 9 MS. STRUTHERS: Doctor, did you hear 16:59:09 10 the question? I think he asked you a question. 16:59:11 11 A. Oh, I'm sorry. I missed your question. 16:59:11 12 Q. (BY MR. SUMMERS) No, that's okay. 16:59:13 13 Who is Jeffrey Heier? 16:59:14 14 A. Jeff Heier is a retina specialist at TUFFs 16:59:15 15 and Ophthalmic Consultants of Boston. 16:59:19 16 Q. He -- he's a colleague of yours, right? 16:59:23 17 A. One more time. 16:59:24 18 Q. He's a colleague of yours? 16:59:25 19 A. He is a colleague of mine, yes. 16:59:26 20 Q. And he's a coauthor on a number of papers 16:59:28 21 with you, as well, right? 16:59:31 22 A. Correct. 16:59:32 23 Q. Okay. And in your declaration, in fact, you 16:59:33 24 refer to a conversation with him you had as 16:59:35 25 reflecting, in your view, skepticism around the Q8 16:59:38 Page 233

1 regimen, right? 16:59:47 2 A. That's correct, paragraph 121: In fact, I 16:59:47 3 recall discussing the design of Regeneron's Phase 3 16:59:52 4 VIEW trials with co-investigator Jeff Heier, before 16:59:55 5 the initiation of the view trials. At that time, 16:59:57 6 we had only preliminary Phase 2 data from 17:00:00 7 CLEAR-IT 2. And I recall that, looking at the rise 17:00:04 8 in means of central retinal thickness, we both 17:00:05 9 thought a VEGF Trap-Eye might last six weeks, but 17:00:07 10 had great skepticism that it would be non-inferior 17:00:10 11 to Lucentis on an eight-week fixed dosing regimen. 17:00:15 12 While we thought monthly dosing of VEGF 17:00:16 13 Trap-Eye would likely work, non-inferior to 17:00:19 14 Lucentis monthly dosing, we viewed the Q8 arm as a 17:00:21 15 long shot. Indeed, as discussed above, when 17:00:26 16 Regeneron ranked its dosing regimens for 17:00:27 17 statistical reporting, it ranked the two Q8 arms 17:00:29 18 below both 2Q4 and 0.5Q4 dosing arms, believing 17:00:32 19 that -- Regeneron believed both arms were more 17:00:40 20 likely than Q8 to hit their primary endpoints. 17:00:42 21 That's correct. 17:00:46 22 Q. Okay. I'm going to hand you a document that 17:00:46 23 you cite. This is Exhibit 2362. 17:00:49 24 MS. STRUTHERS: Thank you. 17:00:54 25 A. Okay. 17:00:56 Page 234	1 And then, Mr. Heier goes on: These 17:04:08 2 components were selected for their high affinity 17:04:11 3 for both VEGF-A and PlGF. 17:04:15 4 A. PlGF. I think it's PlGF, by the way. 17:04:22 5 Q. Oh, thank you. That makes more sense, PlGF. 17:04:24 6 Do you see where I'm at? 17:04:30 7 A. Yes. 17:04:31 8 Q. So, before today, were you unaware of -- 17:04:32 9 that -- of Mr. Heier's representation here that the 17:04:36 10 components of VEGF Trap-Eye were selected based on 17:04:41 11 their high affinity for VEGF-A and PlGF? 17:04:45 12 A. Repeat the question. 17:04:50 13 Q. Yeah. Before today, were you unaware of 17:04:51 14 Mr. Heier's representation here that -- 17:04:53 15 A. No, I mean, I knew that Regeneron -- 17:04:54 16 MS. STRUTHERS: Let him finish his 17:04:57 17 question, please. 17:04:58 18 Q. (BY MR. SUMMERS) Go ahead. 17:04:59 19 A. Sorry. 17:04:59 20 Q. No. Go ahead. I think you heard the 17:04:59 21 question. 17:05:01 22 MS. STRUTHERS: I actually didn't. 17:05:01 23 Could you please repeat the question? 17:05:03 24 Q. (BY MR. SUMMERS) Sure. So in forming your 17:05:04 25 opinions -- sorry. 17:05:06 Page 236
1 Q. (BY MR. SUMMERS) This is a document with 17:00:57 2 the title, VEGF Trap-Eye for Exudative AMD. 17:00:59 3 Do you recognize this document, Dr. Brown? 17:01:08 4 A. I do not. I don't know if I've ever seen 17:01:12 5 it. 17:01:18 6 Q. Okay. Well, let me direct you to the second 17:01:18 7 page of this document. It's page 2 of 17:02:29 8 Exhibit 2362. 17:02:39 9 Do you see there's a section entitled, VEGF 17:02:40 10 Trap Design? 17:02:45 11 A. Hold on a second, let me get there. 17:02:48 12 (The witness peruses the document.) 17:03:09 13 A. Okay. I'm there. 17:03:09 14 Q. (BY MR. SUMMERS) Okay. Do you see where 17:03:38 15 Figures 1 and 2 are bolded? 17:03:41 16 A. Figures 1 -- 17:03:43 17 Q. The words, Figures 1 and 2, on page 2, are 17:03:47 18 in bold. 17:03:51 19 Do you see that? 17:03:52 20 A. Yeah. 17:03:52 21 Q. Okay. So this section is discussing the 17:03:52 22 VEGF Trap-Eye design. And it says: As seen in 17:03:56 23 Figures 1 and 2, this results in two identical 17:03:58 24 arms, each constructed from select pieces, VEGF-R1 17:04:01 25 and VEGF-R2. 17:04:08 Page 235	1 Were you unaware, prior to today, of 17:05:20 2 Mr. Heier's statement here, that the components of 17:05:22 3 VEGF Trap-Eye were selected based on their high 17:05:27 4 affinity for both VEGF-A and PlGF? 17:05:30 5 MS. STRUTHERS: Objection; document 17:05:36 6 speaks for itself. 17:05:37 7 A. Yeah. I had no idea that Jeff wrote an 17:05:37 8 article in Retina Physician, which is typically a 17:05:44 9 non-peer-reviewed journal that appears in our 17:05:48 10 mailbox free. 17:05:51 11 So I had idea he wrote this article. I've 17:05:52 12 never seen it. And if I referenced it or looked at 17:05:54 13 it before, I didn't remember. But it's 17:05:56 14 well-written, though. 17:05:58 15 Q. I'll represent to you this is -- this was 17:05:59 16 submitted by Regeneron. 17:06:03 17 So, did you understand that it was published 17:06:06 18 to a POSA, that these arms were selected based on 17:06:14 19 their high affinity for both VEGF-A and PlGF? 17:06:17 20 MS. STRUTHERS: Objection, beyond 17:06:22 21 the scope. The witness has testified he hasn't 17:06:23 22 seen the document before. 17:06:25 23 A. You know, like I said, I haven't seen the 17:06:26 24 document before. I will point to you a couple of 17:06:39 25 things in the document. 17:06:41 Page 237

1 He -- you know, Jeff says -- or the writer 17:06:41 2 for Jeff says, placental growth factor PlGF -- and 17:06:43 3 this is in the VEGF family and its biologic 17:06:49 4 function, in the end of the -- right below the VEGF 17:06:51 5 family and its biologic function, there is the 17:06:54 6 first -- first full paragraph. 17:06:56 7 It says: Placental growth factor has been 17:06:57 8 prescribed as promoting pathologic angiogenesis, 17:06:59 9 but its role is less understood than that of 17:07:03 10 VEGF-A. Some more recent studies, including, 17:07:06 11 animal models, have implicated placental growth 17:07:08 12 factor purely in disease-related angiogenesis, such 17:07:12 13 as ischemia, inflammation, wound healing, and 17:07:17 14 cancer, implying that it's not -- and thought to be 17:07:19 15 implicated in wet macular degeneration. 17:07:24 16 Although it's -- it's certainly possible, I 17:07:26 17 guess. 17:07:29 18 Q. And then you see over on page 3, under VEGF 17:07:29 19 Trap-Eye Mechanism of Action, Mr. Heier is, again, 17:07:44 20 discussing both the unique binding properties of 17:07:50 21 VEGF Trap-Eye and predictive modeling studies that 17:07:57 22 indicate it should have a longer duration of 17:08:00 23 activity -- 17:08:03 24 A. So where is that under the VEGF 17:08:03 25 Trap-Eye mechanism -- I'm sorry, I was -- 17:08:05 Page 238	1 properties and the studies indicating it has a 17:09:18 2 longer duration, that this is something that 17:09:20 3 supports the idea that it may be able to produce 17:09:25 4 stainable improvements in visual acuity and/or 17:09:30 5 reduced injection frequency? 17:09:33 6 MS. STRUTHERS: Objection; beyond 17:09:34 7 the scope, the document speaks for itself. 17:09:35 8 A. Yeah. And particularly talking about 17:09:37 9 predictive modeling strategies, which I'm not an 17:09:45 10 expert in and -- and don't offer an opinion on 17:09:47 11 them. Most of them don't work, but maybe this one 17:09:49 12 would. 17:09:51 13 Q. (BY MR. SUMMERS) Was it beyond the scope of 17:09:51 14 your report to consider the characteristics of VEGF 17:09:55 15 Trap-Eye as they were known to a POSA when 17:10:00 16 evaluating reasonable expectation of success? 17:10:02 17 MS. STRUTHERS: Objection; 17:10:03 18 mischaracterizes the testimony. 17:10:05 19 A. I did consider the characteristics of VEGF 17:10:05 20 Trap-Eye. 17:10:08 21 Q. (BY MR. SUMMERS) And -- 17:10:08 22 A. And knew -- and knew that it blocked 17:10:08 23 placental growth factor, and didn't think it a 17:10:13 24 pathologic role in wet AMD, according to the best 17:10:14 25 of my knowledge. And this paper doesn't convince 17:10:19 Page 240
1 Q. VEGF Trap-Eye Mechanism of Action, on page 17:08:05 2 3. Let me know when you're there. 17:08:07 3 So you see the header there. It's just the 17:08:09 4 second sentence that I'm referring to you. 17:08:11 5 A. I see the sentence, yeah. 17:08:13 6 Q. Okay. So again, like Dixon, like the PIER 17:08:30 7 paper that we were looking at, there's, again, a 17:08:32 8 reference to the unique binding properties of VEGF 17:08:36 9 Trap-Eye and predictive modeling that indicates 17:08:42 10 that it should have a longer duration of activity, 17:08:45 11 right? 17:08:47 12 MS. STRUTHERS: Objection; beyond 17:08:47 13 the scope, document speaks for itself. 17:08:48 14 A. Repeat the question. 17:08:49 15 Q. (BY MR. SUMMERS) Sure. Like the PIER paper 17:08:50 16 we looked at in Dixon, you see, again, Mr. Heier is 17:08:53 17 referring to both the unique binding properties of 17:08:58 18 VEGF Trap-Eye and predictive modeling that 17:09:02 19 indicates that VEGF Trap-Eye should have a long 17:09:05 20 duration of activity? 17:09:12 21 MS. STRUTHERS: Objection; beyond 17:09:12 22 the scope, document speaks for itself. 17:09:13 23 A. Yeah, I see the words, yeah. 17:09:14 24 Q. (BY MR. SUMMERS) Okay. And he -- he's 17:09:15 25 indicating here, again, that the unique binding 17:09:16 Page 239	1 me otherwise. 17:10:20 2 Q. Okay. Can you show me where in your report? 17:10:20 3 A. What I can show on my report is that in 17:10:26 4 section 6: State of the art, A, The Prior Art 17:11:03 5 Treatment of Angiogenic Eye Disorders With 17:11:06 6 anti-VEGF Therapies. Angiogenic eye disorders, 17:11:09 7 characterized by pathologic growth of abnormal 17:11:13 8 blood vessels and had vascular leakage from damaged 17:11:14 9 blood vessels, present significant risk to 17:11:17 10 patients' vision, absent treatment. 17:11:19 11 Angiogenic eye disorders and neovascular 17:11:21 12 eyes diseases include conditions such as iris 17:11:22 13 neovascularization, retinal vein occlusion, 14 diabetic retinopathy, diabetic macular edema, 15 neovascular glaucoma, wet AMD, and retinopathy 16 prematurity. A shared feature of angiogenic eye 17 disorders is the presence of elevated ocular levels 18 of VEGF, a molecule that plays a critical role in 19 the pathology of angiogenesis and vascular 20 permeability. 21 By 2005 -- I'm going to page 8, No. 27 -- it 22 was recognized by the POSA that treating patients 23 with certain anti-VEGF agents, which reduce ocular 24 VEGF levels, could reduce the incidence of 25 pathologic angiogenesis and vascular permeability, Page 241

1 and prevent loss of vision, and even in many cases, 2 improve vision. 17:12:16 3 Before the use of anti-VEGF agents, 17:12:16 4 treatments for angiogenic eye disorders included 5 methods such as laser ablation and photodynamic 6 therapy. These treatments generally did not 7 improve vision. 8 And -- and so, our entire history of 17:12:16 9 anti-angiogenic eye disease is, the only effective 17:12:21 10 agents were Anti-VEGFs. This is the first agent to 17:12:25 11 block placental growth factor, if it's important, 17:12:30 12 to get the improved vision and maintenance of 17:12:34 13 vision. 17:12:39 14 In the standard of care Lucentis arm, we got 17:12:39 15 that with a pure VEGF-A blocker that blocked 17:12:42 16 nothing else. And in my opinion -- and I think 17:12:47 17 most POSAs -- that's the primary impetus for 17:12:50 18 macular degeneration intervention. 17:12:54 19 Q. So your report on reasonable expectation of 17:12:56 20 success has five sections. None of those five 17:13:13 21 sections evaluate a POSA's consideration of 17:13:19 22 beneficial properties of VEGF Trap-Eye, as we've 17:13:28 23 been discussing them, right? 17:13:33 24 MS. STRUTHERS: Objection; document 17:13:35 25 speaks for itself. 17:13:36 Page 242	1 body, right? 17:15:42 2 A. Repeat the question. I'm sorry, you kind of 17:15:43 3 faded on me there. 17:15:45 4 Q. Yeah, that's okay. 17:15:46 5 So we've -- we've gone through Dixon, the 17:15:47 6 papers you coauthored on CLEAR-IT 2, and 17:15:50 7 Mr. Heier's paper that we were just discussing in 17:15:55 8 Exhibit 2362. And all three of them discuss the 17:16:02 9 potentially advantageousness properties of VEGF 17:16:07 10 Trap-Eye, when it comes to binding and having a 17:16:10 11 longer duration in the human body, right? 17:16:14 12 MS. STRUTHERS: Objection; 17:16:16 13 mischaracterize the documents. Objection to form, 17:16:18 14 and the documents speaks for themselves. 17:16:21 15 A. So, the paper authored Heier, that is 17:16:22 16 probably written by the writing assistant, so 17:16:31 17 Alicia Woods, Ph.D., it's so well-written -- not 17:16:35 18 that Jeff couldn't write it himself -- you know, 17:16:36 19 talks about all these characteristics of -- of VEGF 17:16:39 20 traps. 17:16:45 21 And then there's a little clinical data, 17:16:45 22 study of wet AMD, the Phase 1. And we talk about 17:16:49 23 the Phase 1 in my -- in my declaration. And we can 17:16:53 24 go there. 17:16:56 25 CLEAR-IT 1 involved administration of a 17:17:00 Page 244
1 A. Irrespective of its molecular weight or pH 17:13:36 2 or binding affinity or molecular structure or human 17:13:54 3 structure, or -- et cetera, the POSA would have 17:14:00 4 understand, in a trial of humans, that fluid 17:14:04 5 re-accumulation, paragraph 117, page 58, between 17:14:06 6 week 4 and week 8, would strongly suggest that VEGF 17:14:11 7 Trap-Eye would not be effective on an eight-week 17:14:16 8 dosing interval. 17:14:21 9 Q. (BY MR. SUMMERS) So, Dixon, the CLEAR-IT 2 17:14:21 10 papers that you coauthored, Mr. Heier's paper, all 17:14:30 11 discuss the potentially advantageousness properties 17:14:36 12 of VEGF Trap-Eye in binding and maintaining 17:14:40 13 duration, and none of them discuss the OCT data 17:14:45 14 that you suggest strongly suggests that Q8 dosing 17:14:51 15 wouldn't work, right? 17:14:59 16 MS. STRUTHERS: Objection; 17:15:00 17 mischaracterizes the documents. 17:15:02 18 Q. (BY MR. SUMMERS) Let me -- let me strike it 17:15:03 19 and make it simple for you. 17:15:10 20 In discussing the potential likelihood that 17:15:12 21 VEGF Trap-Eye could be used for extended dosing, 17:15:17 22 we've seen Dixon, CLEAR-IT 2, Mr. Heier's paper, 17:15:21 23 all discussing the potentially advantageous 17:15:35 24 properties of VEGF Trap-Eye, when it comes to 17:15:37 25 binding and having longer duration in the human 17:15:39 Page 243	1 single injection of VEGF Trap-Eye to only 21 17:17:00 2 subjects who were assessed six weeks later. Dixon 17:17:04 3 does not -- 17:17:05 4 Q. (BY MR. SUMMERS) Are you reading from your 17:17:05 5 declaration? 17:17:06 6 A. It's page 61, paragraph 124. CLEAR-IT 1 17:17:06 7 involved administration of a single injection of 17:17:09 8 VEGF Trap-Eye to only the 21 subjects, who were 17:17:12 9 assessed six weeks later. Dixon does not disclose 17:17:16 10 specific information about CLEAR-IT 1 dosing, but 17:17:18 11 states that CLEAR-IT 1 was a sequential cohort 17:17:20 12 dose-escalation study, assessing 21 patients for 17:17:25 13 six weeks, designed to evaluate the safety, 17:17:28 14 tolerability, and biologic activity of intravitreal 17:17:30 15 VEGF Trap-Eye, in the treatment of neovascular AMD. 16 The POSA would have understand, based both 17 on the disclosure of Dixon and on general knowledge 17:17:39 18 about Phase 1 clinical trials, that the Phase 1 17:17:42 19 clinical study was not designed to meaningfully 17:17:45 20 assess the efficacy of even a single injection that 17:17:46 21 it tested, explaining that the Phase 1 studies are 17:17:49 22 designed to assess safety in dosage. 17:17:51 23 Moreover, Dixon reports that CLEAR-IT 1 best 17:17:53 24 corrected visual acuities results, on which 25 Dr. Chaum, relies were measured six weeks after the 17:18:04 Page 245

62 (Pages 242 - 245)

1 study participants received the injections. These 17:18:05 2 results, therefore, did not provide any information 17:18:06 3 where VEGF Trap-Eye would be more durable for eight 17:18:08 4 weeks. Even a small number of participants 17:18:14 5 injected in CLEAR-IT 1. 6 I hold that human trials, CLEAR-IT 1, 17:18:17 7 CLEAR-IT 2, offer way more examples, or way more 17:18:22 8 evidence, of the potential duration or dosing 17:18:25 9 regimen of a drug than any preclinical molecular 17:18:28 10 characteristic. 17:18:37 11 Q. And your conclusion, based on those human 17:18:37 12 trials, including CLEAR-IT 2, was that the 17:18:41 13 potential duration was sufficient to support dosing 17:18:43 14 the 2-mgs every eight weeks, and that it would be 17:18:47 15 as effective as monthly dosing, right? 17:18:51 16 MS. STRUTHERS: Objection; 17:18:54 17 mischaracterizes the testimony. 17:18:55 18 A. That's -- you must not have been listening 17:18:55 19 to me for the last seven hours. 17:18:57 20 But we said it's worth trying, but unlikely 17:18:59 21 to work. Three doses and then Q8 were unlikely to 17:19:03 22 be non-inferior to monthly ranibizumab, as was seen 17:19:09 23 in MARINA and ANCHOR, gold standard with visual 17:19:11 24 acuity gains that were maintained without 17:19:14 25 fluctuation. 17:19:17 Page 246	1 reductions in retinal thickness and improvements in 17:20:58 2 visual acuity and was well tolerated in patients 17:21:02 3 with neovascular... 17:21:05 4 That's the conclusions of that paper. 17:21:07 5 Q. (BY MR. SUMMERS) You also said, based on 17:21:09 6 the data from CLEAR-IT 2, on page 1095, that there 17:21:22 7 was data supporting that the duration that VEGF 17:21:30 8 Trap-Eye was sufficient to raise the possibility 17:21:37 9 that dosing with 2-mgs every eight weeks may be as 17:21:39 10 effective as a monthly dosing, right? 17:21:44 11 MS. STRUTHERS: Objection; the 17:21:52 12 document speaks for itself. 17:21:52 13 A. That makes sense. 17:21:52 14 Q. (BY MR. SUMMERS) Yeah. While I understand 17:21:54 15 what you're saying, in your opinion, that the 17:21:55 16 clinical trials provide the best evidence of 17:21:58 17 duration, you don't disagree that in discussing the 17:21:59 18 likelihood that VEGF Trap-Eye would support 17:22:05 19 extended dosing, multiple authors, including 17:22:11 20 yourself, discussed it's binding affinity and 17:22:16 21 likely longer duration in the human body, right? 17:22:23 22 MS. STRUTHERS: Objection to form, 17:22:27 23 vague, mischaracterizes documents. 17:22:28 24 A. I'm lost. What was the question? 17:22:30 25 Q. (BY MR. SUMMERS) Sure. You don't disagree, 17:22:34 Page 248
1 Q. (BY MR. SUMMERS) Right. But you say on 17:19:17 2 Exhibit 2 -- 2296, page 1095, that the data from 17:19:20 3 the human clinical trials, which you -- 17:19:25 4 A. Where are we again? 2396, which one is it? 17:19:28 5 Q. The -- this is your paper. 17:19:30 6 A. I wrote a bunch of papers. Tell me which 17:19:33 7 one. 17:19:35 8 Q. On CLEAR-IT 2. 17:19:36 9 A. 2296? 17:19:40 10 Q. Yeah, 20 -- 2296, page 1095. 17:19:40 11 A. Got it. 2296, 1095. Okay. 17:19:44 12 Q. And this is data -- from what you just told 17:19:49 13 me, is the preferential human trials, when it comes 17:19:51 14 to learning about the duration of the molecule, 17:19:54 15 right? 17:19:57 16 MS. STRUTHERS: Objection; document 17:20:01 17 speaks for itself. 17:20:05 18 (The witness peruses the document.) 17:20:05 19 A. The important parts of a paper are in the 17:20:26 20 abstract. In the abstract, we say the reduction in 17:20:31 21 central retinal thickness, with the 2-milligram Q4, 17:20:39 22 and the .5-milligram Q4 were significantly greater 17:20:43 23 than each of the quarterly dosing regimens. 17:20:46 24 And the conclusion, repeated monthly 17:20:53 25 injections over 12 weeks demonstrated significant 17:20:55 Page 247	1 as we've seen today, from Exhibit 2297, for 17:22:37 2 instance -- let's start there. 17:22:42 3 A. 2297. 17:22:44 4 Q. 2297, exactly on the page that we've been 17:22:45 5 looking at the whole time, 1104. 17:22:50 6 2297 is a paper on which you're a coauthor, 17:22:57 7 right? 17:23:00 8 A. So what are we looking at again? 17:23:00 9 Q. So we're looking at the first full paragraph 17:23:11 10 in the right-hand column. 17:23:13 11 A. Of the discussion. 17:23:14 12 Q. Yeah. And it starts: The 52-week results 17:23:15 13 from a CLEAR-IT 2 study suggests that the efficacy 17:23:18 14 of VEGF Trap-Eye, established with an initial fixed 17:23:21 15 dosing regimen, is maintained with PRN dosing, and 17:23:25 16 that VEGF Trap-Eye has an extended duration of 17:23:28 17 action. 17:23:31 18 Do you see that? 17:23:31 19 MS. STRUTHERS: Objection; document 17:23:34 20 speaks for itself. 17:23:35 21 A. I see that. 17:23:35 22 Q. (BY MR. SUMMERS) Okay. So, this paper, on 17:23:36 23 which you were a coauthor, cited to the fact that 17:23:39 24 the data from CLEAR-IT 2, in fact, suggested that 17:23:43 25 VEGF Trap-Eye has an extended duration of action, 17:23:49 Page 249

1 right? 17:23:51	1 witness give his answer before you determine 17:26:21
2 MS. STRUTHERS: Objection; document 17:23:52	2 whether or not it's responsive. 17:26:22
3 speaks for itself. 17:23:53	3 Q. (BY MR. SUMMERS) Okay. Go ahead. 17:26:23
4 A. I read the sentences, yeah. 17:23:53	4 MS. STRUTHERS: Thank you. Go 17:26:24
5 Q. (BY MR. SUMMERS) Okay. And you go on in 17:23:59	5 ahead. 17:26:26
6 this paper that you coauthored to discuss the high 17:24:00	6 A. Okay. So you're telling me that we should 17:26:26
7 binding affinity of VEGF Trap-Eye, in the next 17:24:04	7 consider placental growth factor, and that blocking 17:26:30
8 sentences, right? 17:24:07	8 that, and blocking additional things, are a 17:26:32
9 High binding affinity of VEGF Trap-Eye, 17:24:07	9 surefire reason why things may work, and you should 17:26:34
10 presumed -- its presumed long intravitreal 17:24:12	10 consider that. 17:26:36
11 half-life, and activity against multiple VEGF 17:24:15	11 I'll direct you to paragraph 149, in the 17:26:37
12 family members, including PIGF, may contribute to 17:24:19	12 declaration about Conbercept. It's another VEGF 17:26:40
13 more sustained and comprehensive VEGF suppression 17:24:22	13 antagonist fusion protein developed by Chengdu 17:26:48
14 and may be achieved with currently used anti-VEGF 17:24:27	14 Kanghong. 17:26:52
15 agents.	15 The -- the specific molecular benefits of 17:26:52
16 Do you see that? 17:24:32	16 Conbercept is it not only blocks VEGF receptor 1 17:26:56
17 MS. STRUTHERS: Objection; document 17:24:32	17 and 2, as aflibercept, so it does block placental 17:27:01
18 speaks for itself. 17:24:33	18 growth factor, but also blocks VEGF 17:27:04
19 A. I see that. 17:24:33	19 receptor 3. So it's thought, maybe you block more 17:27:06
20 Q. (BY MR. SUMMERS) So in the context of this 17:24:33	20 stuff, you should do better. 17:27:09
21 paper, you had both data from clinical trials, 17:24:35	21 So Kanghong tested Conbercept in two global 17:27:10
22 suggesting an extended duration, and you were cited 17:24:38	22 Phase 3 trials. The studies were designed to 17:27:16
23 understanding of a POSA that VEGF Trap-Eye had 17:24:43	23 evaluate the efficacy and safety of two different 17:27:18
24 beneficial characteristics such as high binding 17:24:47	24 levels of the Conbercept intravitreal injection, as 17:27:19
25 affinity and a presumed long half-life, right? 17:24:50	25 compared to the approved vascular endothelial 17:27:22
Page 250	Page 252
1 MS. STRUTHERS: Objection; document 17:24:53	1 growth factor antagonist active control, 17:27:27
2 speaks for itself. 17:24:54	2 aflibercept -- 17:27:27
3 A. I read the paragraph, yeah. 17:24:54	3 Q. Hold up. Are you reading from your 17:27:27
4 Q. (BY MR. SUMMERS) Okay. And as we look at 17:24:56	4 declaration again? 17:27:28
5 Dixon, Dixon also discusses high binding affinity 17:25:03	5 A. I am, yeah, yeah. Page 71, paragraph 149. 17:27:29
6 and the presumed longer individual half-life in its 17:25:10	6 MR. SUMMERS: I'm going to move to 17:27:33
7 discussion whether VEGF Trap-Eye could be used for 17:25:15	7 strike this as nonresponsive -- 17:27:34
8 extended dosing, right? 17:25:18	8 MS. STRUTHERS: It's -- 17:27:35
9 MS. STRUTHERS: Objection; document 17:25:20	9 MR. SUMMERS: It's not -- this a 17:27:36
10 speaks for itself. 17:25:40	10 section of his declaration that's talking about 17:27:37
11 (The witness peruses the document.) 17:25:40	11 secondary considerations and not reasonable 17:27:40
12 Q. (BY MR. SUMMERS) If it would help -- 17:25:59	12 expectation of success. My question is about 17:27:42
13 A. So in my deposition, I do discuss -- 17:26:00	13 Dixon. 17:27:44
14 Q. So you mean your declaration? 17:26:07	14 MS. STRUTHERS: Please don't 17:27:45
15 A. -- the Conbercept -- 17:26:08	15 interrupt the witness. Let him finish his 17:27:47
16 Q. Sorry. 17:26:09	16 response. 17:27:49
17 A. Well, going back to the declaration, page 17:26:09	17 Go ahead, Doctor. 17:27:49
18 71, Conbercept -- 17:26:11	18 A. Yes. So we're discussing block in the 17:27:50
19 Q. Okay. My question is actually -- it's about 17:26:13	19 additional targets. And this one certainly blocks 17:27:52
20 Dixon. So -- 17:26:15	20 placental growth factor. And big Phase 3 trial, 17:27:55
21 MS. STRUTHERS: Yeah. 17:26:17	21 they spent a lot of money. Also blocks VEGF 17:27:58
22 Q. (BY MR. SUMMERS) -- with all do respect, 17:26:17	22 receptor 3, which should give you even a bigger, 17:28:03
23 this is not responsive. 17:26:19	23 more impressive blockade. 17:28:05
24 Dixon has got -- 17:26:20	24 They gave three loading doses of 17:28:10
25 MS. STRUTHERS: You -- let the 17:26:20	25 .5-milligram Conbercept at four-week intervals, 17:28:13
Page 251	Page 253

64 (Pages 250 - 253)

1 followed by half-milligram doses every eight weeks. 17:28:16 2 They gave three loading doses of 1-milligram 17:28:19 3 Conbercept at four intervals, followed by one every 17:28:21 4 12 weeks. And then, three loading doses of 17:28:24 5 2-milligram of aflibercept, followed by 2-milligram 17:28:26 6 doses every eight weeks, which, as you know, is the 17:28:29 7 Eylea label. 17:28:32 8 On April 9, 2021, Kanghong announced it was 17:28:34 9 stopping the Panda trials globally. The announce 17:28:37 10 noted that as many as 68 trial centers, more than 17:28:39 11 half the subjects' vision changes from baseline 17:28:42 12 after injection or equal to or even lower than 17:28:43 13 zero. And the steering committee on which I served 17:28:46 14 believed that the Panda trial has failed to achieve 17:28:49 15 its expected goals. 17:28:52 16 I -- I mention that because you take 17:28:53 17 something with placental growth factor that blocks 17:28:56 18 everything that aflibercept blocks, plus something 17:28:59 19 else, and it fails miserably. So just because you 17:29:04 20 have hypothetical reasons why something may work, 17:29:07 21 when you put it in humans, it often doesn't. 17:29:09 22 Q. (BY MR. SUMMERS) Okay. My question, to 17:29:11 23 which your answer is completely nonresponsive -- 17:29:13 24 MS. STRUTHERS: Objection to that 17:29:15 25 characterization. 17:29:18 Page 254	1 Dixon, and in your paper on the PIER study, you 17:31:13 2 agree that all three authors thought it noteworthy 17:31:20 3 that VEGF Trap-Eye had a higher binding affinity 17:31:26 4 and a perceived longer duration in the human body, 17:31:31 5 correct? 17:31:34 6 MS. STRUTHERS: Objection; calls for 17:31:34 7 speculation. The documents speak for themselves. 17:31:37 8 A. Yeah, I see that all the authors put it in 17:31:39 9 page -- almost the last page of each -- each. So 17:31:41 10 they must have thought it incredibly important. 17:31:44 11 Q. (BY MR. SUMMERS) Okay. And it's your 17:31:46 12 conclusion from this that you, in performing your 17:31:49 13 reasonable expectation of success analysis, can 17:31:56 14 ignore the evidence of the contemporaneous belief 17:32:00 15 that the improved properties would also improve the 17:32:03 16 chance that it could be extended, right? 17:32:06 17 MS. STRUTHERS: Objection; 17:32:08 18 mischaracterizes the testimony. 17:32:09 19 A. So I've seen no data to ever support the 17:32:10 20 placental growth factor increases duration, either 17:32:15 21 experimentally or in humans. 17:32:19 22 Q. (BY MR. SUMMERS) What about the data here, 17:32:20 23 beyond placental growth factor, that POSAs 17:32:22 24 understood that VEGF Trap-Eye had both a higher 17:32:27 25 binding affinity and believed that it had a longer 17:32:31 Page 256
1 Q. (BY MR. SUMMERS) I'm going to move to -- 17:29:18 2 I'm going to move to strike your answer. 17:29:18 3 But if you look at Dixon -- and you're 17:29:20 4 welcome to pull it up, it's Exhibit 1006. I'm on 17:29:22 5 page 1577, I'm on the right-hand column. 17:29:26 6 A. I see -- 17:29:32 7 Q. Dixon also discusses VEGF Trap-Eye's high 17:29:33 8 binding affinity, doesn't it? 17:29:38 9 MS. STRUTHERS: Objection; document 17:29:40 10 speaks for itself. 17:29:41 11 A. I see that. 17:29:41 12 Q. (BY MR. SUMMERS) Okay. You also see, if 17:29:50 13 you will return to Mr. Heier's paper that we were 17:29:55 14 looking at, Exhibit 2362 -- 17:29:59 15 A. 2362. 17:30:12 16 Q. -- on page 3, we just looked at this, that 17:30:13 17 under VEGF Trap-Eye mechanism of action, Mr. Heier 17:30:18 18 also discusses VEGF Trap-Eye's higher binding 17:30:22 19 affinity, as well as a belief in longer duration of 17:30:30 20 activity, based on predictive modeling, right? 17:30:32 21 MS. STRUTHERS: Objection; document 17:30:34 22 speaks for itself. 17:30:56 23 A. I see that. 17:30:56 24 Q. (BY MR. SUMMERS) Okay. So, in 17:30:57 25 Exhibit 2362, Mr. Heier's paper, in Exhibit 1006, 17:31:05 Page 255	1 duration in the human body? 17:32:34 2 MS. STRUTHERS: Objection; documents 17:32:35 3 speak for themselves. 17:32:37 4 A. I see it in the papers. 17:32:39 5 Q. (BY MR. SUMMERS) And is it your testimony 17:32:40 6 that that's irrelevant to a POSA's reasonable 17:32:42 7 expectation of success? 17:32:47 8 A. I think a much higher -- no offense to Jeff 17:32:47 9 Heier -- consideration is what we saw in human 17:32:57 10 studies. CLEAR-IT 2 is the best study we had, 17:32:59 11 where we tested multiple doses with different 17:33:02 12 intervals. 17:33:06 13 And it's the OCT findings that -- that would 17:33:07 14 give the POSA a reasonable -- not have given the 17:33:22 15 POSA a reasonable expectation of successfully 17:33:27 16 achieving the Q8 dosing regimen claimed by the '681 17:33:29 17 patent until after Regeneron actually conducted its 17:33:36 18 VIEW 1 and VIEW 2 trials. 17:33:39 19 Q. Okay. With all due respect, you owe 17:33:40 20 apologies to yourself as well, right, as an author, 17:33:42 21 in discussing the likelihood that VEGF Trap-Eye 17:33:44 22 could be used for extended dosing. You also 17:33:50 23 discussed, in Exhibit 2297, the high binding 17:33:52 24 affinity of VEGF Trap-Eye and its presumed long 17:34:00 25 intravitreal half-life, right? 17:34:06 Page 257

1 MS. STRUTHERS: Objection; document 17:34:07 2 speaks for itself. Can you point us to where 17:34:09 3 you're referring to? 17:34:10 4 MR. SUMMERS: Sure. We've looked at 17:34:11 5 it numerous times. Exhibit 2297, right-hand 17:34:12 6 column, first full paragraph on page 7. 1104 is 17:34:21 7 the page of this study. 17:34:25 8 MS. STRUTHERS: And could you repeat 17:34:29 9 your question, please? 17:34:30 10 A. Repeat the question one more time. I have 17:34:42 11 to apologize to myself? Is that the question? 17:34:43 12 Q. (BY MR. SUMMERS) Yeah, yeah, you said 17:34:45 13 apologies to -- you said apologies to -- 17:34:46 14 A. I -- I don't think I need to apologize. 17:34:46 15 Q. -- Mr. Heier, right? 17:34:49 16 A. I don't think I need to apologize to myself. 17:34:50 17 No, I said -- I used the word higher, like 17:34:52 18 H-I-G-H-E-R. I was playing a pun on words. But 17:34:56 19 the -- no apologies to myself. 17:34:58 20 I -- I think in many discussions, we do 17:34:59 21 hypotheses of why something may or may not work 17:35:01 22 or -- or may potentially explain the -- something 17:35:04 23 that's happening. 17:35:08 24 I -- this in no way is a level of scientific 17:35:09 25 evidence that it's actually doing anything, when we 17:35:14 Page 258	1 Dr. Brown? 17:36:22 2 MS. STRUTHERS: I'm confused. Where 17:36:25 3 is there? 17:36:34 4 A. One more time. 17:36:34 5 Q. (BY MR. SUMMERS) Dr. Brown, was your 17:36:35 6 testimony -- 17:36:36 7 A. Can you repeat the question? Yeah. 17:36:36 8 Q. Well, no. I want to know what your answer 17:36:37 9 was. 17:36:39 10 A. Tell me what your question was, so I make 17:36:40 11 sure I know what your answer was. 17:36:43 12 Q. Okay. I said, you -- you don't discuss the 17:36:45 13 OCT data that you point to in the last part of this 17:36:49 14 article, or anywhere else, as it relates to whether 17:36:54 15 VEGF Trap-Eye will likely maintain visual acuity 17:36:57 16 gains with less frequent dosing, right? 17:36:59 17 A. We discuss, in the abstract, which was what 17:37:01 18 most people read, and the -- and the -- the 17:37:04 19 overlying summary of the article, that -- is that 17:37:08 20 we discuss in the Brown, et al, paper, the 17:37:16 21 reduction in central retinal thickness in the 17:37:24 22 2 milligram Q4 and the .5 milligram Q4 regimens 17:37:28 23 were significantly greater than each of the 17:37:30 24 quarterly dosing regimens. 17:37:34 25 The conclusion, and again that's boldfaced, 17:37:34 Page 260
1 put it in the last parts of a discussion, or in a 17:35:17 2 non-peer-reviewed article on what exactly this new 17:35:25 3 molecule coming out from Regeneron that's written 17:35:29 4 by a -- a medical author that looks like it was 17:35:32 5 paid for Regeneron, along with Jeff. And I'm sure 17:35:36 6 he read it. It's well-written. So... 17:35:38 7 Q. So -- so this is -- according to you, the -- 17:35:40 8 the last parts of the article and I suppose -- 17:35:42 9 A. The discussion, yeah. 17:35:44 10 Q. -- can -- can never be ignored, but you -- 17:35:45 11 you don't discuss at all the OCT data that you keep 17:35:48 12 pointing to in this last part of the article or 17:35:52 13 anywhere else, as it relates to whether VEGF 17:35:54 14 Trap-Eye will likely maintain visual acuity gains 17:36:00 15 with less frequent dosing, right? 17:36:04 16 MS. STRUTHERS: Objection; 17:36:06 17 mischaracterizes the documents. And objection to 17:36:08 18 form. 17:36:10 19 A. Yeah, I don't see it there. So... 17:36:10 20 THE REPORTER: Say that again. I'm 17:36:13 21 sorry. 17:36:13 22 MS. STRUTHERS: What -- 23 MR. SUMMERS: He said, I don't see 17:36:15 24 it there. 17:36:15 25 Q. (BY MR. SUMMERS) Right? Is that correct, 17:36:17 Page 259	1 conclusions, repeated monthly intravitreal dosing 17:37:36 2 of VEGF Trap-Eye over 12 weeks demonstrated 17:37:41 3 significant reductions in retinal thickness and 17:37:44 4 improvements in visual acuity and was well 17:37:48 5 tolerated in patients with neovascular AMD. 17:37:49 6 So we talk about retinal thickness and 17:37:53 7 improvements in our conclusion and in our results 17:37:57 8 in our -- in our abstracts, which is the most -- 17:37:58 9 which is the summary of the article. 17:38:01 10 MS. STRUTHERS: I just want to ask 17:38:03 11 the videographer to give us a time on the record, 17:38:04 12 please. 17:38:06 13 THE VIDEOGRAPHER: Six hours, 57 17:38:08 14 minutes. 17:38:24 15 MS. STRUTHERS: Thank you. 17:38:26 16 Q. (BY MR. SUMMERS) So I'd like to turn your 17:38:27 17 attention to Exhibit 2286. 17:38:29 18 MS. STRUTHERS: So -- so, Counsel, 17:38:32 19 just before you ask your question, I'm -- I'm going 17:38:33 20 to let you know, we are going to be cutting you off 17:38:35 21 at seven hours. 17:38:37 22 MR. SUMMERS: Okay. Counsel, let me 17:38:38 23 ask my question then. 17:38:39 24 MS. STRUTHERS: Go ahead. 17:38:40 25 Q. (BY MR. SUMMERS) In the conclusion for your 17:38:41 Page 261

1 summary of the PIER study year 2, which I 17:38:44 2 understand -- 17:38:47 3 A. Which -- which paper are we on again? 17:38:47 4 Sorry. PIER? 17:38:50 5 Q. Yeah, PIER. Which I understand you're 17:38:51 6 saying -- 17:38:52 7 A. Regillo, got it. 17:38:53 8 Q. Yeah, the most important. In the conclusion 17:38:54 9 for the Regillo study, the part that you have told 17:38:58 10 me that people read, it is the most important, you 17:39:02 11 say, ranibizumab administered monthly for three 17:39:07 12 months, and then quarterly provided significant VA 17:39:11 13 benefit for patients with AMD-related subfoveal CNV 17:39:13 14 and was well tolerated, right? 17:39:19 15 MS. STRUTHERS: Objection; document 17:39:21 16 speaks for itself. 17:39:24 17 A. In the results, we say: Ranibizumab 17:39:24 18 arrested CNV growth and reduced leakage from CNV. 17:39:27 19 However, the treatment effect declined in the 17:39:31 20 ranibizumab groups during quarterly dosing; e.g., 17:39:35 21 at three months, the mean doses -- the mean changes 17:39:38 22 from baseline VA had been gains of 2.9 and 4.3 17:39:41 23 letters for the .3 and .5-milligram doses 17:39:47 24 respectively. 17:39:51 25 Q. (BY MR. SUMMERS) None of that is in the 17:39:55 Page 262	1 time, Counsel. 17:41:05 2 MR. SUMMERS: Okay. Let me make a 17:41:09 3 statement on the record before we go off, that 17:41:10 4 there's been a great deal of obstruction in getting 17:41:14 5 through this declaration, and we reserve the right 17:41:21 6 to hold open the deposition and seek more time. 17:41:24 7 MS. STRUTHERS: Counsel, I will 17:41:27 8 state on the record that we are closing the 17:41:28 9 deposition, that you've spent an inordinate amount 17:41:30 10 of time today asking questions that had nothing to 17:41:33 11 do with the scope of the doctor's declaration. So 17:41:35 12 any shortage of time is a matter of your own 17:41:37 13 making. 17:41:40 14 This deposition is closed. 17:41:40 15 THE VIDEOGRAPHER: Mr. Summers, did 17:41:45 16 you want your video synced with the transcript? 17:41:47 17 MR. SUMMERS: Yeah. 17:41:51 18 THE VIDEOGRAPHER: Ms. Struthers, 17:41:53 19 did you want to order a video? 20 (Discussion with multiple voices.) 17:42:02 21 THE VIDEOGRAPHER: Ms. Struthers, 17:42:03 22 did you want to order? 17:42:05 23 MS. STRUTHERS: Yes, I do want to 17:42:06 24 order it. 17:42:07 25 (Discussion with multiple voices.) 17:42:18 Page 264
1 conclusions, right? 17:39:57 2 A. Results and conclusions are all in the 17:39:58 3 abstract. 17:40:01 4 Q. Okay. And if we look back at the 17:40:02 5 CLEAR-IT -- CLEAR-IT 2 paper we've been referring 17:40:12 6 to, Exhibit 2297, the conclusions there are PRN 17:40:14 7 dosing VEGF Trap-Eye at weeks 16 to 52 maintained 17:40:21 8 the significant anatomic -- 17:40:25 9 A. Which one -- which one are we at now? 17:40:28 10 Sorry. Which one of the two -- 17:40:29 11 Q. 2297. 17:40:29 12 A. 2297. 17:40:30 13 Q. The conclusion -- 17:40:31 14 A. Got it. 17:40:31 15 Q. You -- the conclusion there is PRN dosing 17:40:32 16 with VEGF Trap-Eye at week 16 to 52 maintained the 17:40:35 17 significant anatomic and vision improvements 17:40:39 18 established during the 12-week fixed dosing phase 17:40:42 19 with low frequency of reinjections, right? 17:40:45 20 A. Yeah. And in the results section, I point 17:40:49 21 you to the most robust improvements and consistent 17:40:52 22 maintenance of vision gains occurred in patients 17:40:56 23 dosed with 2 milligrams every 4 weeks. 17:40:59 24 Q. Sure. 17:41:02 25 MS. STRUTHERS: I believe we're at 17:41:04 Page 263	1 THE VIDEOGRAPHER: Okay. This 17:42:18 2 concludes today's videotaped deposition. The total 17:42:19 3 number of media units used was seven and will be 17:42:21 4 retained by Veritext Legal Solutions. We're off 17:42:24 5 the record at 5:41 p.m. 6 (The deposition concluded at 5:42 7 P.M.) 8 9 -- SIGNATURE REQUIRED -- 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 Page 265

67 (Pages 262 - 265)

1 CHANGES AND SIGNATURE 2 WITNESS NAME: DR. DAVID M. BROWN 3 DATE OF DEPOSITION: DECEMBER 13, 2023 4 _____ 5 _____ 6 _____ 7 _____ 8 _____ 9 _____ 10 _____ 11 _____ 12 _____ 13 _____ 14 _____ 15 _____ 16 _____ 17 _____ 18 _____ 19 _____ 20 _____ 21 _____ 22 _____ 23 _____ 24 _____ 25 _____ Page 266	1 COUNTY OF HARRIS 2 STATE OF TEXAS 3 4 REPORTER'S CERTIFICATE 5 6 I, AMY PRIGMORE, Certified Shorthand 7 Reporter in and for the State of Texas, hereby 8 certify that this transcript is a true record of 9 the testimony given by the witness named herein, 10 after said witness was duly sworn by me. 11 I further certify that the deposition transcript 12 was submitted on _____, _____ to 13 the witness or to the attorney for the witness for 14 examination, signature, and return to me by 15 _____, _____. 16 I further certify the amount of time used 17 by each party at the deposition is as follows: 18 Zach Summers - (07h02m) 19 Abigail Struthers - (00h00m) 20 21 I further certify that I am neither 22 attorney nor counsel for, related to, nor employed 23 by any of the parties to the action in which this 24 testimony was taken. Further, I am not a relative 25 or employee of any attorney of record in this cause, nor do I have a financial interest in the Page 268
1 2 _____ 3 DR. DAVID M. BROWN 4 5 THE STATE OF TEXAS) 6 SUBSCRIBED AND SWORN TO BEFORE ME, the undersigned 7 authority, by the said DR. DAVID M. BROWN on this 8 the _____ day of _____, 9 _____. 10 11 _____ 12 Notary Public in and for 13 the State of Texas 14 15 My Commission Expires: _____ 16 17 18 19 20 21 22 23 24 25 Page 267	1 action. 2 SUBSCRIBED AND SWORN TO by the undersigned 3 on this the 14th day of December, 2023. 4 5 6  AMY PRIGMORE, Texas, CSR Expiration Date: 4/30/2025 7 Firm Registration: 571 8 Veritext Legal Solutions 9 300 Throckmorton Street, Suite 1600 10 Fort Worth, Texas 76102 11 Phone. 817-336-3042 12 13 14 15 16 17 18 19 20 21 22 23 24 25 Page 269

68 (Pages 266 - 269)

&	100:25 105:14	178:25 179:20	1101 155:25
& 1:21 2:4,9 6:11,13	106:3 116:1,5	219:4,7,15	170:21
0	119:21 122:23	10,130,681 1:7	1104 157:14
0 154:17	123:21 130:10	3:11 16:23,24	158:21 164:13
0.2 135:14	130:13 131:21	100 80:22	168:11,12
195:23	135:9 140:12	151:4 201:11	169:2 170:10
0.3 94:21	140:15 142:18	1001 3:11	178:25 181:22
0.5 32:10 37:15	143:2 150:12	53:23 114:6	249:5 258:6
39:3 94:23	169:9 170:1,11	218:18	113 132:2
140:11 190:16	171:4 182:2	10019 2:10	115 143:18
190:23	190:11,18,18	1006 3:14	116 150:23
0.5q1 230:23	190:18,18	103:1,7 228:1	152:18,18
0.5q2 152:4	192:15 198:3	255:4,25	171:13 230:10
0.5q4 152:8	200:4,10,23	101 20:3 24:5	117 184:15
231:2 234:18	201:5,23,25	36:13 38:3	243:5
00h00m 268:18	202:3 215:2	39:9 226:2	12 3:19 65:12
07h02m 268:18	220:23,24,25	102 85:8	94:19,21 95:6
1	221:14 225:25	103 3:14	127:23 133:4
1 3:2,17 4:3	226:6 228:14	105 137:8	134:8 135:14
5:12 20:6	228:17 229:7	107 24:10	136:12,18
24:16,19 25:16	229:22 231:10	108 101:14	140:13,16,18
25:22 35:5	231:21 232:23	1093 148:23	142:19 152:5
36:3,16 37:17	233:5 235:15	1095 142:15,16	154:7 155:11
38:6 39:6	235:16,17,23	142:21 148:25	157:21 158:9
41:17 45:22	244:22,23,25	247:2,10,11	160:6 161:5
46:1,2,13,18,25	245:6,10,11,18	248:6	163:25 165:8
47:12 51:19	245:18,21,23	10:29 53:16	169:13 176:25
52:3 54:21	246:5,6 252:16	10:40 53:19	182:17,24
55:4,15,23	254:2 257:18	10th 2:4	184:3,9 189:7
56:8,9,24,24	1,200 103:19	11 95:7 116:2	195:21 197:9
57:10,15,19	1-5 113:18	119:21	197:10 198:13
58:8 65:4 81:6	1.6 94:22	11.3 135:11	199:8 200:14
97:24 99:11,21	195:22	110 24:18	219:15 230:24
	10 116:2	1100 156:21	247:25 254:4
	119:21 160:6		261:2 263:18

263:23 12-13-2023 5:5 121 31:18 184:25 186:11 187:25 188:22 189:24 234:2 122 25:14 124 245:6 128 43:19,20,21 12:09 107:2 12:43 107:5 12:45 108:16 12:47 108:19 13 1:12,18 56:7 56:14,20 57:3 58:1,13 189:7 198:14 266:3 133 3:16 134 47:19,21 139 3:17 13th 215:12,14 14 3:10 54:8,14 54:21 57:16,18 81:6 216:1 141 3:20 149 252:11 253:5 14th 269:3 15 54:8,14,22 90:7 91:16 93:2 103:4 113:15,17,22 114:21 115:4 115:11,13,23 116:13,15	117:9 118:3,13 118:19,22,23 121:1,12 125:12 146:19 193:2 1576 102:25 103:8 1577 228:3,6 255:5 16 140:23 152:10 154:18 157:1 263:7,16 1600 269:8 17 27:24 18 122:18 19 195:9 196:2 192 4:1 1990 9:4,9 1993 8:24 1995 9:9 1:40 139:17 1:58 139:20 2 2 3:2,17,17 10:21 11:2 20:6,18,19 23:6,6 24:6,7 24:16,19,23 25:15,16,22 31:11,22,23 32:9,10 33:10 33:10,12,16,18 34:9 35:15,16 35:20 36:3,12 36:17 37:3,4,8	37:17 38:7,17 38:18,22 39:6 39:17 56:9,24 65:4 71:15 86:16,21 94:23 95:3,5 97:4,7,8 98:11,12,25 99:16,21 100:2 100:3 101:1,20 103:23 106:3 116:1 119:21 122:24 123:21 130:10,13 131:22 135:11 135:12 140:4,6 140:7,8,9,11,14 141:1,2 144:1 144:3,5,10,11 144:13 148:25 149:2,6 150:11 150:12,24 151:3,5 152:1 152:9,22 153:1 153:17,24,24 155:9,9 158:19 160:14 161:17 164:10 166:18 169:14,21 170:1,11,24 171:4,5,14,25 173:23 176:12 176:16,17 177:13,15 178:24 179:19 179:20 180:16	182:2,7,9,15,25 184:22 185:4,4 187:18 189:1 189:16 190:11 190:20,22 192:4 200:4,10 200:22,23,24 201:4,5,7,23,25 202:3,4 209:22 209:24 210:1,5 210:15 211:15 211:24 226:1,6 226:16,17,24 227:2,4,5,12 228:14,17 229:7,22 230:10 231:10 231:21 232:23 233:5 234:6,7 235:7,15,17,17 235:23 243:9 243:22 244:6 246:7,12,14 247:2,8,21 248:6,9 249:13 249:24 252:17 254:5,5 257:10 257:18 260:22 262:1 263:5,23 2.5 184:6 2.6.3 103:9 2.9 262:22 20 53:13 80:16 91:25 112:11 125:13 196:2
--	--	--	--

247:10	87:18,23 88:9	197:22 198:24	263:12
2002 10:20	110:22 112:11	215:2	23 54:25
71:14 107:13	118:11 136:24	2185 3:12 59:2	234 4:4
2004 194:18,20	137:2,3,9,9,17	59:19 61:10,14	2362 4:4
2005 11:16	137:17,23	63:8	234:23 235:8
68:4 241:21	138:3,14,19	2189 3:13 60:6	244:8 255:14
2006 3:16	140:18 142:5	60:20 61:2	255:15,25
71:12 87:14	142:10 155:24	62:19	2396 247:4
94:10,12	159:10 161:14	22 54:25	24 27:24 41:25
107:14 115:3	162:19,21	2212 3:16	42:2,3,14
115:10 133:2	164:6 166:12	133:11,23	54:25 126:4
133:15 199:2,6	178:1 180:3	227 173:2	127:21 129:13
2007 79:7	202:10,12	2286 261:17	135:10,11
188:8 194:20	229:6,16	2296 3:20	136:8 194:23
199:2	2012 66:8	140:19 141:11	215:15
2008 188:8	2017 188:4	141:12,14	243 198:5,7
192:22 199:3	2021 3:13 60:8	143:9,19	245 197:23
2009 142:8,8	60:12 65:18	148:22 151:5	247 193:2
2010 142:9	254:8	152:2,22 156:6	196:8
188:4	2023 1:12,18	161:14 172:1	248 215:15
2011 3:12	175:6 266:3	173:19 180:17	24e 215:12
11:25 59:4	269:3	186:3,7 247:2	25 67:12 70:18
61:15 62:22	202300442 5:17	247:9,10,11	92:1 125:13
63:4,15,18,24	20328 269:5	2297 3:17	250 2:9
64:16,24 65:3	2050 14:1,9	140:24 150:8	26 54:21 55:4
65:8 66:3,13	2055 3:10	154:20 155:4	55:15,23 136:8
67:7 69:2,10	14:11 113:19	156:1 157:15	266 3:3
72:9,11,13,20	122:21	162:25 163:3	268 3:3
72:24 73:7,10	2060 3:10 8:14	168:2 170:10	27 114:12,15
74:3,22,24	21 54:25 57:16	172:2 173:3	115:19 199:2,6
75:6,23 76:14	57:18,19 58:7	181:4,23 183:6	241:21
76:16 77:23	197:2 199:4	183:20 186:3,6	28 129:4
78:5,11,24	245:1,8,12	201:16 249:1,3	2b 156:5,9
79:8,15 80:8	2131 4:1 192:8	249:4,6 257:23	2q 164:7
81:9,14 87:2,4	192:9 196:6,23	258:5 263:6,11	

2q12 152:4 154:3 164:7 230:23 2q4 185:16 231:2 234:18 2q8 185:15 201:21,23 202:3	3's 211:20 30 92:1 115:19 160:8 300 269:8 31 119:9 32 144:17 33 114:12 338 83:1,5,21 84:21 34 119:10 140:8 37 219:16 221:12 38 130:4,6 3:01 180:24 3:18 181:2 3b 145:2,4 148:23 149:15 149:18 150:9 156:1,8 167:20 168:17 170:21 3q8 200:14,17 200:17,23 201:5	218:21,22,25 219:2,9 230:12 230:21 243:6 263:23 4-6 122:17 4.3 262:22 4.5 94:18 4/30/2025 269:6 40 113:20 115:14 127:16 4000 1:22 5:19 41 70:5 42 132:18 44 45:20,23 4460 7:5,6 45 17:12 40:5 45:19,23 164:22 46 77:11 80:22 122:15,18 47 20:2 77:11 80:22 96:13 196:3 48 85:5 49 93:24 137:8 4:21 214:19 4:33 214:22 4q12 152:4 230:23	140:14 144:22 145:11,21 157:8 172:1 179:16 194:22 197:8 198:14 201:20 247:22 253:25 260:22 262:23 5.2. 165:18 5.4 165:17 5.4. 179:17 5.55. 201:19 50 24:10 151:4 195:8 196:3 50,000 111:15 52 24:18 95:15 140:23 157:22 158:10,18 163:2 165:3,10 197:2 199:5 200:5,11 249:12 263:7 263:16 53 3:11 55 140:2 55th 2:9 56 152:17 230:10 57 152:17 261:13 571 269:7 58 57:20 134:14 136:7 219:5,8 243:5
3			
3 3:21 25:4 31:12,13,20 33:12 44:6 64:9,9 65:19 71:15 86:25,25 89:12 94:19 95:3,5 100:5 101:18 103:9 106:13 116:2 119:21 130:22 135:13 141:18 144:16 145:1 152:22 153:2,8 155:25 167:7 168:9 169:16 169:23 170:23 177:5 180:16 182:1 185:1 190:12 194:22 195:21 221:12 226:20 234:3 238:18 239:2 252:19,22 253:20,22 255:16 262:23	4 4 56:8,14,19,20 57:4 58:1,13 116:2 119:21 140:12,15 150:25 151:11 152:3 154:11 154:17 171:15 172:3,13 177:18 178:5 184:5 197:23	5 5 24:23 95:4 104:1 116:2 119:21 135:9 135:11,12	

59 3:12 135:2 164:22 5:00 164:20 5:20 164:19 5:41 265:5 5b 163:24 165:5 5q12 144:21,21 5q4 144:20 165:17 185:16	61:4 70:10 81:6,13 97:23 102:11,18 103:15 104:14 113:25 114:7 117:25 118:25 119:4 120:2 218:18 220:23 220:25 226:5 257:16	172:3,13,17 177:18 178:5 179:21 182:14 184:9 230:12 230:21 241:21 243:6 8.3 145:9 8.8 145:9 817-336-3042 269:9 83 70:5 117:14 84 132:17,19,20 865 2:4	abandoned 164:6 abbreviated 228:18 abby 123:6 abigail 2:8 6:11 268:18 abigail.struth... 2:10 ability 139:6 159:21 170:5 ablation 242:5 able 25:7 37:19 44:11 95:16 108:2 167:6 240:3 abnormal 67:14 241:7 above 1:17 32:7 144:20 165:17,18 185:13 197:10 216:14 228:4 234:15 absent 67:17 241:10 absolutely 91:13 127:16 abstract 247:20 247:20 260:17 263:3 abstracts 66:2 261:8 academy 142:5
6	69 125:19	83 70:5 117:14	
6 3:6 27:16,18 27:19,24 116:2 119:21 241:4 6.52. 201:20 6.6 135:10 60 3:13 31:18 118:17 136:8 61 245:6 64 129:4 65 47:19 68 254:10 681 17:1,4,7,10 17:17 18:5,20 19:2,18,22 20:5 35:4 36:15 38:6 44:4 46:18,25 48:25 49:16 50:1,4,13,19 52:4,15,24 53:21 54:4 55:23,25 56:15 57:3,5,16 59:21 60:22	6:00 164:20	84 132:17,19,20 865 2:4	
	7	9	
	7 56:2 67:12 114:7,8,14,15 115:16,19 116:2 119:9,21 121:19 258:6 700 1:22 5:19 71 251:18 253:5 73 140:7,8 75 190:11 76102 269:8 77002 5:20 78 116:15 79 130:7 7:40 164:19	9 116:2 119:21 179:23 193:2 254:8 90 9:9 90017 2:5 93 9:5,7 95 9:7 96 80:22 98 77:10 82:5 82:13 84:5 86:12 99 77:10,18 81:4,10 82:5 84:5 86:12 9:07 1:18 5:4	
	8	a	
	8 3:10 95:4 116:2 119:21 140:13 151:1,9 152:3 154:11 154:17 171:16	a.m. 1:18 5:4 53:16,19 aao 142:8	

[acceptable - administration]

acceptable 135:22 136:3 193:16 acceptance 100:18 access 30:16,18 73:25 75:15,16 78:9,13,14 accumulation 171:23 172:2 172:12 177:18 178:6 230:18 230:21 243:5 achieve 24:11 46:11 95:17 110:20 118:2 137:18 196:18 199:22 254:14 achieved 110:8 137:19 144:2,3 144:11 149:1 172:7 173:9 250:14 achieving 20:4 35:3 36:15 38:5 97:22 117:20 118:12 144:10 150:21 226:4 257:16 acid 41:18 acknowledge 122:23 acknowledges 100:11	acted 209:23 action 5:25 238:19 239:1 249:17,25 255:17 268:22 269:1 active 116:18 116:21,25 117:2,4 216:13 217:7 223:9,10 253:1 activities 113:10 activity 95:11 139:6 160:6,8 238:23 239:10 239:20 245:14 250:11 255:20 actual 179:15 199:12 actually 12:7 13:1 14:3 32:24 37:16 39:6 40:15 45:10 55:12 99:20 120:14 133:10 134:9 146:4 170:8 178:25 179:8 179:16 181:5 186:22 189:25 206:4 211:25 213:1 236:22 251:19 257:17 258:25	acuties 111:2 245:24 acuity 86:23 89:12 91:12 92:24 94:15,19 110:8,21 113:23 114:23 117:10,22 118:4 121:2 122:3 124:2,2 126:23 127:24 134:23,24 135:10,13 144:2,11,16,23 147:19 149:1 150:15,17 153:7,10,12,16 153:20,20,22 157:21 161:24 162:1,5,8 163:1,13 165:3 165:9 166:1 169:15,16 172:16 173:22 174:6 175:13 175:24 176:4,7 176:11,15,25 177:1,12,22,24 179:3 182:16 182:23 183:6 183:21 193:11 194:4,12 195:6 195:18 196:5 198:2 240:4 246:24 248:2	259:14 260:15 261:4 ad 185:23 188:17 add 201:18 added 62:21 addition 20:18 23:5 24:6,24 35:15 37:3 38:17 60:13 98:10 118:11 152:10 226:16 additional 25:1 25:9 62:20 252:8 253:19 additionally 210:15 address 7:4,5 administer 106:19 administered 24:23 103:23 104:2 140:10 193:9 196:9 262:11 administering 63:9,19 64:18 64:25 66:14 69:1,9 administration 65:23 101:10 116:8 133:17 134:1 190:16 244:25 245:7
--	--	---	---

[adopt - anatomically]

adopt 89:23	254:5,18	147:10 158:24	226:9 235:2
adopted 100:21	age 3:15,22 4:2	163:7,8 167:10	240:24 241:15
132:7	59:12 61:19	175:10,12	244:22 245:15
adoption 100:9	87:21 141:20	236:18,20	261:5 262:13
132:3	192:14 227:22	252:3,5 253:17	amended 197:6
advantage	231:15	261:24	199:5
100:22 132:9	agency 29:19	aimed 232:13	amendment
advantageous	31:4 33:14	air 126:18	197:15
243:23	59:11	al 66:6,7 151:5	amendments
advantageous...	agent 13:13	155:22 156:10	197:5 198:25
243:11 244:9	68:13 74:19	215:6 260:20	american 142:4
adverse 110:5	110:2 113:11	alani 128:5	192:21
193:16,17	166:8 170:5	alcon 205:15	amino 41:18
affect 225:1,8	242:10	205:20	amount 116:17
225:18 229:12	agents 68:5	alicia 244:17	148:14 264:9
affected 150:17	78:19 111:14	align 203:6	268:16
affiliations 6:5	241:23 242:3	alleged 186:10	amy 1:19 5:22
affinity 159:3,7	242:10 250:15	allergan 177:9	268:6 269:6
159:10,15,17	ago 65:12 83:6	allow 169:12	analogous
159:23 160:4	83:23 203:18	alter 173:12	104:7
228:13 232:22	agree 5:10 14:6	amazing	analysis 20:14
236:2,11 237:4	48:12 81:11	195:17	28:15 35:11
237:19 243:2	84:10 118:21	amd 4:4 20:11	36:24 38:13
248:20 250:7,9	164:12 170:7	35:9 36:21	43:18 45:16,18
250:25 251:5	171:9 184:7,14	38:11 61:23,23	98:6 100:25
255:8,19 256:3	200:2 228:25	62:3,10 67:22	128:10 226:11
256:25 257:24	256:2	69:1,9 72:2	256:13
aflibercept	agreements	87:3,12,13,15	anatomic 86:22
31:14 49:4	188:13	87:25 97:20	122:10 150:14
59:11 68:19	ahead 8:4,9	98:4 103:20	153:19 263:8
122:8 166:23	15:5 17:13	114:19 120:14	263:17
190:15,20,21	28:4 77:9	132:23 135:23	anatomical
190:22 191:3	80:21 103:10	136:1,11,17	162:5 176:13
192:3 202:19	142:17 145:15	151:20 171:21	anatomically
252:17 253:2	146:11 147:9	191:16 196:11	109:16 110:4

[anatomy - approaches]

anatomy 111:3 153:11	109:25 112:10 113:24 114:19	31:9 32:20 33:8 34:7,25	232:12 241:6 241:23 242:3,9
anchor 47:11 71:3,18 84:13 95:14,17,19 106:14 108:6 110:12 113:5 113:10 118:16 120:11 123:18 124:3,7 125:25 126:6 127:2,5 135:7 179:25 195:6,16 196:6 196:13 197:6 197:10 198:11 198:19 213:1,3 246:23	116:8 119:1,6 120:10 121:5 135:23 136:3 151:20 171:21 178:10 230:16 241:5,6,11,16 242:4,9 angiograph 193:12 angiographic 194:13 angiography 157:11 animal 238:11 announce 254:9 announced 254:8 answer 7:18,23 8:4,5,9 15:3,5 16:11,14 20:22 23:19 54:18 68:23 69:16,22 72:4 105:4 108:21 115:7 136:10 145:24 150:3 190:8 208:24 252:1 254:23 255:2 260:8,11 answered 18:23 19:12 21:6 30:15	36:10 37:25 39:15 40:1 41:15 46:21 48:17 49:2,19 50:3 56:18 57:7 58:5,17 77:25 84:24 92:8 136:14,20 137:21 138:4 174:10 176:9 187:1,7 188:2 189:5,20 191:25 204:23 206:25 207:9 207:19 208:8 208:19 224:13 answering 120:25 antagonist 252:13 253:1 anti 13:13 30:4 33:16 35:22 68:5 70:24 71:5 74:19 75:18,22,25 76:16,23 77:2 77:7,20 107:14 108:2 111:14 120:10 122:24 124:4,14 126:7 128:15 138:17 166:7 178:11 197:25 228:12	242:10 250:14 anytime 8:7 166:16 apologies 257:20 258:13 258:13,19 apologize 76:6 76:9 202:2 258:11,14,16 appeal 1:2 appearance 6:3 appearances 3:2 6:5 appears 18:19 237:9 applied 26:6 28:12 29:22 30:3,10 31:7 32:17 33:1,5 34:4,22 35:19 36:7 37:20 39:12,23 84:7 90:20 applies 116:23 apply 13:12 22:25 23:12,25 82:7,12 84:2 90:24 appreciate 181:18,21 approaches 128:16

[appropriate - attention]

appropriate 117:3	118:19 127:18 131:8,21 135:9	35:7 36:18 38:8 43:24	233:10
approval 31:4 31:13 45:8 59:11 61:14 62:13,17 63:4 69:17,23 73:25 78:10 79:6 113:21 132:21 135:4 194:18	135:11,12 147:25,25 164:11 179:16 185:12,15,16 185:18 189:25 195:21,23 200:14,18,23 201:5 226:1 234:14 242:14	56:4 98:1 101:9 116:7 226:7 241:4,4 article 237:8,11 259:2,8,12 260:14,19 261:9	asking 8:12 14:24 15:25 16:1 32:25 39:22 50:7 97:6 98:17 147:8 186:23 208:2,3 216:19 264:10
approve 32:22		artificial 147:22	assess 245:20 245:22
approved 29:20 31:5 59:15 63:25 68:21 71:11 73:11 78:25 87:10,13 100:23 105:22 130:20 132:11 132:11,24 133:2,3 134:6 134:16 136:11 136:16 177:15 252:25	arms 24:22,25 25:1,9,12 32:10,12 117:24 132:14 144:23 151:10 151:12 152:4,4 152:6,8 172:4 172:4,5,17 174:22 185:16 185:18 190:15 201:7,21,23 202:3 230:22 230:22,25 231:1 234:17 234:18,19 235:24 237:18	asked 9:13,17 18:22 19:11 21:5 30:14 31:9 32:20 33:7 34:6,24 36:9 37:24 39:14 40:1 41:15 46:20 48:16 49:1,18 50:3 53:20 56:17 57:6 58:5,17 72:23 77:24 84:23 92:8,22,23 125:2 136:13 136:19 138:4 174:9 176:8 186:25 187:6,9 187:11 188:1 189:4,19 191:24 204:22 206:25 207:9 207:19 208:8 208:19 224:12	assessed 245:2 245:9 assessing 245:12 assistant 244:16 associated 45:4 95:11 110:7 assume 30:21 56:11 64:12 69:3,10 90:21 assumption 116:23 attached 1:24 attempt 126:4 attempts 20:9 35:8 36:18,19 38:9 68:11 98:2 99:8 226:8 attention 114:3 114:7,10 150:14 193:1 261:17
approximate 134:22			
april 254:8			
area 10:2,3,4,6 80:13,14	arnold 1:21 2:9 6:11,13		
argue 222:21	arnoldporter.... 2:10		
argumentative 102:20 176:2 186:13	arrested 262:18		
arm 32:6,9,10 32:12 94:21	art 19:17,22 20:8 30:20		

[attorney - begins]

attorney 6:6 17:24 268:13 268:21,24 attorneys 56:11 audience 175:19,21 audio 5:9 august 194:20 author 33:17 35:21 37:9 38:23 71:2,3 79:2,22 128:4 140:25 142:12 155:14,15 161:15 173:6 173:19 180:17 186:2,5,6 192:24 194:2 210:17,18,19 215:8 257:20 259:4 authored 71:2 173:8 202:18 244:15 authority 267:7 authors 56:25 57:11,12,25 65:16 71:4 172:24 180:8 248:19 256:2,8 availability 73:13 available 11:23 12:2 31:15 33:15 34:8	65:18 71:10,11 74:3,6,9,18,19 76:16 78:2,3,4 78:6,19,19 84:9 91:9 92:3 104:12 105:23 106:12,20 110:3 191:17 avastin 11:11 11:14 76:3,5 107:17 137:11 137:13,18,20 138:8,10,15 139:7 average 71:6 94:18 95:4,8 110:12,16 112:24 118:11 123:16 124:2 126:5,9 127:3 127:24 129:23 134:24 139:10 151:14 196:15 200:14,15,18 200:23 201:6 202:5 aware 82:24 135:24 187:17 187:21 188:23 189:13	babies 181:19 back 39:8 40:5 40:5 45:19 53:18 61:10 64:14 66:6 70:2 80:5,21 83:23 95:21 107:4,6,8 108:18 136:23 137:2 138:14 139:19,21 148:20 152:21 154:14 161:14 162:25 167:19 181:1,3,22,24 206:2 209:19 214:21,23,24 214:25 215:5 218:24 223:21 251:17 263:4 background 44:9 116:6 banks 205:5 bar 120:11 164:4 barn 107:23 base 117:2 based 30:3 33:20 70:9 86:20 102:3 106:13 116:20 117:16,19 126:13 144:15 150:8 160:4 166:21 168:7	172:11 182:8 182:22 197:19 236:10 237:3 237:18 245:16 246:11 248:5 255:20 baseline 94:22 94:24 145:5 153:2 163:2 195:22,24 254:11 262:22 basically 197:17 basis 28:15 88:17,19,23 89:8,9,11,13,17 92:12 96:1,2,5 96:23 97:12 98:21 128:15 162:9 169:11 224:7 bayer 131:1 bcva 145:5 153:2 182:13 beast 145:25 beg 27:22 226:25 began 94:17 140:23 171:15 182:17,24 195:20 230:11 beginning 6:6 94:12 157:1 begins 228:11
	b b 3:8 10:25,25 11:2 76:6,6 79:21 144:16 168:9 227:20		

[begun - blocks]

begun 150:25	113:22 118:23	207:8,18 208:7	bioepis 1:4
behalf 6:16 7:9	121:2 126:15	208:18 211:8	bioepsis 5:15
205:13	128:24 139:6	212:4,16 213:9	6:9 53:23
belief 229:6,18	148:4,4 197:12	213:18 214:5	biologic 238:3
231:8 255:19	240:24 245:23	215:24 216:17	238:5 245:14
256:14	248:16 257:10	216:19 217:2,9	biological
believe 6:13	better 14:6	218:7,13	160:6
8:15 85:24	125:10 126:11	219:19 221:5	bissonnet 7:6
101:24 127:1	148:2 151:25	221:15 225:3	bit 9:2 10:16
162:9 218:22	153:12,13	225:10,19	40:5 52:12
220:18 263:25	166:1 175:16	227:15 229:9	58:20 70:21,21
believed 32:11	179:2 180:5	229:23 237:20	71:24 81:4
185:17 234:19	223:12 252:20	239:12,21	130:1 143:17
254:14 256:25	bevacizumab	240:6,13	162:20 163:21
believing	68:15 74:18,21	256:23	164:8,17
234:18	74:25 75:3	biased 70:25	167:17
bell 126:12	76:5,6,17	biases 92:11	blind 70:20,21
bellaire 7:6,6	77:22 78:15	223:8,13	blinded 223:3
beneficial	107:16 177:8	big 10:9 45:7	blinding 70:19
242:22 250:24	beyond 9:19	128:25 211:19	76:20
benefit 43:24	12:16 13:15,21	253:20	block 111:14
71:13 134:23	14:18 15:9,19	bigger 146:1	229:1,21
134:24 169:20	16:7,16 17:21	253:22	242:11 252:17
193:11,23	18:6,23 19:12	binding 159:7	252:19 253:18
194:4,12	41:7,14 44:18	159:10,15,17	blockade
196:11,15,19	46:3,7 47:8	159:20,22	229:14 253:23
199:23 262:13	51:21 52:6,17	160:4 228:13	blockage
benefits 196:5	53:3 58:4,16	232:22 238:20	228:14
211:4 252:15	59:23 60:23	239:8,17,25	blocked 240:22
best 10:20 11:3	61:5 97:8	243:2,12,25	242:15
71:10,15 78:1	120:7,23	244:10 248:20	blocker 242:15
78:18 84:9,11	121:13 139:8,9	250:7,9,24	blocking 70:24
106:11,12,20	159:11 160:16	251:5 255:8,18	231:10 252:7,8
109:14,21	188:21 206:9	256:3,25	blocks 232:22
111:9 112:9	206:15,24	257:23	252:16,18

[blocks - case]

253:19,21 254:17,18 blood 67:14,15 76:22 80:2 241:8,9 blow 177:10 blue 142:3 155:23 board 1:2 82:24 83:7,10 83:16 board's 83:22 83:24 84:18 boards 185:23 188:17 body 244:1,11 248:21 256:4 257:1 bold 235:18 bolded 235:15 boldfaced 260:25 bond 186:18 border 147:19 boston 233:15 bottom 54:7 162:23 bought 203:25 bounce 151:13 bouncing 130:1 boyer 66:6,7 branch 79:10 79:15,16 87:7 87:19	bravo 79:21 120:15 144:16 145:2 172:1 break 8:7,10 53:13,17 101:6 106:23,25 107:3 108:17 139:15,18 164:16 167:14 167:18 180:21 180:25 181:16 183:15 208:25 209:10,13 214:16,20 breaks 8:6 181:6,9,12 breakthrough 45:12 132:23 bring 148:20 152:21 britni 2:13 5:20 broaden 52:11 brolocizumab 177:8 brown 1:11,15 3:6,11 5:13 6:20 7:1,3 14:2 14:9,12 32:14 33:2 34:20 42:12 53:20 59:7 60:10 107:7 138:2 139:21 140:18 141:22 151:5 155:18,21	156:9 181:3 192:16 195:25 209:19 214:23 220:13 235:3 260:1,5,20 266:2 267:3,7 bunch 127:20 179:22 247:6 burden 100:16 128:2 129:24 business 7:4,5 118:18 busy 211:18	cancer 191:16 238:14 capped 104:11 169:17 care 70:12,16 71:9,16,23 72:2,8,21,25 73:8,14,22 74:10,22,25 75:2,10,18 76:15,21 77:2 77:6,17,19,22 78:1,16,20,23 79:14,19 80:16 81:8,16,23 85:2,18 88:6,7 88:12,22,24 89:6 95:17,25 106:11 107:10 107:11 108:8 108:22 109:4 109:10,20 110:1,10,21 111:5,11,24 112:4,9,13,18 112:22,23 113:2 117:19 118:6 179:25 242:14 careful 15:21 carries 135:17 case 1:6 5:17 12:24 13:10 71:22 72:1,24 110:19 139:24
		c	
		c 2:1 5:1 76:6 79:2 ca 2:5 call 114:10 142:3 227:3 called 10:22 11:1 65:15 147:21 148:4 227:6 calls 22:1,8,16 23:3 26:10,20 27:5 28:23 29:6,14 30:1 40:10 90:13 93:11 97:1,15 98:24 124:8,21 191:13,25 231:22 232:5 256:6 canada 74:20 103:20 107:16	

[case - claim]

140:2 152:24 155:15 cases 68:9 75:20 242:1 catastrophic 75:21 177:6 197:24 cause 1:17 178:6 268:25 caused 79:16 causing 111:16 caveat 136:21 center 79:17,18 79:18 95:2,4 127:17 172:9 centers 254:10 central 31:25 78:21,23,25 87:6,20 151:17 151:21 157:5 171:18,19 185:6 201:10 230:13,14 234:8 247:21 260:21 certain 22:12 25:10,25 68:5 93:1 110:20 115:25 119:10 119:19 156:17 241:23 certainly 26:1 39:16,18 41:1 57:8 62:13 65:14 69:23	74:15,18,22 77:1 89:2 99:9 99:12 131:13 131:19 138:6 159:21 164:7 165:18 166:6 166:21 169:21 174:20 176:24 177:23 199:10 211:22 212:9 226:2 227:17 229:11,25 238:16 253:19 certainty 21:19 21:25 22:4,7 22:19,22 26:7 26:17 27:2,8 169:24 certificate 3:3 268:4 certified 268:6 certify 268:8,11 268:16,20 cetera 69:25 105:16,16,16 107:16 181:20 212:7 218:6 223:11 226:21 243:3 challenge 81:13 163:21 challenged 85:9 chance 10:23 39:5 256:16	change 135:11 145:5 153:2,7 160:22 162:3 165:15 166:22 changed 163:22 changes 3:3 153:22 157:4 180:15 254:11 262:21 266:1 changing 164:11 characteristic 246:10 characteristics 117:1 159:3 231:9 240:14 240:19 244:19 250:24 characterizati... 23:22 254:25 characterized 67:13 194:3 241:7 characterizing 32:24 charge 205:5 chart 114:24 116:3 119:12 119:15,22 120:21 121:21 145:21,25 148:5,9,12 156:4,5	charts 145:11 146:17 chaum 101:14 101:21 122:23 245:25 check 74:5 133:7 checked 148:15 checking 148:12 181:19 chengdu 252:13 child 181:19 choose 124:24 chronic 178:16 circle 64:14 circumstance 22:11 circumstances 89:19 cite 41:17 52:18 143:19 234:23 cited 25:23 186:1 249:23 250:22 civil 1:23 claim 18:20 41:17 45:21,22 46:1,2,13,18,25 47:12 48:25 49:16 50:1,13 50:19 51:19 52:3,15,24 56:15,16 57:5 57:15,19 58:8
---	---	---	---

[claim - cognizant]

59:21 60:22 61:4 80:23 83:25 85:8,11 86:14 105:14 220:23,24,25 221:14 claimed 20:5 27:13 35:4 36:15 38:5 40:9,18,23 42:16,17,23,25 43:5,6,14,15,24 44:1,4 45:15 97:23 99:19 101:17 102:2,7 102:10,17 103:15 104:20 226:5 257:16 claims 17:4,7 17:17 18:5 19:2,4,6 41:2 45:16 49:6 50:7 51:1,9 54:13,21 55:4 55:15,23 56:10 57:1,3,13,15 58:2,3 81:6,13 82:19 85:9 104:13 105:17 118:25 119:3,4 206:3,5 207:25 clarify 136:5 187:24 204:3 class 18:12	classic 157:10 193:14,14 201:13 classify 80:12 clear 3:17 9:25 12:10 15:25 20:19 21:11 23:6 24:7 25:15 30:6 31:11,15,23 33:10,16,18 34:9 35:16,20 36:12 37:4,8 38:2,18,22 39:17 67:1 86:16,21 97:4 97:7,8,18 98:12,25 99:3 99:16 100:2 101:1,20 122:7 122:10 135:15 137:16,21 140:4,6,7,8 141:2 150:13 150:24 154:2 155:9 158:19 160:13,14 166:10 169:14 169:21 170:1,1 171:5,14 176:16 177:1 178:24 182:9 182:25 184:22 185:4 187:18 189:1,11,16	200:22,24 201:4,7 202:4 209:22,24 210:1,5,15 211:15,24 226:17,24 227:2,3,4,5,6,8 227:9,12,18 230:10 234:7 243:9,22 244:6 244:25 245:6 245:10,11,23 246:5,6,7,12 247:8 248:6 249:13,24 257:10 263:5,5 clinic 73:14,23 78:1 100:9 140:21 clinical 12:4 25:3,15 29:17 31:1 70:9 73:24 74:16 75:5 78:8,13 87:17,19 88:9 88:13 89:2,13 89:16,21,24 90:4 93:24 94:7 100:21 105:24 106:13 117:17 122:24 123:9,14 124:4 124:14 125:22 126:14,15 127:21 132:4,8	135:4,5 146:18 147:21 148:17 169:20 190:4 190:10 191:4 191:10,22 194:24 195:9 202:19 210:14 213:21,23 214:7 225:2,7 225:13,17 244:21 245:18 245:19 247:3 248:16 250:21 clinically 157:20 158:9 167:4 193:22 clinician 161:6 clinics 8:25 close 116:22 126:1,3 144:24 165:23 closed 264:14 closely 102:21 closing 264:8 cme 76:8 cnv 193:12 262:13,18,18 coauthor 160:1 210:16 233:20 249:6,23 coauthored 243:10 244:6 250:6 cognizant 224:1
---	--	--	---

[cohort - compromise]

cohort 156:8 245:11	145:21 148:3 154:18 181:24	commonly 229:1	complete 20:22 56:4 224:2
cohorts 106:4 123:15 197:12	209:19 211:5 220:22 222:19	community 44:10 137:10	completed 20:13 25:22
collaborative 25:6	223:21	138:5,6,21 197:11	35:10 36:23 38:12 44:5
colleague 6:12 127:19 233:16	comes 106:10 107:22 108:1	company 130:19 159:16	86:25 98:5 106:3 199:7
233:18,19	243:24 244:10 247:13	comparable 137:19	226:11
colon 57:21	coming 259:3	comparative 159:20 161:11	completely 254:23
column 56:2,7 56:14,19,20	comment 162:3 173:19,21	compare 45:25 56:14 117:13	complex 202:2
57:3,16,18,19	174:8	140:9 194:20	compliance 129:20 223:16
58:1,7,13	commented 174:11	compared 33:22 37:14	compliant 129:12
103:9 114:7,14	commenting 172:24	104:1 134:21	complicated 10:7
114:15 115:16	comments 141:8 220:7	165:3,10	complications 128:9,13,25
115:19 116:5	commercial 44:1	190:13,14	comply 222:17
119:9 121:19	commercially 11:23 12:2	194:8 195:5	224:11
142:23,23,24	74:4,6,9 78:6	200:3,9,21	component 193:14
156:23 158:17	commission 267:15	201:3 252:25	components 236:2,10 237:2
158:21 163:3,4	commitments 224:5	comparison 57:2 154:16	composing 227:21
181:25 219:4,7	committee 141:6 188:11	164:12 196:4	composition 56:6
219:15,15	188:12 197:21	compensated 202:17,20,21	comprehensive 135:3 250:13
228:11 249:10	254:13	202:23,24	compromise 139:3
255:5 258:6	common 146:16 228:24	203:2,4,20	
columns 54:25		204:15	
combination 128:16		compensation 204:4,8	
combined 157:19 158:8		competitive 100:22 132:8	
come 34:18 40:4 69:18			
74:16 95:20			
107:8 127:20			
129:13 145:10			

[compromises - context]

compromises 180:9	263:13,15	confirms 24:19	178:12 179:24
conbercept 251:15,18 252:12,16,21 252:24 253:25 254:3	conclusions 248:4 261:1 263:1,2,6	confused 105:1 145:18 260:2	263:21
concept 168:14	conclusive 28:19 29:2,10 29:16	conjunction 84:21 157:8	constancy 116:23 148:8
concepts 166:20	concomitant 111:1 191:17	conjunctivitis 217:15 218:6	constructed 235:24
concern 178:6 184:7	concur 48:12	connection 139:14	construction 80:23 83:9,15 83:25 84:2,19 85:11 86:14
concerned 111:20	condition 130:13 131:9	consent 211:3,8 224:3	consultant 203:2,9,15,21 209:23 212:24
concerning 170:4	conditional 130:9	consider 16:11 83:8,14 84:18 116:13 121:4 191:18,20 227:7,13 231:5 231:7 240:14 240:19 252:7 252:10	consultants 233:15
conclude 196:17	conditioner 126:18	consideration 88:21 135:19 233:4 242:21 257:9	consulting 202:21 205:1,4 211:23
concluded 99:18 144:9 265:6	conditions 67:19 241:12	considerations 46:19 175:3 253:11	consuming 45:5
concludes 265:2	conduct 25:2	considered 74:10 99:9 117:25 209:6 226:24 227:2 230:6	contemporan... 256:14
conclusion 26:11,21 27:6 29:14 30:2 40:11 44:2 81:12 163:13 164:24 169:8 178:24 179:7 190:17 196:9 196:22 199:20 246:11 247:24 256:12 260:25 261:7,25 262:8	conducted 20:6 35:5 36:2,16 37:17 38:6 97:24 99:21 190:12 226:6 257:17	consistency 117:23	contemporan... 172:23 196:6
	confidence 131:8,14,21	consistent 71:8 74:21 113:11	contend 116:12
	confidentiality 188:13		contends 101:15
	confirm 28:4 54:10		content 71:20
	confirmatory 153:20		contention 118:22
	confirmed 94:25		context 114:18 119:1,5 120:25 206:7,13,18 208:9 219:10 250:20

[contingent - counsel]

contingent 204:6,9	194:23 253:1	42:12,13 51:12	178:7 182:25
continuation 156:4	controlled 4:1	52:15 53:1,9	186:3,4,7,8
continue 5:10	29:18 31:2	54:15 55:6	187:8 192:24
110:3 152:12	32:18 33:6	59:15,16 61:15	192:25 194:5,9
209:1 218:16	34:5 87:16,18	61:20 62:23	196:23 198:6,7
continued	87:24 88:8,13	63:3 69:14	198:24 199:16
134:21 140:22	88:18 90:3	74:11 75:1,7,8	199:17 200:6
140:23 157:3	113:7 148:15	76:4,5 79:9,12	200:12,19,20
172:8 196:16	151:14 192:13	79:13 80:1,11	200:25 201:6
continues	223:2	81:1 84:22	201:25 202:8
151:10 152:5	conversation	87:17 88:9,10	204:7,11,12
230:24	186:10,24	90:8,9 91:12	209:25 215:10
continuing	187:4 189:12	91:17,18,20	222:18 224:14
151:15	233:24	92:19 96:3,12	233:22 234:2
contradict	conversations	96:19,20 102:7	234:21 256:5
69:18	5:7 189:7	104:4,11,16	259:25
contrary 115:2	convince	110:11 112:8	corrected
115:9	240:25	119:2,7 122:4	113:23 118:4
contrast 151:20	convinced	122:14 123:3	118:23 121:2
171:21 230:17	37:15 39:5	123:12,22	245:24
contribute	cookie 181:17	124:16 126:25	correlate 153:1
250:12	copernicus	127:4,10,15	correlated
contributed	64:10	129:21 130:16	108:3
20:14 35:12	cornea 10:1	133:4 134:8	corresponding
36:24 38:13	80:3,3,6,6	136:18 142:13	71:4 152:14
98:6 226:12	corneal 79:24	143:9 145:6	corresponds
control 91:6	80:2,10	149:14 150:9	151:18,22
116:18,21	corner 54:7	152:19 153:3,8	171:19 230:14
117:1,2,4	correct 7:9,10	154:5,6,9,13,19	230:18
127:18 129:8	8:19 11:7	156:6 157:22	cost 25:3
147:25 164:11	16:23,24 17:5	158:19 159:4	costly 45:5
179:2,9 180:5	17:9,18 18:21	160:1,2 162:6	counsel 5:14
193:23 194:8	19:18,23,24	162:7 168:17	6:4 8:1,3 16:9
	27:21,25 31:3	170:12,15	18:8 72:19
	34:15,17 41:24	171:13 174:2,7	106:23 133:8

[counsel - data]

149:22 181:8 181:14 208:23 216:16 218:12 218:16 219:21 220:5 261:18 261:22 264:1,7 268:21 counsel's 7:18 143:16 country 21:12 74:15 county 268:1 couple 7:13 28:16 100:8 108:21 142:8 203:17 237:24 course 112:8 197:3 court 5:22 6:18 7:15,22 118:8 185:24 cow 107:23 cr 157:6 cr2 152:10 created 20:19 23:7 24:7 35:16 37:4 38:18 56:10 76:22 98:13 151:19 171:20 226:17 230:16 creating 57:1 credence 161:6 223:2	criteria 17:8,18 17:20,25 18:5 18:14,19 19:6 41:6,13 49:12 49:13 51:11,20 51:24 52:3,9 52:14,24 53:8 57:20 58:3,9 58:14,24 66:19 75:7 84:7 92:24 108:21 109:9 118:17 140:22 156:12 156:14,15,18 156:22,24 157:12 201:17 206:8,14,17,18 206:23 207:7 207:17,25 208:6,14 209:12 212:14 213:17 214:3 215:19 216:12 217:19,25 218:5,23 219:16,22 220:18 221:3,7 221:13 222:2 critical 68:1 241:18 criticism 224:7 cross 127:8 197:7 crossed 134:9 198:15,18	crossing 198:22 crossover 199:1,1,7,12 crt 31:24 151:21 152:13 171:22 172:13 173:15 177:18 230:17 cruise 79:1 120:15 crvo 66:7 114:19 csr 1:19 269:6 curing 178:14 currently 250:14 currents 134:14 curriculum 3:10 curve 126:12 curves 152:4 230:22 cut 9:23 cutting 261:20 cv 8:15,20 213:12 cytokines 229:12	dash 11:1 data 22:10,14 27:11 30:6,24 31:7,22 33:15 33:20,21 34:8 34:11 35:19 37:7,7,10 38:21 39:18,21 40:2 58:1 62:16 65:14 66:25 69:17 70:10 86:16,17 86:18 90:17 91:2 93:14,20 94:2,9,10,13 99:9,12,14,17 99:23 100:3 101:1,22 104:12 117:17 117:22 122:10 125:9 134:12 135:4 141:1 143:12 148:24 149:12 152:10 159:15 160:13 161:7,16,24,24 162:2,22 163:13 165:6 166:5,11 167:20,22,24 168:8,16 170:3 170:20,22 171:5 172:19 172:25 173:20 173:22 174:5,5
		d	
		d 5:1 65:15 damaged 67:15 241:8 darpin 177:9	

[data - depends]

174:22,25 175:1,5,23,24 178:7 179:15 184:16,22 185:4 187:18 188:20 189:1 189:16 195:2 195:11,12,13 195:16 197:9 197:10,20 199:9 210:9,14 234:6 243:13 244:21 247:2 247:12 248:6,7 249:24 250:21 256:19,22 259:11 260:13 date 11:25 62:1 62:8,13 63:4,7 63:12 72:10 120:15,16 266:3 269:6 dates 74:5 79:5 david 1:11,15 2:8 3:6,11 5:13 6:12,20 7:3 14:2,12 266:2 267:3,7 day 16:12 140:12,15 214:6 267:8 269:3 days 160:8 223:22	deal 10:9 264:4 deals 31:11 33:10 36:12 38:2 97:17 death 175:17 december 1:12 1:18 266:3 269:3 decide 212:19 decisions 83:22 declaration 3:10 12:18 13:23 14:2,4 14:12,20,21 15:1 16:10 17:5 18:10 19:3,16,20 22:24 23:12,24 26:3,14,24 27:16 28:13 29:24 33:4 34:3,19,23 39:13,20 40:6 43:13 47:20 48:12 52:25 55:3,10,11,13 55:22 56:13 58:19 59:3 60:2,8 67:2 70:3,6,16 77:9 80:18 81:11 82:7,12 83:9 83:15 84:17 85:6 96:12,18 97:11 98:16	99:5 112:19 113:15,17 121:16 122:16 125:15 130:4 132:3,18 137:8 143:19 152:19 152:20 161:9 162:20 170:19 171:11 177:16 184:16 187:16 194:17 196:1 197:3 199:4 204:5,9 207:2 209:3,8,15,16 209:20 213:21 216:18,21 219:23 220:1,4 220:19 221:9 221:18 225:22 225:24 230:1 233:23 244:23 245:5 251:14 251:17 252:12 253:4,10 264:5 264:11 declarations 184:21 187:11 decline 94:18 declined 95:3 262:19 decrease 95:2 151:17 171:18 172:17 230:14 decreased 128:2	decreasing 111:18,18 defined 120:20 121:20 191:5 defining 28:2 definition 18:14 21:15 123:14 degeneration 3:15,23 4:3 59:13 61:20 68:18 70:18 87:21 113:6 141:20 192:14 227:22 229:3,8 230:17 231:16 238:15 242:18 deliver 36:19 36:20 demonstrate 24:12 25:16 118:5 123:20 demonstrated 62:17 122:25 247:25 261:2 demonstrating 123:10 denuyl 2:8 6:13 depend 100:9 132:4 dependent 207:24 depends 138:16 192:2
--	---	--	--

[depose - discuss]

depose 14:24 deposed 7:11 deposition 1:11 1:14 5:13,18 112:19 209:4 212:8 218:14 218:16 219:24 251:13 264:6,9 264:14 265:2,6 266:3 268:11 268:17 depositions 83:5,21 described 156:9 description 3:9 56:5 design 24:19 31:19 37:9 116:25 169:15 169:22 174:23 177:15 188:7,9 191:4 202:25 203:2 225:13 226:20,21 234:3 235:10 235:22 designated 156:25 designed 25:16 79:21 128:5 140:9 188:10 190:12 194:20 245:13,19,22 252:22	designing 25:4 116:19 190:10 202:21 designs 31:12 detect 128:19 determination 46:15,17,24 52:2,13,23 54:12 55:2,14 55:21 58:12 90:18 91:2 101:2 determine 37:21 43:13 46:1 56:15 57:4 67:3 91:9 93:14,19 107:11 138:21 157:2 174:22 252:1 determining 23:13 29:22 36:7 176:12 develop 20:9 35:8 38:9 58:1 98:2 226:8 developed 107:15 128:8 252:13 developing 57:12 130:19 deviating 211:10 deviations 91:7 211:10	diabetic 60:13 62:25 63:1 64:18,25 65:23 66:14,19,22,23 67:4,5,6,21,21 68:17 73:8,10 73:15 74:4 75:19 76:12,15 76:17,20,21,25 77:1,4,5,21 78:5,17 87:7,8 87:9,10,11,20 114:22 148:6 241:14,14 diagnosis 111:20 112:8 diana 65:16 difference 94:22 195:24 differences 227:18 different 75:16 75:16,17 88:25 110:25 156:10 159:19 161:1,1 166:8 190:14 212:10 223:24 224:22 227:20 229:12 252:23 257:11 differs 228:11 dilated 127:21 129:14 diminish 174:18	direct 96:12 151:2 193:1 196:7 216:10 235:6 252:11 directed 115:16 directly 153:1 disagree 97:16 101:21 118:21 183:5,19,25 186:21 222:7 248:17,25 disappointing 94:13 195:13 disclose 102:7 245:9 disclosed 101:9 101:17 178:4 226:1 discloses 102:2 102:10,17,21 103:14 104:15 105:25 disclosure 56:4 245:17 disclosures 142:7 discounted 222:22 discuss 12:18 16:17 39:19 46:9 49:6,7 51:23 52:8 53:5 58:21,23 99:7,7,16 112:18 128:24
--	--	--	--

[discuss - document]

140:3 158:18 176:6 207:1 221:7 227:17 230:7 243:11 243:13 244:8 250:6 251:13 259:11 260:12 260:17,20 discussed 20:8 32:7 36:17 38:8 98:1 165:6 171:9 181:7 185:13 185:20,21 194:17 226:6 229:16 231:18 231:21 234:15 248:20 257:23 discusses 159:2 170:13 251:5 255:7,18 discussing 31:19 55:11,11 61:18 101:2 107:9 132:22 150:13 161:8 171:4 183:21 185:1 234:3 235:21 238:20 242:23 243:20 243:23 244:7 248:17 253:18 257:21 discussion 157:14 158:1,3	160:14 162:3 162:25 167:21 167:23 168:6,8 168:13 169:1,5 169:7 171:11 172:20 173:8 174:11 175:4 176:5 177:25 180:14 193:3 220:8 230:2 249:11 251:7 259:1,9 264:20 264:25 discussions 160:18,19 174:21 188:3,8 188:11 232:1 258:20 disease 89:19 110:1 112:9,10 112:10 130:21 139:6 178:16 238:12 242:9 diseases 107:18 111:1 241:12 disorder 10:19 11:5 44:3 47:5 68:13 70:19 76:12 79:11,25 80:11,13,25 81:20 82:9,14 83:3,11,17 84:3,20 105:15 113:24 120:10 121:6 135:23	136:4 disorders 44:23 46:10 48:6 49:4 50:24 51:4 67:13,18 67:19,24 68:14 68:20 69:4,12 70:18 73:1,3 114:19 116:9 119:2,6 178:11 241:5,6,11,17 242:4 disparity 135:7 distinguish 12:1 distinguished 156:18 dive 164:16 divide 71:23 dixon 99:24,25 101:9,17,22 102:2,7,8,10,13 102:15,16,25 103:3,6,14,18 104:4,5,6 105:6,25 132:1 154:15 178:4 226:1 227:23 228:2,4 229:16 231:18,21 239:6,16 243:9 243:22 244:5 245:2,9,17,23 251:5,5,20,24 253:13 255:3,7	256:1 dme 65:5 74:21 74:22,24 75:2 114:20 120:14 do's 81:11 doc 155:17 doctor 135:24 147:11 233:9 253:17 doctor's 264:11 doctors 141:7 document 14:1 14:13 17:14,23 24:4 28:5,6 41:16 42:4 43:9 51:13 54:1 55:18 58:18 59:7,9 60:9,11 67:11 77:14 81:2 82:1 93:23 97:2 101:13 102:23 103:11 103:16 105:13 115:5 121:22 125:17 133:6 141:13,21,24 142:1,2,15 143:5 155:18 157:23 158:5 158:14,25 159:5,25 160:9 161:21 163:10 163:18,20 165:13 166:3
---	---	--	--

[document - dosing]

166:15 167:18 168:1,14 170:16,25 171:8 173:5 174:1,10,13 176:2,23 179:11,11 180:6,8 183:1 183:9,10,23 184:11 190:9 192:12,16,18 192:19 193:2,3 194:6,14,16 196:8,25 199:25 215:12 215:14 219:6 219:12 220:10 221:16 232:17 232:25 234:22 235:1,3,7,12 237:5,22,24,25 239:13,22 240:7 242:24 247:16,18 248:12 249:19 250:2,17 251:1 251:9,11 255:9 255:21 258:1 262:15 documentation 186:10,16 documents 176:9,21,21 243:17 244:13 244:14 248:23	256:7 257:2 259:17 doggy 149:7 doing 91:10 104:8 106:22 109:21 111:5 111:10 153:21 181:17 211:18 227:7 258:25 dollars 204:21 dosage 133:16 133:25 245:22 dose 94:20 95:7 99:13 101:17 116:25 135:21 138:24 140:14 140:16 144:1,3 144:10,12,14 148:25 149:2 151:7,11 152:13 154:1,4 154:7,10,17,18 156:15 161:2 164:8 172:10 173:15 178:17 179:22 182:7 182:14,15,16 193:21 245:12 dosed 3:19 20:21 23:8 24:9 35:18 37:6 38:20 39:4 48:18 98:14 155:10 166:23,25	201:22 226:19 263:23 doses 25:21 46:12 47:9 94:16 101:11 103:22 104:1 108:2 122:8 139:11 140:10 140:13 152:12 154:16 161:1,4 163:15 165:8 165:24,25 166:8,24 167:1 169:25 178:15 178:17,19,20 178:22 179:1 180:4 182:21 192:5 194:21 195:18 196:15 198:10 200:5 200:11 201:22 202:4 246:21 253:24 254:1,2 254:4,6 257:11 262:21,23 dosing 3:20 20:5,10,16 24:12,14,15,21 24:24 25:10,12 25:18,20 27:14 30:7 31:17 32:3,4,6,8,10 32:11,12 33:22 35:4,8,13 36:1 36:15,20 37:1	37:14 38:5,10 38:15 39:3 44:4,8,17 46:10 47:6,8 63:9,19 64:17 64:24 65:22 66:14 69:1,8 69:25 85:25 94:17 95:1 97:5,23 98:3,8 99:8,20 100:1 100:13,13 101:9,11,25 102:2,7,10,17 103:15,24,25 104:10,11,14 104:20 105:7 105:18,25 116:10 117:24 122:25 123:1 123:11,19,21 124:6,7,15,19 125:6,11 126:22 127:4 132:25 134:7 134:13,21,21 135:16 136:1,2 136:12,17,24 137:6,10,12,18 137:20,23 138:2,8,9,14,17 138:22 139:2,4 139:11 140:20 144:5,6,13 149:5 152:3,8
---	---	---	--

[dosing - easier]

154:14 155:11 156:10,14,17 156:19,22,25 157:3 158:11 160:23,23 161:9,12,17,18 162:10,11 163:16 164:9 167:23 168:7 168:15 169:6 169:12,25 170:15 171:6 172:4,5,15 173:2,22,24 175:7 176:4,12 176:17,18 177:20 178:3 179:5,8,18 182:8,22 184:19,24 185:9,10,12,14 185:16,17 187:19 189:3 189:18 190:15 190:19 191:1 193:9,10 194:22 195:15 195:20 196:14 196:16,17 199:21 226:1,4 226:8,14 230:22 231:1 232:2,11 233:5 234:11,12,14 234:16,18	243:8,14,21 245:10 246:8 246:13,15 247:23 248:9 248:10,19 249:15,15 251:8 257:16 257:22 259:15 260:16,24 261:1 262:20 263:7,15,18 double 4:1 192:12 205:5 223:3 doubt 170:22 171:5 dr 1:11,15 3:6 5:13 6:20 7:1 14:9 32:14 33:2 34:20 42:12 53:20 59:7 60:10 81:3,5,11 84:10 101:14 101:21 107:7 112:20 122:23 129:17,18 138:2 139:21 141:22 155:18 181:3 192:16 195:25 209:19 214:23 220:13 223:20 224:10 235:3 245:25 260:1,5 266:2	267:3,7 draft 173:7 drastic 135:6 draw 114:3,6 drift 164:1,2 drop 25:11 dropping 144:22 drug 3:13,16 14:22 29:20 31:5 32:22 60:8 62:5,6 71:14 88:14 109:15 116:17 130:21,24 131:4,25 132:10 133:15 150:21 153:19 159:16,17 173:16 175:15 177:9,15 223:9 223:10 246:9 drugs 15:12 177:7 dry 137:16 138:12 139:4 drying 151:18 152:14 171:20 230:15 dryness 172:6 due 33:24 75:15 257:19 duly 1:16 6:21 268:10	durable 246:3 duration 91:17 142:19 143:2 158:11 169:19 176:13 238:22 239:10,20 240:2 243:13 243:25 244:11 246:8,13 247:14 248:7 248:17,21 249:16,25 250:22 255:19 256:4,20 257:1 e e 2:1,1 3:5,8 5:1 5:1 65:15 76:6 79:2 258:18 e.g. 116:1 119:21 262:20 earlier 30:25 53:21 61:18 95:24 107:9 155:4 183:18 197:2 199:20 218:20,25 219:17 222:14 223:15 early 72:13 74:3 94:10,11 114:22 148:6 211:17 easier 7:14,22 13:16 152:1
---	--	--	--

[easiest - either]

easiest 54:6 easily 133:10 easy 125:20 150:16 economics 131:25 edema 62:24,25 63:10,20 64:18 64:25 65:24 66:7,22 67:4,6 67:21 68:16,17 73:9,11,16 74:4 75:19 76:25 77:4 79:17,18 87:8 87:8,11,21 111:18,22 113:5 151:9,13 153:14 241:14 edition 60:16 education 8:23 effect 92:18 117:4 150:22 150:24 171:14 182:16 184:3 230:11 262:19 effective 20:20 23:8 24:8,11 27:14 35:18 37:5 38:20 44:11,14 68:13 68:15,20 81:14 81:15,21,22 82:20 84:9 85:9,16 87:2,5	92:4 94:6 98:14 99:20 100:14,19 105:19 107:24 110:2 111:17 113:23 115:4 115:12 118:15 118:24 120:16 121:3,5 128:11 132:6 133:17 134:1,17 135:22 137:13 144:6,14 149:6 149:8 152:7 161:18,25 162:10,16 164:6 172:6,14 173:1,10,23 176:18 177:20 184:18,24 189:2,18 195:4 226:18 231:1 232:11 242:9 243:7 246:15 248:10 effectiveness 95:9 100:12 110:4 115:23 120:10 170:6 176:13 effects 113:11 140:10 174:20 177:7,11 efficacious 69:3 69:11	efficacy 28:19 29:3,11,16,19 31:2 32:18 33:6 34:5 62:2 62:9,15,17 63:8,21 64:19 65:1,7,22 66:16,22 67:4 68:25 69:8 81:7 82:20 85:2 87:22,24 88:12 89:16 90:10 91:2,19 91:24 92:25 93:3,9,21 95:1 96:23 97:13 98:21 99:25 100:6,10 101:18,20,23 103:21 104:21 105:8 109:3,8 112:22 113:2 114:20 116:1 116:11,14 119:10,20 120:6,20 121:10,18 122:2,25 123:10,20 124:6,19 132:5 142:19 232:14 245:20 249:13 252:23 efforts 36:19	eight 24:15 25:19 27:14 32:3 45:1 48:9 48:20 49:5 51:7,18 100:1 100:10,13,14 101:11 103:25 110:14 127:5,9 127:14 132:5 132:13,25 137:11,12,17 138:8,9 144:4 144:5,12,13 146:4,6,12 147:4 149:2,6 161:18 162:10 170:6,15 171:6 172:15 173:2 173:23 175:6 176:17 177:20 182:13,15,22 182:23 183:7 183:21 185:9 187:19 189:3 189:18 190:22 201:22 202:4 234:11 243:7 246:3,14 248:9 254:1,6 eileen 2:13 6:14 either 66:2 70:22 128:15 132:12 202:15 204:10 217:16 256:20
--	--	---	--

[element - evaluate]

element 45:15 45:15,17,17 46:1 elevated 67:25 241:17 eligibility 215:19 216:12 217:19,24 218:4 eligible 78:14 emanuel 2:4 6:8 embodied 50:19 55:16,24 embodies 42:23 42:24 43:5,6 43:14,15 45:14 46:2,18,25 49:16 50:1,13 54:13 56:16 57:4 143:13 embodiments 115:25 119:10 119:14,20 120:2,5,5,19,19 121:10,15 embody 51:8 employed 26:15,25 268:21 employee 268:24 encouraging 176:24	ended 104:8 163:25 endophthalm... 217:16 endothelial 3:18,21 111:15 141:19 155:9 252:25 endpoint 3:20 117:11,11,20 117:22 118:2 140:17 141:18 191:2 endpoints 185:19 224:18 225:2,9,18 234:20 ends 179:17 199:21 england 71:1 enroll 78:7 224:1 enrolled 75:5 200:17 enrollment 190:17 ensure 213:7 entails 34:10 entire 40:9 41:1 41:2,17 57:8 90:20 122:9 169:5 214:7 219:17 220:17 242:8	entirely 94:16 195:19 entirety 60:18 entitled 192:12 207:23 208:23 235:9 entity 91:19 entry 217:19,24 218:4 equal 24:14 25:19 126:9 132:12,13 157:7 254:12 equaled 112:25 equipoise 191:5 191:5 equity 202:11 202:16 equivalent 104:21 105:8 escalation 245:12 especially 116:9 150:11 essentially 56:10 81:3 89:10 118:18 127:3 156:4 establish 65:22 66:22 100:6 established 62:2,10 63:9 63:21 64:19 65:1,8 66:15 69:2,9 70:1	71:4 88:8 90:11 91:15,20 92:25 197:11 228:12 232:13 249:14 263:18 estimate 117:4 estimated 160:4 estimates 116:20 et 66:6,7 69:25 105:16,16,16 107:16 151:5 155:21 156:9 181:20 212:7 215:6 218:6 223:11 226:21 243:3 260:20 etdrs 113:22 114:23 115:4 115:11 116:3 117:10 118:3 119:12,15,22 120:21 121:2 121:21 145:11 145:20,25 146:17 148:5 201:12 ethical 190:4 191:10 ethically 213:22 ethics 197:1 evaluate 103:21 242:21
--	---	--	--

[evaluate - expect]

245:13 252:23 evaluated 122:1 135:1 157:1 169:10 evaluating 96:21 97:9 98:19 143:7 145:10,20 240:16 evaluation 59:17,19 60:20 61:2 96:1,4 events 110:5 177:6 193:16 193:17 everybody 160:25 197:17 222:12 evidence 44:19 44:20 90:3 115:23 180:10 188:23 189:14 231:14 246:8 248:16 256:14 258:25 exact 27:7 39:16 74:5 89:18 92:2 155:22 191:14 exactly 11:15 45:17 63:13 65:12,17 72:5 78:10 82:3 105:4 109:12 140:21 159:21	160:18 174:15 203:17 204:1 204:13 205:3 212:8,19 213:23 223:5 249:4 259:2 exam 108:5,24 examination 3:6 6:22 92:14 106:17 126:15 268:14 examinations 201:9 examine 90:16 92:2 105:20 106:7,18 125:8 128:19 210:12 examined 56:22 examiner 210:11 213:5 examining 95:12 122:24 124:14 example 46:16 46:24 56:7,8 56:14,20 57:4 58:1,13 90:5 190:11 218:21 218:22,25 219:2,9 examples 56:2 56:3,23 57:9 246:7	exams 129:14 except 144:18 excite 125:25 excluded 75:6 exclusion 17:8 17:18,20,25 18:4,14,19 19:5 41:6,13 41:20 49:12,13 51:11,19,24 52:3,9,14,24 53:6,8 57:20 58:2,8,14,24 206:8,14,17,18 206:23 207:6 207:16,25 208:5,14 209:12 212:14 213:17 214:3 218:23 219:16 219:22 220:18 221:3,7,13 exclusions 208:11,20 excuse 49:22 82:10 exhibit 3:9,10 3:10,11,12,13 3:14,16,17,20 4:1,4 8:14 14:1 14:9,11 53:23 59:2,18,19 60:6,20 61:2 62:19 63:8 103:1,7 113:19	114:6 122:19 133:11,23 140:19,24 141:11,14 143:9,19 144:1 148:22 150:8 151:5 152:2,22 154:20 155:4 156:1,6 157:15 161:14 162:25 170:10 172:1,2 173:2,19 180:17 181:4 181:23 183:6 183:20 186:3,6 186:7 192:8 196:6,23 197:22 198:24 201:16 214:25 215:2,4 218:18 227:24 234:23 235:8 244:8 247:2 249:1 255:4,14,25,25 257:23 258:5 261:17 263:6 exhibited 193:21 exhibits 114:21 121:25 exist 42:22 43:4 expect 86:21 109:1 110:16 120:12
---	--	--	---

[expectation - eye]

expectation 19:16,21,25 20:1,4 21:4,8 21:14,18,24 22:6,18 23:1 23:10,14 24:1 26:7,16 27:1 27:13 28:3,12 28:20 29:4,12 29:23 31:10 32:15 33:3,9 34:2,10,13,22 35:1,3 36:8,11 36:14 37:22 38:1,4 39:12 39:24 40:8,14 40:17,22 82:18 85:7,23 86:6,8 86:19 88:6 89:7 95:21 96:11,18,22 97:10,17,19,22 98:20 99:2,15 99:19 101:3,16 104:19,23 105:6,10 106:2 122:2 139:23 143:8,23 166:23 178:21 225:25 226:3 230:6,8,9 231:4 240:16 242:19 253:12 256:13 257:7 257:15	expectations 25:24 86:15 122:6 expected 254:15 expecting 195:15 expense 25:8 experience 30:4 39:9 152:12 166:6 172:8 203:24 experienced 128:17 experimental 11:8 experimentally 256:21 expert 3:10 7:8 14:2,12 30:23 33:16 35:23 80:3 101:14 131:25 188:25 189:16 228:4 240:10 expertise 80:14 expiration 269:6 expires 267:15 explain 258:22 explained 94:3 195:2 197:9 explaining 182:20 245:21	explains 134:16 193:20 explanations 86:19 expound 95:15 184:2 expounded 81:3 expressed 84:4 187:18 188:24 189:15 extend 45:9 136:24 137:10 138:7,19,23 139:3 extendable 99:11 extended 20:10 20:16 24:11,21 25:18 35:8 36:20 38:10,15 44:17 85:25 94:5 98:3,8 99:8 123:19 124:5,14 126:22 137:6 137:22 138:2 140:19 142:19 143:2 170:14 171:6 226:8,14 232:2 233:4 243:21 248:19 249:16,25 250:22 251:8 256:16 257:22	extending 24:14 35:13 37:1 44:8 122:25 175:7 232:14 extensiveness 60:15 extent 7:24 162:8 169:19 exudation 95:11 113:6 128:17 exudative 4:4 235:2 eye 3:14,19,22 4:4 9:24 10:18 11:5 20:19,20 23:6,7 24:7,8 25:12 32:1,5 35:16,17 37:4 37:5 38:18,19 44:3,23 46:10 47:5 48:6 49:4 50:24 51:4 67:13,18,18,24 68:13 69:4,12 70:11 73:1,3 76:12 79:11,25 80:5,11,12,25 81:20 82:8,14 83:3,11,17 84:3,20 98:12 98:13 99:10 100:4,15,20 103:22 105:15
--	---	---	--

[eye - feasible]

106:16 109:25	244:10 245:1,8	eylea's 63:4	44:16 68:11
112:10 113:24	245:15 246:3	f	98:2 99:8
114:19 116:8	248:8,18	f 11:2	100:24 126:5
117:18,24	249:14,16,25	fab 10:22 11:1	226:8 254:14
118:4 119:1,6	250:7,9,23	fact 31:18 74:3	fails 122:23
120:10 121:5	251:7 255:17	90:7 124:18	254:19
128:18 132:7	256:3,24	137:9 152:6	failure 43:23
135:23 136:4	257:21,24	159:25 160:3	94:25
140:10 141:19	259:14 260:15	160:22 161:16	failures 24:11
143:13 145:25	261:2 263:7,16	172:4 173:12	35:9 36:22
147:11 148:5,9	eye's 132:3	173:21 176:16	38:11 98:4
150:25 155:10	255:7,18	184:25 186:5	226:10
156:25 157:1,3	eyeballs 177:10	213:22 229:18	fair 72:18
157:4 159:4,8	eyes 106:16	230:24 233:23	95:14 204:2
159:10 169:20	125:20 241:12	234:2 249:23	familiar 7:12
171:15 172:14	eylea 3:12,13	249:24	56:8 59:6,25
173:1 177:19	11:18,21,23	factor 3:19,22	60:9,14 141:21
178:10 179:6	12:2 31:14	111:15 141:19	215:22
184:18,23	44:24 45:1,8	155:10 231:14	family 238:3,5
185:7,11 189:2	46:11,17,25	238:2,7,12	250:12
189:17 190:13	47:6,24 48:4,7	240:23 242:11	fan 123:5
216:14 217:16	48:9,14,18,20	252:7,18 253:1	203:12
226:17,18	48:24 49:15,16	253:20 254:17	far 116:9
228:11,25	49:22,25 50:12	256:20,23	fast 10:16
229:19 230:11	50:19,25 51:7	factors 113:13	68:10,11
231:8 232:3,21	52:2,14,23	228:14,17	favor 175:5
234:9,13 235:2	59:3,15,17	229:7,13,22	fda 31:5 32:22
235:22 236:10	60:7,12 62:2	231:10,21	45:10 59:10
237:3 238:19	62:10 63:7,9	232:23	62:16 69:23
238:21,25	63:19 64:18,25	facts 16:1 36:5	116:20 117:6
239:1,9,18,19	65:23 66:14	36:7 37:21	135:3,18
240:15,20	67:4 69:1,9	fade 126:1	fda's 134:15
241:5,6,11,16	110:2 111:17	faded 244:3	feasible 133:20
242:4,9,22	111:21 132:21	failed 20:9 35:7	134:4,20
243:7,12,21,24	139:10 254:7	36:18 38:9	136:22

[feature - fluid]

feature 67:24 241:16	figures 135:15 152:21,22	10:17 11:4,13 11:17,20 12:12	146:13,21,23 147:12,15
features 20:12	235:15,16,17	33:17 37:9	198:11 201:12
february 199:2	235:23	44:25 48:8,19	202:5 242:20
199:6	filed 5:16 81:9	49:5 51:6	242:20
federal 1:23	85:3	59:12 60:16	fixed 3:20
feel 16:20 97:4	final 143:25	61:10 71:2,3	20:15 24:13
169:23	180:18	79:2,22 87:13	25:18 32:3
fellow 9:6	financial	94:8,10 104:9	35:13 37:1
felt 43:23 44:7	130:12 131:9	127:23 132:24	38:15 47:8
44:18,20 45:2	202:9,14	133:19,25	94:3 98:8
47:15,25 48:4	268:25	134:3,6,19	123:1,10,20
48:10,15,21	financially 5:25	142:12,12,14	124:6,19
49:15,25 51:8	131:12	142:21,22	132:25 133:3
149:4 203:4	find 44:11	147:14 155:21	134:7 135:16
fewer 114:22	55:13 100:17	156:23 157:18	136:12,17
fifths 216:11	123:19 139:4	158:17,23	138:24 139:4
figueroa 2:4	175:23 176:3	161:5 165:25	139:11 155:11
figure 22:11	finding 138:24	169:9 170:4	156:13,22,24
72:5 106:18	findings 83:24	173:6,8,18	160:23,23
135:9,12	153:22 173:11	176:25 193:7	165:8,24
144:16 145:1,2	173:13 210:14	194:10 195:10	179:18 182:8
145:4 148:23	257:13	195:12 198:10	185:9 194:21
150:9 151:2,3	fine 50:10	199:18 200:5	195:3 226:13
151:5,25 152:1	220:20	200:11 203:8	234:11 249:14
153:1,2,8,24,24	finger 89:4	203:15 211:1	263:18
154:3 155:25	finish 8:9 77:12	228:9 238:6,6	flip 45:19 62:18
156:1,8,9	93:6 145:14	242:10 249:9	154:20
163:24 164:21	146:8 236:16	258:6	floor 2:4
165:5 167:20	253:15	five 25:23	fluctuate 113:7
168:9,17	firm 5:23	110:14 126:23	fluctuation
170:21 171:25	204:19 269:7	127:2,7,8	84:15 113:1
172:1 175:15	firmly 232:12	134:22,23	120:13 246:25
188:6 197:23	first 6:21 7:16	137:15 138:12	fluid 108:4,23
198:3	9:12,17 10:13	139:8 145:25	128:20 151:19

[fluid - full]

151:22 152:2 157:8,9 171:22 172:2,12,12 177:17 178:5 178:19 201:13 230:15,18,21 243:4 fluids 171:20 fluorescein 157:11 focal 75:19,23 focus 200:17 follow 168:23 followed 44:25 48:8,19 49:5 51:6 76:23 95:7 101:11 163:16 182:21 193:10 194:21 212:3,13,15 213:8,14,17 214:3 254:1,3 254:5 following 6:14 56:2 59:11,20 60:21 61:3 62:24 63:10,20 66:7 67:5 79:1 103:25 134:25 157:4 190:19 192:4 follows 6:21 84:1 268:17 footnotes 142:6	foreign 25:8 forgotten 183:17 form 13:14 23:15 24:3 40:16,17,19,21 40:22,25 48:1 48:24 49:9,14 49:21,24 50:2 51:16 52:22 58:2 62:4,12 63:11,22 64:20 65:25 66:17,24 69:5 72:16 73:2 86:3,11 88:1,15 90:23 91:4 92:7 93:22 96:6 97:1,15 98:24 104:24 105:12 109:5,11 110:24 111:25 112:6 119:17 122:5 123:13 123:23 127:11 131:17 133:5 145:23 149:20 150:10 153:9 156:7 160:17 167:3 173:4 187:23 191:12 200:7,13 201:1 203:23 232:4 244:13 248:22 259:18	formation 11:9 formed 32:14 33:2 34:1 50:12,18 121:9 forming 22:23 23:11,23 26:8 26:17 27:2 28:18 29:2,10 34:22 41:5,11 43:11 45:13 46:18 47:1 48:23 55:21 82:6,11 230:5 231:3 236:24 formulation 11:8 fort 269:8 forth 55:22 56:3 117:15 forward 10:16 167:7 177:5 found 134:11 137:12 138:9 186:1 198:19 229:21 four 24:24 25:12 44:24 48:8,18 49:4 50:25 51:5 100:10,12,19 103:24 104:2 127:2 132:5,6 132:12,14 133:19 134:3 134:19 137:15	138:11 139:8 140:11,13 157:2 167:1 190:19,20,21 190:25 191:8 201:18 253:25 254:3 fourth 152:13 172:9 foveal 95:2,4 frame 72:2 free 237:10 frequency 240:5 263:19 frequent 45:3 48:11,22 101:19 108:2 116:10 138:22 163:16 167:23 168:7,14 169:6 179:4 259:15 260:16 frequently 128:4 front 17:12 19:8 28:17 61:12 70:4 80:19 114:4 148:1 227:23 full 142:17,22 143:25 158:17 158:23 162:23 163:4,6 170:9 181:25 182:6 228:9,9 238:6
---	--	--	--

[full - go]

249:9 258:6 fully 177:25 function 111:4 153:12,13 238:4,5 functional 122:11 functionally 109:16 110:4 fund 25:6 131:1,4 funding 131:23 funds 25:5 further 39:25 81:14,21 152:14 160:21 169:18 197:14 217:14 219:23 219:25 268:11 268:16,20,23 fusion 252:13	195:17 198:9 gained 90:7 91:16,25 126:23 127:9 127:14 145:22 gaining 111:2,4 gains 90:8 94:16 95:18,18 105:19 110:14 117:22,23 120:12,13 122:3 123:17 124:2 129:1 169:15 176:15 176:25 177:2 177:22,24 179:3,16,17 182:23 183:6 183:21 195:6 195:19 246:24 259:14 260:16 262:22 263:22	245:17 generally 29:17 145:19 204:14 242:6 generic 76:9 genuinely 146:15 147:3 getting 106:20 109:13 147:18 151:9 160:25 161:2 164:16 210:13 211:3 223:9,10 264:4 give 7:4,18,22 9:17 12:3,7,14 13:12 15:12 18:13,18 19:15 19:20 39:11 41:22 42:10 46:16,23 80:23 82:13 90:5 96:10,17 97:8 102:15 108:2 119:18 131:3 138:14 147:11 151:11 154:23 155:2 163:7 196:4 209:11 223:1 252:1 253:22 257:14 261:11 given 11:10,18 11:21 16:21 49:4 50:6 83:1 83:10,16 84:20	140:15 156:13 190:24 200:19 200:24 207:23 227:10 257:14 268:9 gives 84:13 106:1 giving 10:17 11:14 29:24 39:12 49:14,24 71:5 76:9 82:17 85:22 86:6 108:7 173:15 178:17 glad 203:6 glaucoma 67:22 241:15 global 252:21 globally 254:9 go 5:11 7:14 8:4,9,16 14:21 15:4 16:18 17:13 28:4 39:18 40:5 42:21 43:19 44:7,13 45:8 45:25 47:15 51:1 54:10 56:7 64:13 68:10 70:13 77:9,10 80:21 81:10 83:23 85:5,15 95:14 98:10,11 99:22 101:24 102:25
g			
g 5:1 258:18 gain 91:12 92:25 93:1 94:14 112:25 113:1 114:24 116:1 119:11 119:14,20 120:6,20 121:11,20 125:24 135:10 146:4,6,12,12 146:16,18 147:5 182:16	galileo 64:10 gap 165:23 genentech 94:9 194:19 195:11 202:25 211:19 211:20 212:25 genentech's 117:11 general 20:14 35:12 36:24 38:13 72:7 98:6 145:9 147:17 226:12		

[go - hand]

103:8,10 108:9 111:7 113:15 114:12 117:14 125:18 135:2 139:8,9 142:17 145:15 146:2 146:11,11 147:9,10,11 151:17 155:25 158:4,24 161:14 163:7,8 164:1 167:9 175:9,12 184:22 195:8 198:3 216:9 220:7,24 223:5 225:13 236:18 236:20 244:24 250:5 252:3,4 253:17 261:24 264:3 goal 44:10 47:7 132:15 goals 254:15 goes 52:20 128:21 158:16 160:3 182:12 236:1 going 5:4 7:17 8:12 13:24 14:7,10,25 15:1,3 16:3 17:15 18:9 20:24 21:1 29:7 39:2 47:8	53:12 84:8,8 87:25 98:17 101:4 103:19 104:15 108:13 124:10 125:22 139:14 140:1 141:10 147:6 162:24 164:15 164:18 167:11 167:13,17 181:4 192:6 207:14 208:1 211:5,6 212:18 212:20 213:22 214:10,13,15 216:9,23 218:13,15 223:5 227:9 234:22 241:21 251:17 253:6 255:1,2 261:19 261:20 gold 246:23 good 5:3 6:7,10 6:24,25 10:11 86:24 150:18 166:6 167:14 186:18 205:14 214:24 gotten 201:21 grab 141:16 grade 216:14 graph 198:2 graphic 125:18	graphs 172:21 great 24:12,20 25:17 32:1 170:8 172:23 185:7 234:10 264:4 greater 24:14 25:19 90:7 95:5,6 157:6,7 169:13 201:11 201:12 247:22 260:23 greatest 159:17 grounds 19:17 19:22 group 93:25 94:23 154:4,11 165:25 184:5 191:6 193:24 194:8,25 222:10 groups 94:20 153:6 157:19 158:8 164:3 182:17 191:9 193:21 200:19 200:22 201:4 262:20 growth 3:18,22 67:14 111:15 141:19 155:10 228:14,17 229:7,13,21 231:10,14,21 232:23 238:2,7	238:11 240:23 241:7 242:11 252:7,18 253:1 253:20 254:17 256:20,23 262:18 guess 238:17 guessing 7:12 guidance 117:6 guidelines 135:5 guy 80:5 125:18 guys 180:11 h h 3:8 11:1 258:18,18 half 103:22 159:4,14,18 160:4 179:17 190:21 195:23 202:6 250:11 250:25 251:6 254:1,11 257:25 hand 8:13 13:24 14:7,9 14:10 53:21 59:1 60:6 103:9 133:10 141:10 170:10 181:25 192:6 228:11 234:22 249:10 255:5 258:5
---	---	--	---

[handing - huh]

handing 14:3 handpicked 127:19 129:7 129:15 221:24 222:7 handpicking 223:15 handy 61:9 hang 177:23 happen 26:2 happened 156:8 199:1,12 199:15 happening 258:23 happy 16:10 39:20 58:21 96:12 150:3 220:7 hard 123:5 223:20 harder 223:11 harris 268:1 hat 177:24 he'll 16:10 head 7:23 110:20 147:2 160:25,25 161:11,12 header 239:3 healing 238:13 healthcare 75:15,17 hear 123:5 137:25 233:9	heard 12:1 236:20 heat's 203:14 heater 126:18 155:6 heater's 227:11 heier 31:21 99:23,24 140:24 154:25 155:3 185:2,20 186:2,11 210:20 233:8 233:13,14 234:4 236:1 238:19 239:16 244:15 255:17 257:9 258:15 heier's 236:9 236:14 237:2 243:10,22 244:7 255:13 255:25 help 47:14 179:8 198:4 203:2 251:12 helped 141:7 helpful 12:11 71:19 74:23 123:7 148:19 hemorrhage 76:18 108:5,24 111:8 122:13 128:18 201:15 hereto 1:25	hide 174:20 hierarchal 130:9 226:21 high 81:7 85:1 112:21 116:10 116:13 129:23 135:17 161:10 229:13 236:2 236:11 237:3 237:19 250:6,9 250:24 251:5 255:7 257:23 higher 159:22 163:25 228:13 229:19 232:22 255:18 256:3 256:24 257:8 258:17 highest 75:24 highly 94:13 195:13 histamine 111:16 historical 117:3 history 106:15 242:8 hit 32:12 74:1 185:18 229:4 234:20 hoc 20:13 35:11 36:23 38:12 98:5 128:10 226:11 hold 72:15 93:5 93:5 114:11	145:13 146:7 220:6 235:11 246:6 253:3 264:6 holder 57:12 honestly 39:4 63:23 64:8 80:4,7 211:16 hope 86:22 109:15 112:8 126:8 hopeful 137:10 138:7 hopefully 7:14 111:4 hoping 111:9 hopkins 65:5 horse 37:16 hospitals 8:24 hour 53:13 101:5 139:14 205:5 214:16 hourly 204:25 hours 212:10 246:19 261:13 261:21 houston 1:22 5:19 141:5 148:9 164:19 210:7 213:5,7 huge 107:19 huh 115:15,17 157:13 210:2 228:7
--	--	---	---

[human - independent]

human 210:9 210:21,24 243:2,25 244:11 246:6 246:11 247:3 247:13 248:21 256:4 257:1,9 humans 159:14 160:5 243:4 254:21 256:21 hundred 157:6 204:21 hundreds 213:13 214:12 hunting 102:25 hurt 164:7 hypotheses 258:21 hypothesizing 160:19 hypothetical 30:16 90:14 91:23 93:12 124:9,22 191:13 192:1 254:20	identical 235:23 identified 59:3 60:7 133:14 identify 69:25 ignore 256:14 ignored 259:10 illumination 148:13,14 image 157:11 imaging 205:16 205:22 immediately 153:15 impact 174:18 impetus 242:17 implants 32:13 implemented 197:4 implicated 238:11,15 implications 52:9 53:5 implore 115:24 implying 238:14 import 135:15 importance 180:15 221:8 221:18 important 174:5,5 175:4 175:14,24 176:3,10,11 177:22 211:7	242:11 247:19 256:10 262:8 262:10 importantly 7:15 117:21 impressive 253:23 improve 68:9 75:20 151:15 153:11 242:2,7 256:15 improved 71:7 108:4,4,23,23 127:24 165:2,9 242:12 256:15 improvement 89:11 111:10 112:15 113:2 144:2,10 149:1 157:20 158:9 163:1 182:13 improvements 84:14 86:22,23 87:9 177:3 240:4 248:1 261:4,7 263:17 263:21 improves 151:8 improving 71:17 111:3 232:14 impugned 229:2 impugning 186:20	incentive 25:11 incidence 193:15 241:24 incidents 68:7 incisions 9:24 10:3 13:5 include 57:21 58:9 62:24 67:19 76:3 207:25 241:12 included 24:22 74:25 242:4 includes 122:12 including 57:8 112:7 122:10 160:15 185:22 185:22 220:2 238:10 246:12 248:19 250:12 incomplete 90:14 91:22 93:12 124:9,22 191:13,25 increase 151:21 157:5 171:22 173:15 222:3 223:16 230:17 increased 25:1 224:16 increases 224:21 256:20 incredibly 177:2,3 256:10 independent 45:22
i			
i.e. 77:18 81:17 185:11 193:13 231:2 idea 147:23 175:6 208:9 231:24 237:7 237:11 240:3			

[index - injections]

index 3:1 indicate 193:8 238:22 indicated 157:9 indicates 151:23 171:23 230:19 239:9 239:19 indicating 32:11 185:17 239:25 240:1 indication 59:12,14 60:14 61:18 71:24 87:13 150:21 indications 62:21 72:7,8 73:1 78:11 indicative 111:23 112:2,3 indicator 115:22 153:10 162:2,5,9 175:16 indicators 162:6 indices 91:9,12 92:15 indicia 41:24 42:11,15,22 43:4,12,22 46:9 47:1,4 52:21 111:8 112:15	individual 13:4 88:19 89:16 90:6 91:8,15 91:20 92:9,13 92:14 93:4,13 96:2,4 105:20 106:7,10 107:12,23 109:2,7,17,21 110:9,18 113:8 113:12 123:19 125:8,9 126:8 126:13,20 128:22 136:25 138:16 150:20 192:2 251:6 individuals 92:24 123:15 124:5,18 industry 43:25 ineffective 118:14 138:10 infection 178:14 infective 217:14 218:5 inferior 32:2,5 70:11 116:18 117:18 118:5 166:24 185:8 185:11 234:10 234:13 246:22 inferiority 100:5 103:20 116:16,19,24	117:5 191:2 inflammation 216:13 217:8 238:13 influenced 231:15 inform 122:7 126:13 information 39:10,25 59:10 59:21 60:21 61:3,15 62:2,8 62:9 169:19,22 207:23 231:13 245:10 246:2 informed 31:12 42:15,21 44:19 89:2,12 106:12 211:2,8 224:3 informing 180:16 230:7 informs 33:12 inherent 223:13 initial 94:14 101:10 154:1 154:16 163:15 165:8 169:15 179:1,7 180:3 182:21 195:17 249:14 initially 59:15 initiated 194:19	initiation 31:21 114:20 116:3 119:13,16,23 120:22 121:24 185:3 234:5 inject 13:6 injected 193:23 194:8 246:5 injecting 10:12 injection 9:10 9:17,18 10:5 10:14,18 11:4 11:14,21 12:3 12:8,13,15 13:7,12,17,20 14:17 15:8,17 16:3,6 44:24 45:1 48:7,9,20 50:25 51:7,17 133:18 134:2 134:18 178:5 197:7 240:5 245:1,7,20 252:24 254:12 injections 10:9 11:11,18 13:11 45:3 48:11,22 51:5 94:4 95:10 133:19 133:20 134:3,4 134:19,19 136:22 137:15 138:11 163:14 165:2,4 190:23 190:24 191:3
--	--	--	---

[injections - irrelevant]

195:4 199:6 200:18,24 201:6,8,10 246:1 247:25 inordinate 264:9 input 211:12 211:14 inside 206:19 206:22 207:5 207:15,20 208:6,21 instance 1:16 41:25 49:11 77:10 82:18,25 101:9 110:7,21 123:18 154:4 229:20 249:2 instituted 189:8 instituting 82:25 instructs 8:3 integrity 186:20 210:10 intensive 107:20,25 interest 197:12 202:9,14 268:25 interested 5:25 212:1 interests 203:6 interim 62:21 190:25	internal 188:15 interpret 21:16 141:7 163:22 interpretation 83:2 97:3 166:5,11 167:22 188:19 interpreted 82:19 interrupt 108:12 253:15 interval 134:13 139:3,4,5,12 160:24 172:15 173:2 176:4 177:20 184:19 184:24 189:3 189:18 210:13 243:8 intervals 100:1 100:10,15,20 101:11 103:24 103:25 132:5,7 132:25 133:3 134:8 136:12 136:18 176:12 178:12,13 187:19 253:25 254:3 257:12 intervene 184:9 intervention 242:18 intimate 21:11 30:5,23 37:8 38:22	intimately 33:17 39:19 intra 15:7 intraocular 216:13 217:8 intraretinal 76:18 intravitreal 9:10,16 10:5,8 10:13,18 11:4 11:11,14,18,21 12:13,14 13:6 13:12,17,20 14:17 15:8,17 16:3,6 44:24 45:1 48:7,9,19 50:25 51:5,6 51:17 94:4 103:22 159:14 191:3 195:3 245:14 250:10 252:24 257:25 261:1 introduce 140:7 introduced 103:6 introduction 173:7 invented 148:6 invention 40:9 40:18,23 41:3 42:17,18,24,25 43:5,7,14,16,25 44:1,19 45:15	56:6 85:17 investigator 12:7 31:20 35:21 64:11 93:25 129:9,10 141:4,5 148:10 148:11 185:2 194:24 210:6 210:25 213:4,6 214:7 222:16 234:4 investigators 12:5 94:7 195:9,14 222:1 investment 205:5 involve 47:4 212:3 involved 33:17 38:24 39:19 70:17 79:18 83:5 94:1 195:1 211:24 229:7 244:25 245:7 involving 205:16 iowa 8:24 9:3 ipr 5:17 ipr2023-00442 1:6 iris 67:19 241:12 irrelevant 257:6
---	---	---	--

[irrespective - language]

irrespective 243:1	155:24 192:21 237:9	55:13 56:23 57:17 60:12,17 61:11 64:8 65:6,11 66:18 68:11 74:14 77:12 78:11 80:4,7,15 88:22 89:22 91:24 92:17,23 93:2,8,16,18,20 102:9,16,21 104:8 111:21 115:21 125:7,9 126:19 129:25 133:21 144:19 146:24 155:6 156:2 157:15 161:1 164:5,15 164:17 165:16 165:16 167:5 177:9 178:18 179:20 182:3 185:25 186:1 187:2,4 188:17 189:6,13 191:14 193:5 198:18 204:1 204:13 208:24 209:10 210:12 211:3,19 212:8 215:4 219:5 223:5,8,9 224:4,21 225:12 227:5 228:4 232:7	235:4 237:23 238:1 239:2 244:18 254:6 260:8,11 261:20
irreversible 128:13 197:14	journals 203:5		
ischemia 76:23	judgment 126:15		
238:13	june 94:12		
ish 11:25 79:7	k		knowledge 21:11 30:5,23 31:14 38:22 240:25 245:17
127:7,8			
issues 75:15	kaiser 185:22		known 17:8,18 67:3 68:12 83:1 138:18 159:9,13 173:14 240:15
issuing 135:4	kanghong 252:14,21 254:8		knows 66:20 164:9
j			kols 45:11
january 72:13	kaye 1:21 2:9		l
72:13,20,24	keep 61:9		label 3:12,13 3:16 12:9 59:4 59:18,25 60:2 60:3,8,12,15 62:22 63:7 127:17 133:15 133:22 134:15 134:16 135:6 135:20 136:21 254:7
73:7,10 76:14	164:18 181:4 259:11		labels 61:9
77:23 78:5,11	keratitis 217:15		lack 177:6
78:24 79:15	key 185:21 197:4		lagging 153:10 162:2,5
80:16 136:24	kicked 155:7 203:12,14		language 135:20
137:3,23	kids 18:13		
138:19	killed 177:7		
jeff 31:20 99:23	kind 71:19 125:18 156:18 202:22 244:2		
99:24 140:24	kinds 223:8		
185:2,20 186:2	knew 159:21 236:15 240:22 240:22		
186:11 188:3	know 7:11 8:7 9:21 12:9 15:3 22:19 28:14 29:15 36:6 47:22 50:11,17		
188:10 210:19			
233:14 234:4			
237:7 238:1,2			
244:18 257:8 259:5			
jeffrey 233:8 233:13			
jobs 213:7			
johns 65:4			
joined 6:12			
journal 71:1 142:3,3,4			

[large - listening]

large 29:18 31:2 32:18 33:6 34:5 90:3 106:13 166:7 laser 70:22 75:19,23 242:5 lasts 175:15 late 107:22 launch 11:24 laundry 220:17 221:2,13 law 18:13 204:19 lawyer 21:8 22:21 27:7 29:15 layman's 21:7 lead 33:13 94:7 97:4 99:14 134:22 161:15 179:2 180:17 186:5,6 191:19 195:9 leader 138:6 leaders 185:22 leading 30:4 62:16 leak 157:10 178:13 201:14 leakage 67:15 111:17,18 179:2,9 180:5 241:8 262:18 learn 9:22	learning 247:14 leave 164:19 167:17 led 11:8 31:12 31:13 101:22 101:23 128:12 left 87:12 142:23 175:4 176:6 228:11 legal 5:21,23 20:2 21:15 22:20 26:10,20 27:5,8,20,23 29:14,16 30:1 40:11 57:11 205:4 265:4 269:7 length 174:16 175:3 lenses 148:1 lesion 230:13 letter 94:18,22 134:23 147:4 195:22,23 letters 90:8 91:16 93:2 94:23 110:14 113:22 114:22 115:4,11,24 116:2,13,16 117:10 118:3 118:13,19,23 119:12,15,22 120:6,21 121:2	121:11,20 125:12 126:23 127:2,9,14 135:10,14 145:9,21 146:1 146:5,6,12,13 146:13,19,19 146:19,21,23 146:25 157:8 165:17 179:17 184:6 198:11 198:12,13 201:12,12 262:23 letting 224:4 level 80:13 81:7 85:1 112:22 116:10,14 163:25 258:24 levels 67:25 68:6 75:17 241:17,24 252:24 life 139:2 148:18 159:4 159:14,18 160:5 175:17 250:11,25 251:6 257:25 likelihood 37:12 222:3 224:17,21 225:2,8,18 229:19 233:4 243:20 248:18	257:21 likely 32:5,12 33:21 35:25 37:13 185:11 185:18 222:17 231:8 234:13 234:20 248:21 259:14 260:15 limitation 51:19 limitations 174:16 line 57:20 69:18 101:6 134:23 145:22 146:1,13,14,17 146:21,21,23 146:25 147:1,5 147:6,12 193:22 219:5,8 lines 66:13 114:11,12,15 115:19 119:9 link 42:17 list 108:21 119:11 219:16 220:17 221:2 221:13 229:14 listed 54:14,21 61:19 155:14 155:15 192:24 216:12 221:3 221:14 listening 246:18
--	--	--	--

[literally - lot]

literally 213:13 literature 30:17 litigation 184:21 187:12 188:25 189:6,9 205:10 littered 20:9 35:7 36:18 38:9 98:2 226:7 little 9:1 10:16 40:5 52:12 60:1 70:21,21 71:20,24 76:18 77:8 96:8 101:5 130:1 143:16 149:25 159:13 162:20 164:17,23 167:17 177:24 183:18 198:16 214:16 231:14 244:21 llp 1:21 2:4,9 loading 25:21 94:15 101:10 122:8 152:12 152:13 154:16 172:8 179:1 180:4 182:21 192:4 194:21 195:18 253:24 254:2,4	location 5:18 long 32:7 43:23 44:7,18,20 45:2 47:15,25 48:4,10,15,21 49:15,25 51:8 83:6,22 164:15 175:15 185:13 189:25 190:5 191:11,22 211:5 234:15 239:19 250:10 250:25 257:24 longer 238:22 239:10 240:2 243:25 244:11 248:21 251:6 255:19 256:4 256:25 longest 159:18 look 11:24 14:6 27:10 57:15 61:8 88:19 89:18 91:8 93:13 102:22 120:17 131:13 131:19 135:3 142:6,11 143:18 153:18 162:20 163:24 164:23 170:8 172:19,21 179:14,19 197:22 251:4 255:3 263:4	looked 14:5 34:19 41:2 46:12 47:11 52:7 53:4 99:3 122:3,9 124:4 124:17 144:19 149:18 154:15 161:15 216:1 219:17 237:12 239:16 255:16 258:4 looking 31:7,23 31:24 56:23 64:15 85:12 91:5,7 99:17 102:9,16 110:5 113:20 120:9 121:19 129:11 138:21 144:22 145:1,4 148:22 148:23,24 149:12 153:23 154:3 156:5 161:6 162:21 163:12 167:19 167:21 168:5,5 168:6,25 169:1 174:21 177:14 185:5 210:14 234:7 239:7 249:5,8,9 255:14 looks 259:4 los 2:5	lose 153:5,15 153:16 losing 116:13 117:23 loss 68:8 71:6 75:21 107:19 110:15 113:22 114:21 115:3 115:11,23 117:9,9 118:3 118:13,20,23 121:1,11,20 134:24 135:13 135:17 153:25 157:7 195:22 195:24 197:14 197:24 198:11 198:12,13 201:11 242:1 losses 122:4 lost 94:16,23 96:9 139:14 145:22 149:25 179:17 195:19 248:24 lot 15:21 16:17 18:12 89:20 99:12 129:10 130:22 132:10 145:8 164:3 170:20 180:8 216:18 224:4 225:12 230:2 253:21
--	--	--	---

[lots - making]

lots 138:20 loud 130:6 loudly 227:10 louisiana 1:22 5:19 love 124:11 low 164:3 179:21 193:15 263:19 lower 164:3 254:12 lt 157:6 lucentis 3:16 12:13 32:3,6 70:12,16,20 71:10 72:2,22 72:25 73:8,24 74:3 75:11 76:14 77:18,22 81:17,24 82:21 85:18 86:2,10 87:1,4,23 88:7 88:8,12 89:6 96:24 97:13 98:22 104:21 105:8 107:10 107:12,17 108:3,8 109:4 109:10,20 110:2,13 111:17,21 112:11,24 113:21 116:22 117:12,19,24 118:6 127:4	133:2,15 134:6 134:16 135:6,9 135:12 136:10 136:16 137:11 137:12,18,20 138:8,10,15 139:8 185:9,12 194:19,23 229:20 234:11 234:14 242:14	231:15 238:15 241:14 242:18 made 16:19 39:17 52:1,13 55:14 62:19 87:16 96:4 123:2 148:24 149:11,19 170:13 183:5 183:20 210:7	maintenance 24:15 25:10,20 44:4 71:17 84:14 93:1 95:18 112:25 120:12 135:21 136:1 242:12 263:22 major 45:11 132:23 majority 99:14 make 7:14,21 8:1 46:15,17 46:24 54:12 55:2,20 56:5 56:12 57:2 58:12 59:17,19 60:1,19 61:1 90:18 91:2 101:1 121:15 130:3 141:8 150:7 164:12 169:23 170:20 183:16 202:2 211:2,13 212:14 213:14 224:7 231:5 243:19 260:10 264:2 makes 166:21 236:5 248:13 making 10:3 13:5 27:11 58:21 211:9 212:2,12
	m	magnitude 13:16 mailbox 237:10 main 7:5 95:1 mainstay 90:2 maintain 125:25 134:13 137:16 138:12 139:5 160:6,7 169:15 259:14 260:15 maintained 71:7 90:8 91:16 153:16 157:21 158:10 163:2 179:4,24 195:7 246:24 249:15 263:7 263:16 maintaining 116:10 170:5 243:12 maintains 110:14	
	m 1:11,15 3:5,6 3:11 10:25 14:2,12 76:6 266:2 267:3,7 m.d. 3:11 14:12 macula 151:19 171:20 230:15 macular 3:15 3:23 4:3 59:13 61:20 62:24,25 63:10,20 64:18 64:25 65:23 66:7,22 67:4,5 67:21 68:16,17 68:17 70:18 73:9,11,16 74:4 75:19 76:25 77:4 79:17,18 87:7 87:8,11,20,21 113:6 141:20 157:11 192:14 201:15 227:22 229:2,8 230:16		

[making - method]

213:16 214:2 264:13 mandated 156:14 157:12 161:4 manner 63:6 210:8 manufacturer 159:16 manuscript 35:22 210:19 210:20 manuscripts 128:23 march 3:13 60:8 194:20 margin 116:17 116:20 marginally 165:17,18 marina 47:11 71:3 84:13 95:14,17,19 106:14 108:6 110:12 113:5,9 120:11 123:18 124:3,7 125:25 126:6 127:1,6 135:8 179:25 195:6,16 196:5 196:12 197:5 197:10 198:11 198:19 213:1,3 246:23	marine 71:18 marked 8:13 13:25 14:11 53:22 59:2 60:7 133:11 141:14 192:7 215:1 mask 210:11 213:5 masked 4:1 12:5,6 192:12 massive 70:25 match 190:25 matter 5:14 55:4,22 67:3 204:6 205:2,20 208:10 264:12 maximal 196:18 199:22 maximum 91:24 92:4,17 93:2,8,21 95:2 mean 22:13 31:24,24 39:1 41:6,13 43:20 49:10 70:15 71:9,15 91:6 99:7 106:9 117:22 119:14 129:7,14 130:17 131:5 135:10,11,13 141:16 145:4 147:13 150:17 150:20 153:2	179:13 185:5 187:24 198:1 201:16,19,20 202:2 210:23 211:16 236:15 251:14 262:21 262:21 meaning 19:13 82:13 107:9 151:14 meaningful 193:22 meaningfully 245:19 means 1:20 12:7 14:25 18:2,5 45:18 114:20 116:1 119:11,20 120:6 144:20 146:6 147:7,13 147:15 166:17 210:7,11 217:25 218:5 234:8 meant 169:16 measure 148:14 measured 157:7 245:25 measurements 148:13 mechanism 238:19,25 239:1 255:17	mechanisms 14:22 15:11 16:18 med 18:12 media 5:12 265:3 medical 9:6 27:10 259:4 meet 88:11 95:25 109:4,9 110:9,21 112:13 224:17 225:2,8,18 meetings 142:9 meets 21:15 member 37:9 members 45:10 197:21 250:12 memorable 12:23 mention 254:16 merit 177:25 met 44:19 109:3,9 118:16 156:15 method 21:19 21:25 22:7 44:2 63:8,19 64:17,24 66:13 78:8 80:24 81:5,12,19 82:8,14 83:3 83:10,16 84:3 84:19 85:1,8 90:11 92:18,21
---	---	---	--

[method - monthly]

94:6 105:14,16 112:21 195:4 methods 56:5 114:18 119:1,5 198:17 242:5 mexico 74:20 mg 144:1,3,10 144:11 148:25 149:2 182:7,14 182:15 mgs 144:5,13 161:17 173:23 176:17 246:14 248:9 microaneurysm 76:19 microns 157:6 201:11 microphones 5:5 middle 147:5 milligram 24:23,23 32:10 94:21,23 103:23 104:1 179:16,19,20 184:5 190:16 190:20,21,22 192:4 194:22 194:22 195:21 195:23 247:21 247:22 253:25 254:1,2,5,5 260:22,22 262:23	milligrams 37:15 39:3 103:23 140:11 140:11,14,15 149:6 152:9 190:24 197:8 263:23 mimic 126:6 mind 72:8 211:1 mine 233:19 minimally 193:13 minimize 128:6 minneapolis 148:11 minus 151:4,4 minute 183:15 minutes 53:13 261:14 mischaracteri... 244:13 mischaracteri... 15:19 mischaracteri... 23:3,16 24:3 26:10,20 27:5 28:23 30:1 31:9 32:20 50:15,22 54:17 55:8 65:10 67:10 69:21 74:13 75:14 83:19 88:16 91:3,22 96:7	99:5 109:24 111:13 112:17 120:24 143:11 161:21 166:3,3 166:14,14 173:5 175:9 176:20,20 178:9 179:11 184:12 190:7 196:25 208:18 214:5 222:6,24 223:19 224:20 240:18 243:17 246:17 248:23 256:18 259:17 miserably 254:19 misnomer 138:23 missed 12:25 111:20 147:13 150:4 233:11 misses 112:7 missing 111:24 112:4 163:14 modalities 163:23 modeling 238:21 239:9 239:18 240:9 255:20 models 238:11 molecular 243:1,2 246:9 252:15	molecule 68:1 160:21 211:25 241:18 247:14 259:3 mom 88:24 money 130:22 130:23 253:21 monitor 110:3 monitoring 197:20 232:11 monotherapy 128:15 month 94:19,19 94:21 95:3,6,7 128:4 195:18 195:21 197:9 197:10 198:12 199:8 monthlies 163:25 201:19 201:20 monthly 25:20 32:4,6 33:23 37:15 39:4 44:12 45:5 47:8,10 71:5 73:15,23 74:25 75:2,25 79:20 92:1 103:25 110:13 112:11 112:24 123:1 123:10,21 124:7,19 125:23 126:7 127:4 128:2,12
--	--	--	--

[monthly - nexus]

133:20 134:4 134:11,19,21 136:22 137:20 138:14,17 139:2 144:3,6 144:12,14 149:2 151:15 152:8,11,13 161:12,18 162:10 163:15 165:1,8,24 166:8,25 169:10,25 172:5,8,9 173:24 176:18 179:8,15 180:1 180:4 182:15 182:21 185:10 185:12 190:15 190:24 192:4 193:9 194:21 196:9,14,16,17 197:18 199:21 200:14 201:9 223:25 231:1 234:12,14 246:15,22 247:24 248:10 261:1 262:11 months 44:25 48:8,19 49:5 51:6 94:15 95:4,5 127:23 133:19 134:3 134:18,22,25	135:10,12,14 170:4 193:10 194:23 196:10 196:14 198:12 198:13,14 262:12,21 morning 5:3 6:7,10,24,25 move 20:24 76:11 78:21 79:10 130:2 150:1 167:6 177:5 253:6 255:1,2 multiple 19:4 44:15,15,16 62:14 87:5,16 87:18,24 88:8 88:13,17 106:17 124:13 125:15 132:2 172:22 185:21 207:24 223:21 248:19 250:11 257:11 264:20 264:25 multiples 145:11,21 mute 5:7 mylan 189:8 n n 2:1 3:5,5 5:1 10:25 name 5:20 7:1 148:5 266:2	named 142:12 173:18 215:8 268:9 names 64:2,7,8 76:7,10 near 95:14 necessarily 153:6 188:18 223:14 necessary 87:23 96:22 97:12 98:20 196:18 199:22 209:14 need 7:17 8:7 28:14 43:23 44:7,13,18,20 45:2,5 47:16 47:25 48:4,10 48:15,21 49:15 49:25 51:8 72:3 73:6 92:10 106:18 116:7 138:22 151:23 157:2 164:18 171:23 191:5 230:19 258:14,16 needed 3:19 8:6 25:2,5 33:5 34:4 104:20 105:7 128:15 137:14 138:11 155:10 198:17	needle 10:6 12:22 negative 94:22 neither 268:20 neo 80:10 neovascular 3:14 4:2 59:12 61:19 67:18,22 95:10 103:19 179:2,9 180:5 192:14 196:11 241:11,15 245:15 248:3 261:5 neovasculari... 67:20 79:24 80:10 157:10 201:14 241:13 neurology 130:18 never 58:23 185:24 202:20 229:13 237:12 259:10 nevertheless 116:7 new 2:10 71:1 76:22 80:2 116:8 148:10 157:9,10,11 201:13,14 232:13 259:2 newer 201:15 nexus 42:16,22 43:3
--	--	--	---

[nguyen - objection]

nguyen 65:16 nice 180:14 nine 134:25 179:16 nod 7:23 nods 147:2 non 32:2,5 70:11 100:5 103:20 112:3 116:16,19,24 117:5,18 118:5 127:17 166:24 185:8,11 191:2 193:16 222:11 223:7,11 234:10,13 237:9 246:22 259:2 nonobviousn... 41:24 42:12,16 43:12 44:21 47:2 52:22 nonresponsive 20:25 253:7 254:23 nonresponsiv... 111:21 112:3 nonserious 193:17 nope 225:22 normal 156:18 notably 144:1 notary 267:12 note 5:5 173:9	noted 100:3 142:20 203:14 254:10 notes 7:13 188:16 noteworthy 256:2 noticing 6:6 november 3:12 59:4 61:15 63:15,18 64:16 64:24 66:13 67:6 nuances 214:11 number 25:2 54:7 62:20 75:21 119:15 128:6,7 181:6 201:16 218:23 233:20 246:4 265:3 numbered 1:17 numbers 145:8 165:15 numerous 258:5 ny 2:10	objection 9:19 12:16 13:14,21 14:18 15:9,18 16:7,15 17:21 18:6,22 19:11 21:5 22:1,8,15 23:2,15 24:2 26:9,19 27:4 28:6,22 29:25 30:14 31:8 32:19 33:7 34:6,16,24 36:9 37:24 39:14 40:10,19 40:24,25 41:7 41:14 43:8 46:3,6,20 47:3 48:1,16 49:1,9 49:18 50:2,14 50:21 51:13,21 52:5,16 53:2 54:16 55:7 56:17 57:6 58:4,16 59:23 60:23 61:5 62:4,11 63:11 63:22 64:20 65:2,9,25 66:17,24 67:9 69:5,13,20 72:16 73:2 74:12 75:13 77:24 82:1 83:18 84:23 86:3,11 88:1	88:15 90:13,23 91:4,21 92:7 92:20 93:11,22 96:6,25 97:14 98:23 99:4 102:12,19 103:16 104:24 105:11 109:5 109:11,23 110:24 111:12 111:25 112:5 112:16 119:17 120:7,23 121:13,22 122:5 123:13 123:23 124:8 124:21 127:11 131:17 133:5 136:13,19 143:10 145:23 149:20 150:10 153:9 156:7 157:23 158:13 159:5,11 160:9 160:16,17 161:20 162:12 163:18 165:13 166:2,13 170:16,25 171:7 173:4,25 174:9,13 175:8 176:1,8,19 178:8 179:10 180:6 183:1,8 183:23 184:11
	o		
	o 3:5 5:1 79:21 205:25,25 oath 15:4 186:14 189:21 object 21:21 23:21 24:2 218:2		

[objection - okay]

186:12,25 187:6,23 188:1 189:4,19 190:6 191:12,24 194:6 196:24 199:25 200:7 200:13 201:1 203:23 204:22 206:9,15,24 207:8,18 208:7 208:17 212:4 212:16 213:9 213:18 214:4 215:24 216:16 217:2,9 218:7 219:19 221:5 221:15 222:5 222:23 223:18 224:12,19 225:3,10,19 227:15 229:9 229:23 231:22 232:4,5,17,24 237:5,20 239:12,21 240:6,17 242:24 243:16 244:12,13 246:16 247:16 248:11,22 249:19 250:2 250:17 251:1,9 254:24 255:9 255:21 256:6 256:17 257:2	258:1 259:16 259:17 262:15 objections 6:1 7:19 8:2 29:5 29:13 143:16 objective 41:23 42:11,15,22 43:4,12,22 47:1,4 52:21 156:17 observation 77:6 182:8,22 183:5,19 observations 196:12 observed 128:16 137:14 138:10 157:5 obstruction 264:4 obtain 73:23 75:3,24 obtained 91:25 92:18 93:21 182:14 obvious 44:5 obviously 68:20 occlusion 62:25 63:10,20 67:5 67:20 68:16 78:22,24 79:1 79:11,15,16 87:6,6,7,19,20 241:13	ocular 67:25 68:6 193:15,16 occult 193:14 occurred 263:22 occurring 160:20 occurs 197:24 oct 33:21 94:25 108:4,23 111:8 111:19 112:3 113:3 122:12 127:22 128:19 150:15,20 151:7 152:25 153:21 157:7,9 161:7,16,24 162:3 167:19 167:24 168:8 168:16 169:8 170:3,20 171:5 172:6,21,25 173:11,13,20 174:5,25 175:5 175:15,23 176:6 177:3,12 178:6 180:14 184:16,22 201:13 205:16 243:13 257:13 259:11 260:13 octs 150:20 ocular 241:17 241:23	odd 147:4 offense 257:8 offer 15:11,22 16:19,20 18:1 18:15,24 19:13 41:18,19 53:8 61:7 206:17 207:10,13,20 208:9,20,22 212:20 213:23 214:12 216:6 217:4,11 218:9 221:17 225:21 225:23 226:22 240:10 246:7 offered 53:10 81:5 112:20 166:12 offering 14:22 226:23 227:1 offers 100:15 100:21 132:8 office 1:1 5:17 7:5 45:6 offices 1:21 oh 42:8 46:7 64:6 123:6 149:23,24 206:1 233:11 236:5 okay 7:21 8:22 9:8 11:10 13:8 16:25 17:7,20 19:1,5,9 21:17 23:23 28:1,10
--	---	---	---

[okay - opinion]

39:21 41:4 42:14 43:3,11 43:18 45:13,25 48:14,23 49:14 50:8 51:10,16 52:11 54:24 57:2,14,18,19 57:24 58:12 59:1,9 60:5,19 61:11 62:1,18 63:16 65:6 66:12 69:15 70:2,15 71:19 74:8,23 75:4,9 76:2,11,11 77:16 78:7,12 78:21 79:23 80:9,15,18 82:4,17,24 83:8 84:1,16 85:4,15,22 87:1,15,22 89:15 90:5,10 90:19 91:14 92:5 93:16,19 96:15,21 98:15 103:13 104:13 104:17 109:2 109:18 114:10 114:17 118:10 119:8 120:1,4 121:18 122:1 122:12,20 125:6 129:5,15 129:22 130:17	131:6 132:20 133:9 134:6 136:5,9,23 137:4 138:13 138:18 142:11 142:14,25 143:4,7,22 144:9 145:4,7 145:17 146:15 146:24 147:3 149:9,16 150:1 152:23 153:23 154:10,14,20 155:14,17,25 156:16 157:18 158:6,16,22 159:1,2,24 160:3,12 161:13 162:8 162:18 163:6 163:11 164:23 167:8 168:3 171:10 174:3 180:2,20,22 181:14,18 182:5,12 183:4 183:14 184:1 184:15 186:2,9 186:15 187:9 189:23 190:4 191:6,8,21 192:3,23 193:1 193:4,7 196:4 196:22 198:8 199:18 200:3	200:21 202:9 202:12,17 203:19 204:13 204:25 205:17 205:19,23 207:3 208:13 209:9,18 210:4 211:12 212:12 213:6,15,25 215:3,7,18,21 216:3,8 217:6 217:13,18 218:15,19 219:4,11,13,14 221:1,10,21 222:1 225:23 228:3,8,21 229:15 230:4 231:3,25 232:8 232:20 233:2,8 233:12,23 234:22,25 235:6,13,14,21 239:6,24 241:2 244:4 247:11 249:22 250:5 251:4,19 252:3 252:6 254:22 255:12,24 256:11 257:19 260:12 261:22 263:4 264:2 265:1 older 227:21	once 45:1 48:9 48:20 51:7,18 94:16 100:23 128:4 153:13 195:19 197:5 197:16 oncologists 175:17 ongoing 169:22 170:23 182:1 onset 157:9 201:13 open 12:9 25:18 116:21 127:17 264:6 operating 10:4 operations 13:4 ophthalmic 233:15 ophthalmology 9:5 142:4,5 155:24 178:1 192:22 opining 227:12 opinion 15:11 15:23,25 16:19 16:21 18:1,15 18:24 19:13,15 19:20 22:24 23:11 27:12 32:15 33:2 34:1,14 40:6 41:18,19 43:22 44:22 47:24 48:3,5,14,24,24
---	---	---	--

49:14,15,22,24 49:25 50:12,18 51:3,17 52:18 58:2 60:1 61:7 73:7 80:23 81:5 82:17 83:2 84:25 85:23 86:6,7 89:7 95:21 96:11,17 99:2 104:19 109:19 112:21 115:2 115:10 120:4 121:9,15 135:18 139:23 143:23 166:22 185:21 188:19 206:8,18 207:11,13,20 208:2,4,10,20 212:20 214:13 216:6 217:4,11 218:9 221:18 225:16,21,24 226:22,23 227:1 228:4 230:5 240:10 242:16 248:15 opinions 18:10 23:24 26:8,18 27:3 28:19 29:2,10,24 34:23 39:13 40:16,21 41:23 42:10 43:12	45:13 46:19 47:1 52:21,25 53:7 55:21 58:21 82:6,11 97:8 207:24 209:3 216:21 220:1 231:3 236:25 opportunity 100:15 163:8 197:7 opposed 153:19 optimistic 179:14 optimize 169:16 option 75:10 135:22 options 100:8 191:17 optos 205:22 oral 1:11,14 order 17:5 25:6 28:14,20 29:3 29:11 104:22 105:9 110:9 131:1 137:15 138:12 264:19 264:22,24 orders 13:16 ordinary 30:19 56:4 135:21 original 148:21 187:15	orleans 148:10 orphan 130:21 outcome 6:1 33:18 37:10 166:1 175:17 204:6 205:21 outcomes 152:25 165:3,9 outside 14:25 39:8 131:1 206:5,7,13,19 206:19,22 207:6,16,21 208:6,11,21 overlying 260:19 owe 257:19 own 84:25,25 264:12 owner 1:9 p p 2:1,1 5:1 205:25 p.m. 1:18 107:2 107:5 108:16 108:19 139:17 139:20 180:24 181:2 214:19 214:22 265:5,7 p1g1 228:18 p1g2 228:18 p1gf 236:3 page 3:1,6,9 8:23 17:12 20:2 24:6,10	24:18 25:14 27:16,17,18,19 27:24 31:18 40:5 45:19,20 45:23 47:19 54:7,8 57:16 57:18 67:12 70:5 85:5 96:13 103:2,8 113:15,16,17 114:8 115:13 118:22 122:18 125:19 129:4 130:4,5,6 132:18 133:22 133:25 137:8 139:25 140:2,8 142:12,15 143:18 148:23 152:17 155:25 156:21 157:14 158:21 164:13 168:11,12 169:2 170:10 170:21 178:25 181:22 193:2,2 195:9 196:2 197:2,23 198:5 198:7 199:4 215:12,12,14 216:11 228:3,5 228:6 230:10 235:7,7,17 238:18 239:1 241:21 243:5
---	---	---	---

245:6 247:2,10 248:6 249:4 251:17 253:5 255:5,16 256:9 256:9 258:6,7 pages 54:14,21 77:11 80:22 98:11 136:8 paid 203:24 259:5 pale 68:10 panda 254:9,14 panretinal 76:24 paper 128:5 140:18,25 154:25 155:3 155:21 161:3 161:13 173:8 174:17 189:14 192:24 202:21 203:3 239:7,15 240:25 243:10 243:22 244:7 244:15 247:5 247:19 248:4 249:6,22 250:6 250:21 255:13 255:25 256:1 260:20 262:3 263:5 papers 66:2 71:1 87:8 176:6,14 178:1 178:2 202:18	202:22 233:20 243:10 244:6 247:6 257:4 par 47:10 81:8 81:16,23 82:21 84:12 85:2,17 86:2,9 87:22 88:12 96:23 97:13 98:22 104:21 105:8 108:8 112:22 123:1,10,20 124:6,19 125:7 para 142:21 168:19 paradigm 70:25 paragraph 20:3 24:5,10 24:18 31:18 36:13 38:3 39:9 41:25 42:1,14 43:20 43:21 47:19 67:12 70:5 77:18 82:13 85:8 93:24 95:15 103:10 113:20 115:14 116:15 117:14 122:15 129:4 130:7,8 131:7 132:2,17 134:14 137:8 140:8 142:18	142:22 152:18 157:18 158:18 158:23 162:24 163:5,6 164:13 164:25 168:4 168:23 169:3 170:9 171:4,13 181:25 182:1 184:15,25 186:11 187:10 187:25 188:22 189:24 190:11 195:8 197:2 199:5 226:2 230:9 234:2 238:6 243:5 245:6 249:9 251:3 252:11 253:5 258:6 paragraphs 27:24 77:10,13 80:22 84:5 86:12 136:7,7 152:18 196:3 pardon 27:22 226:25 paren 193:15 parens 114:23 193:13 216:14 parentheses 25:18 116:22 116:22 pars 9:24 10:2 12:22 13:3,5,6 13:9	part 9:25 10:1 24:5 41:4,11 57:14 60:1 65:5 66:3 69:16 71:14 77:1 93:25 115:18 138:5 143:20 146:17 159:19 160:13 194:25 214:1 224:3 226:23 227:1,12 232:1 259:12 260:13 262:9 partially 197:19 participants 200:25 246:1,4 participate 191:18 participated 93:24 194:24 203:1 particular 70:19 110:7 111:22 159:3 particularly 170:3,4 195:5 240:8 parties 5:10 268:22 parts 10:1 39:16 106:17 247:19 259:1,8
--	---	--	--

[party - patients]

party 5:24 268:17 pass 50:4 passages 26:5 26:14,24 past 68:11 116:20 patent 1:1,2,7,9 3:11 5:16 16:22,22 17:2 17:4,7,10,17 18:5,15,20 19:2,18,22 20:5 21:10 35:5 36:16 38:6 40:9 41:1 41:2 44:5,9 46:13,18,25 47:12 48:25 49:17 50:1,4 50:13,20 52:4 52:8,15,24 53:5,21 54:4 55:9,24,25 56:11,15,23,25 57:3,5,8,11,12 57:16,25 58:13 58:22 59:22 60:4,22 61:4 70:10 72:9,12 81:7,9,13 83:1 83:1,6 84:21 85:3 97:23 102:11,18 103:15 104:14	113:25 114:7 115:22 116:5 117:15 118:1 118:25 119:4 119:14 120:2 120:16,19,20 121:10,16 137:5 187:16 203:10,16,21 204:16 205:10 205:21,22 206:7,13,19,22 207:6,16,20 208:6,11,11,21 218:18 219:18 220:23,25 226:5 257:17 patentee 205:19 patents 205:15 path 68:7 pathogenesis 229:8 pathologic 67:14 68:7 238:8 240:24 241:7,25 pathology 68:2 241:19 pathophysiol... 229:2 patient 13:19 14:16 15:7,16 16:2,5 17:25 57:21 58:9	78:13 80:25 81:20 82:9,15 83:4,12,17 84:4,20 88:19 88:20,21,23 89:9,10,25 90:16,18 91:8 91:10 92:2,9 92:13,14 93:4 95:9 96:4 103:19 105:15 105:18,20,21 105:23 106:7 106:10,21 107:12,24 108:1 109:2,8 109:14,17,21 110:9,13,18,25 111:6 113:8,13 114:21 117:1 118:13 121:25 125:8,10 126:5 126:13,16 127:16 128:22 135:1,22 136:1 138:17,24 139:10 145:10 145:20 146:4 146:16 148:1 151:14 175:13 175:20 176:10 227:8,13 patient's 67:16 106:15	patients 13:4 25:2 43:25 44:3,22 48:6 49:3 50:24 51:3 68:5 70:20 71:13 74:14 75:4,9 75:16,23 90:7 90:10 91:1,15 91:20 93:1 94:14 100:16 104:9 106:5,8 107:21 108:6 117:20 118:17 123:19 125:5 126:11,21 127:8,13,20,23 127:24 128:3,8 128:14,17,22 128:25 129:6 129:11,13,15 134:10,10 136:25 137:7 137:14 138:11 138:15,16,22 139:1 142:20 144:17 150:18 156:9 157:1 165:1,7 169:9 169:13,14,17 172:7 175:22 178:12 190:5 190:18 191:11 191:22 192:3 193:12 194:4
--	---	---	--

[patients - photodynamic]

194:12 195:17 196:11,18 197:7,25 199:7 199:22 200:17 200:22 201:4 210:12 212:7 212:19 214:10 221:23 222:18 223:8,10,22 224:2,11 227:21 241:10 241:22 245:12 248:2 261:5 262:13 263:22 pay 150:14 peer 237:9 259:2 pending 8:5,8 16:13 42:6 125:1 149:21 216:24 220:6,9 people 89:22 124:12,12 178:19 198:15 198:21 211:2 260:18 262:10 perceived 256:4 percent 118:17 perfect 133:13 performance 116:21 performed 47:10 65:4 210:8 211:9	performing 9:16 113:9 256:12 period 94:5 95:1 permanent 135:17 permeability 68:3,8 241:20 241:25 permitted 132:24 134:7 persistent 44:10 79:19 157:9,10 178:13 195:7 201:13,14 person 30:20 135:20 personally 30:7 30:11 31:6,14 35:25 pertains 21:10 83:24 97:3 98:25 109:25 208:10 218:10 pertinence 51:23 58:23 peruses 14:13 17:14,23 24:4 28:5 41:16 42:4 55:18 58:18 60:11 67:11 77:14 81:2 93:23	97:2 101:13 102:23 103:11 105:13 115:5 125:17 133:6 143:5 158:25 163:10,20 176:23 183:10 190:9 192:19 194:16 219:6 219:12 220:10 235:12 247:18 251:11 peter 185:22 petitioner 1:6 1:16 2:3 5:14 6:8 ph 243:1 ph's 159:20 ph.d. 244:17 pharmaceutical 90:1 pharmaceutic... 1:8 5:15 6:17 pharmacolog... 175:14 phase 3:17,21 10:21 20:18 23:6 24:6 25:4 31:11,12,13,20 31:22 33:10,12 33:12 35:15 37:3 38:17 44:6 64:4,9,9 65:4,19 71:15 71:15 86:16,21	86:25,25 89:12 98:11 99:11 100:3,5,25 101:18 103:9 106:13 130:22 140:9 141:1,18 142:18 143:2 150:11,12,12 153:17 155:9 156:22,25 164:10 166:18 167:7 169:16 169:21,23 170:23 176:12 177:5,13,15 180:16,16 182:1,9 185:1 185:4 190:12 211:20 226:16 226:20 234:3,6 244:22,23 245:18,18,21 252:22 253:20 263:18 phenomenally 126:10 phil 71:2 127:19 phone 269:9 phones 5:7 photocoagula... 70:22 76:24 photodynamic 70:23 242:5
---	--	---	---

[photography - posa]

photography 127:22	212:23,24 213:15 214:1	23:22 27:15,18 93:6 98:18	poorly 72:23 150:18
phrase 81:19 83:2	215:2,19 216:13 239:6	163:8 183:17 220:12 236:17	populate 222:2 populating 224:9
physician 17:24 59:20 60:21 61:3 78:12,18 112:7 237:8	239:15 256:1 262:1,4,5 pivotal 117:12 place 5:10 9:23 30:19 182:4	236:23 253:14 258:9 261:12 plgf 236:4,4,5 236:11 237:4 237:19 238:2 250:12	population 88:17,23 89:8 89:13 90:21 91:5 92:6,10 92:12,17 93:9 93:21 96:1,23 97:12 98:21 104:22 105:9 106:4 110:17 117:1 123:3,11 123:15,17,24 124:3 126:12 127:3 223:16 223:24 224:23 225:1,7,17 227:8,13,19,19
physician's 156:21	placental 228:14,17 229:7,13,21 231:10,14,20 232:23 238:2,7 238:11 240:23 242:11 252:7 252:17 253:20 254:17 256:20 256:23	plus 146:13 254:18 point 10:21 12:21 14:21 43:18 55:10 95:2,5 116:14 117:6 129:2 153:5 155:20 165:7 171:11 192:20 228:5 237:24 258:2 260:13 263:20	populations 90:3 227:18 porter 1:21 2:9 6:11,13 portfolio 203:10,16,22 204:16 portion 73:21 89:7 97:11 115:1,9 131:16 157:14 158:11 218:22
physicians 77:3 100:17	places 74:8 plainly 135:6 207:22 plana 9:24 10:2 12:22 13:3,5,6 13:9 plane 74:16 player 211:21 playing 258:18 plays 68:1 241:18 pleasant 164:20 please 5:5,7 6:2 6:19 7:1 8:4,6 15:4 16:14	pointed 56:21 112:19 187:10 187:20 188:22 pointing 26:4 26:14,24 259:12 points 39:18,22 65:12 116:25 122:11 150:14 155:21 poking 10:5 pool 224:23 225:1,7,17	posa 20:3,15 27:12 30:16
pick 5:6 222:18 224:10			
picked 222:12 223:22			
piece 189:14			
pieces 235:24			
pier 4:3 44:16 90:6,11 91:14 92:25 93:16,18 93:19,25 94:2 94:3,8 95:13 124:24 125:4 134:9 135:8,13 135:16,19,25 166:7 178:18 192:14,20 193:8 194:3,19 194:25 195:2 195:10 196:5 196:13 197:16 197:17 198:9 200:4,10,15,19			

[posa - presented]

35:2 36:13,25 38:3,14 68:4 68:12,19 69:3 69:10 70:10 81:14 84:11 85:15 97:4,18 97:21 98:7 99:18 101:15 101:24 113:21 115:3,10 116:12 117:16 117:17,25 118:22 121:1 135:16 172:11 173:13 177:17 178:21 188:25 226:3,13 231:12 237:18 240:15 241:22 243:3 245:16 250:23 257:14 257:15 posa's 233:3 242:21 257:6 posas 172:19 174:4 231:8 242:17 256:23 position 174:4 209:11 positive 65:14 100:4 113:11 177:2,3,4,11 possibility 99:15 100:11 144:4,13 149:5	149:8 161:17 161:25 162:15 173:10,22 176:17 248:8 possible 7:24 26:2 71:16 129:12 148:4 167:23 168:7 168:15 169:6 232:2 238:16 possibly 149:7 post 20:13 35:11 36:23 38:12 61:14 73:24 98:5 128:10 226:11 potent 111:16 potential 110:5 174:18 211:4,4 243:20 246:8 246:13 potentially 99:10 132:13 163:15 165:23 185:23 188:15 223:25 229:12 243:11,23 244:9 258:22 powered 166:19 practice 59:21 60:22 61:4 100:9,21 132:4 132:8 136:25 137:6,22,23	138:1,2,18 156:19 practiced 55:5 practices 48:25 52:2,14,23 58:14 praise 43:25 45:9 pre 73:25 140:22 precede 153:22 preceded 65:19 preclinical 246:9 preclude 111:1 predicted 160:5 predictive 238:21 239:9 239:18 240:9 255:20 predominantly 33:20 90:2 101:1 130:18 193:13 230:9 preferential 247:13 preliminary 31:22 185:4 234:6 prematurity 67:23 241:16 prepare 15:16 16:2,5 17:5	prepared 15:12 15:23 16:20 18:2,16,18,25 19:14 41:20 51:24 52:10,19 53:6,10 58:24 121:17 206:20 207:2,11,13,21 208:12,22 212:11 214:13 217:5,12 218:10 220:21 221:9,19 225:14 prescribed 78:15 238:8 prescribing 59:10,20 60:21 61:3,14 62:1,8 62:9 presence 67:25 241:17 present 2:12 6:4 94:10 135:3 195:12 241:9 presentation 79:3 94:1 195:1 presentations 62:14 87:5 210:16,17 presented 65:13,17 73:12 79:4 101:22
--	---	---	--

[presented - properties]

142:7 172:22 199:10 presents 67:16 presumably 10:16 30:18 231:12 presume 54:2 149:17 presumed 250:10,10,25 251:6 257:24 pretty 73:10,12 74:6 102:21 107:21 144:23 149:7 169:17 prevent 68:8 107:19 169:11 242:1 prevented 71:6 75:20 previous 227:20 previously 13:25 14:7,11 53:22 59:2 60:7 69:24 83:10,16 141:13 142:7 192:7 202:24 price 100:22 132:8 prigmore 1:19 5:22 268:6 269:6	primary 3:20 32:13 33:18 35:21,21 37:10 38:23,24 45:6 45:6 62:15 117:10,11,20 118:2 140:17 141:18 155:20 171:11 185:19 191:2 210:17 210:18,18 211:1 234:20 242:17 principal 12:6 35:20 141:5 210:6,25 213:4 213:6 214:6 prior 19:17,22 20:8 24:11 35:7 36:18 38:8 43:24 54:11 65:3 70:19 75:18 78:10 79:8,8 82:25 98:1 101:9 107:13 123:21 184:20 188:24 189:15 194:18 197:24 202:10 226:7 237:1 241:4 private 5:6 prn 25:6 104:10,11 125:23 126:1,3	128:10 140:20 140:20 156:16 156:19,20,20 157:12 158:11 160:25 164:1,5 167:2,2 169:11 169:11,18 179:18 201:7 249:15 263:6 263:15 probability 161:10 probably 11:15 21:11 30:17 66:20 100:17 144:19 151:25 164:18 179:22 184:3 188:5,5 188:14 203:17 204:19 205:7,8 216:1 224:22 244:16 problem 80:6 178:22 224:16 procedure 1:23 10:7 13:10 45:4 proceeding 6:2 192:8 215:1 proceedings 82:25 84:21 187:17 218:10 process 7:13 151:20 171:21 174:25 224:3	230:16 produce 240:3 produced 1:15 product 42:23 42:24 43:5,14 43:15 45:14,16 46:1 54:13 55:5,16,24 products 43:6 program 232:11 programs 73:25 78:9,15 169:16 proliferative 76:20,21 77:5 promise 167:6 promoting 238:8 pronto 124:24 126:3,21 127:9 127:14,16 128:1,9,10,23 221:22 222:15 222:21 224:7 proof 28:19 29:2,10,16 properly 103:3 properties 238:20 239:8 239:17 240:1 242:22 243:11 243:24 244:9 256:15
--	--	--	---

[proportion - quarterly]

proportion 117:19	180:4 197:6 199:6 246:2	155:22 172:21 174:17,25	q4s 201:19
proposed 85:25 105:25	248:16	192:21 196:23	q8 20:5,21 23:8 24:9,24 25:10
prospective 20:15 35:13 37:1 38:15 98:8 226:13	provided 28:13 86:1 169:21 196:10 200:5 200:11 262:12	198:24 199:2 199:11 237:17	30:7 31:17 32:6,9,12 33:22 35:4,18 36:1,15 37:6 37:13 38:5,20 39:2 44:3 46:12 47:9 97:5,23 98:14 99:19 101:24 122:8 139:11 161:9 166:24 169:25 182:7 184:18,24 185:12,18 189:25 192:4 226:4,19 233:25 234:14 234:17,20 243:14 246:21 257:16
protected 210:9,9	provides 193:11 194:11 196:15	publishing 142:10	quan 65:15
protein 252:13	providing 39:9 55:3 57:24 67:2 99:2 104:18 184:20 187:11,15 194:3	pull 17:13 255:4	quarterly 94:4 94:17 95:1 125:6,11,23 135:16,21 152:3 163:14 165:4,11 172:3 193:10 194:22 195:3,15,19 196:10 230:22 247:23 260:24 262:12,20
protocol 129:12,20 147:22 197:4,6 197:15 198:25 199:5 200:4,5 200:10,11 201:22 202:3 211:10,11,13 211:15 212:2,6 212:13,15 213:8,14 222:17 223:20	provisions 1:24 prudent 131:12 ptd 118:16 public 267:12 publication 38:24 66:10 79:3,20 94:2 140:18 142:2 173:6,18 185:25 189:14 195:1 199:19 215:9	pulling 198:21 pun 258:18 pure 242:15 purely 238:12 purposes 22:24 23:12,24 29:23 55:3 67:2 83:9 83:15 84:17 85:22 86:5 97:10 99:1 104:13 192:7	
prove 29:19 31:2 32:18 33:6 86:24 92:11 130:24 132:12 166:20	publications 44:15 62:14 publish 141:8 published 25:14 66:8 73:12 79:4 95:18 135:25	put 30:19 56:3 112:12 149:18 173:12 197:13 254:21 256:8 259:1 putting 89:4 147:25	
proved 36:2 proven 69:14 74:21		q	
provide 56:3 104:22 105:9 169:18 178:4 178:25 179:1		q12 136:1 q4 32:10,10,11 152:9 185:17 247:21,22 260:22,22	

[ques - ranibizumab]

ques 102:14 question 8:4,5 8:8 10:12 14:14 15:2 16:13 17:16 19:19 22:3 23:11,17,18,22 26:12,22 28:25 29:8 32:25 33:25 37:11 40:12,20 41:9 42:5,9 46:22 48:2 49:20 50:7 52:12 54:19 55:19 58:6 60:25 62:5 63:12,15 64:21 66:12 69:6 72:16 74:2 80:9 82:10 83:13 86:4 88:3,7 89:5 93:6 96:9 97:9 98:17 102:15 104:25 109:6 112:1 115:6 119:18 120:25 123:25 124:25 127:12 131:18 133:8 136:9,15 137:1 137:22 145:7 145:14,16,18 146:8,10 148:21 149:21	149:23 150:3,5 171:2 183:11 183:12,17 187:15 189:11 191:10 200:8 201:2 203:12 205:14 206:11 207:3,12,13 216:24 220:6,9 220:12,14,15 221:11 225:5 231:19 233:10 233:10,11 236:12,17,21 236:23 239:14 244:2 248:24 251:19 253:12 254:22 258:9 258:10,11 260:7,10 261:19,23 questioning 73:4 209:5,17 216:22,24 questions 7:17 14:25 16:9 18:9 28:16 209:3,7,14,16 216:19,20 218:13 219:25 264:10 quinn 2:4 6:8 quinnemanue... 2:5	quite 29:8 58:19,20 81:4 83:6 98:10 109:12 130:20 164:2 170:20 212:25 quote 99:23 101:19,20 128:14 132:1 r r 2:1 5:1 10:25 11:1 65:15 79:2,21 258:18 r1 235:24 r2 235:25 race 37:16 raise 162:15 248:8 raised 144:12 149:5 161:17 161:25 170:22 171:5 173:9 176:16 raises 10:11 173:22 raising 144:4 149:7 ran 37:16 162:16 194:19 212:11 214:12 randomization 222:10 223:15 randomize 222:10	randomized 4:1 29:18 31:1 32:17 33:5 34:4 88:18 89:24 92:10,12 105:24 106:5 127:17 129:8 165:1,4 190:18 192:12 222:8,9 222:11 223:1,3 223:7,11,12 224:24 randomizing 191:6,8,22 192:3 ranibizumab 4:2 10:21,25 11:6,9 33:22 37:14 39:3 47:10 68:15 70:24 71:5 73:15 75:3 76:17 78:3,4 78:10,25 79:20 94:4,20 95:7 100:7,22 104:1 107:16 125:22 128:11 132:9 136:2 160:7 161:12 166:25 180:1 190:14 190:16,23,25 192:13 193:8 193:21 196:9 196:19 197:8
--	--	--	---

[ranibizumab - receiving]

197:13,18 199:23 232:15 246:22 262:11 262:17,20 ranibizumab's 94:25 95:8 ranked 32:8,9 185:14,15 234:16,17 ranking 130:9 226:21 rare 139:7,9 rarely 214:9 rate 193:16 205:1 rather 121:11 128:2 147:5 197:13 228:10 ratio 190:19 rationale 170:14 182:7 182:20 rave 79:3 reaccumulation 151:22 152:2 reached 77:6 93:10 read 17:4 19:1 19:4 28:1 41:1 41:2 57:8 65:15,22 66:18 66:21 77:15 103:10 104:5 112:1 114:12 115:24 123:9	125:21 142:17 158:24 159:1 163:8,9,11 170:18 172:20 220:17 250:4 251:3 259:6 260:18 262:10 reading 39:8 77:12 95:22 98:16 104:3,6 118:7 129:3 136:6 152:16 152:17 195:25 219:9 245:4 253:3 readout 94:8 195:10 reads 149:4 158:5 193:7 ready 13:19 14:16 15:7 115:7 167:15 real 65:19 99:9 100:11 148:18 really 9:21 10:8 83:7 90:15 92:3 105:19 107:24 125:21 129:11 141:6 150:6,13,16,18 150:18 153:18 160:24 164:1 164:12 174:21 210:25 211:18 224:4 227:19	realtime 6:15 139:15 181:14 reason 68:18 144:21 148:17 160:15 174:19 184:8 224:15 252:9 reasonable 8:11 19:16,21 19:25 20:1,4 21:3,8,14,18,24 22:6,17,18,21 22:25 23:10,14 23:25 25:24,24 26:6,16 27:1 27:13 28:2,11 28:20 29:3,11 29:23 31:10 32:15 33:3,9 34:2,10,13,21 35:1,3 36:8,11 36:14 37:22 38:1,4 39:11 39:23 40:7,14 40:16,22 69:2 69:10,19 82:18 85:7,23 86:6,8 86:15,19 88:5 89:6 95:21 96:11,17,22 97:10,16,19,22 98:19 99:2,15 99:18 101:2,16 104:19,22 105:6,9 106:1	122:2,6 139:23 143:8,23 160:20 166:23 169:24 225:24 226:3 230:5,8 230:8 231:4 240:16 242:19 253:11 256:13 257:6,14,15 reasonably 25:10 reasons 153:17 222:21 254:20 recall 9:8,12,15 10:11,12,17 11:13,15,20 12:4 31:19,23 64:1,2,6 65:21 66:1,18,21 79:5 174:15 184:25 185:5 203:17 228:23 234:3,7 receive 9:15 14:17 15:7,16 16:2,6 197:8 197:13 received 13:20 92:4 94:8 124:5 152:11 165:8 195:10 200:23 201:5,7 246:1 receiving 9:16
--	--	---	--

recent 238:10	187:13,17	redundant 25:8	reflected
receptor	188:14,23	refer 17:1,7,17	134:15 153:7
252:16,19	198:4 214:18	41:23 42:11	226:20
253:22	214:22 220:7	54:6,24 61:10	reflecting
recite 27:9	261:11 264:3,8	70:2,15 80:6	233:25
recited 37:21	265:5 268:8,24	85:11 130:12	reflects 147:18
52:3,15 58:3	recorded	157:13 162:24	199:19
58:14 81:6,12	185:24 187:13	181:22 214:25	refracted 148:5
recites 57:19	recording 5:9	223:14 228:3	refraction
58:8 218:22	recount 124:13	233:24	147:22
reciting 51:19	186:11	reference 51:11	refractionist
recognize 8:14	recruiter	62:19 168:16	147:23
54:4 192:16	191:19	170:14 239:8	refractionists
216:4,6 235:3	recruiting 25:8	referenced	223:9
recognized	recurred	132:1 141:10	refresh 66:5
20:12,17 35:10	178:19	237:12	103:13
36:22 37:2	recurrent	referred 61:22	regard 109:19
38:11,16 44:14	95:10 128:17	74:14 77:17	regarding
68:4 98:4,9	153:14 157:8	119:8 123:17	20:15 36:25
99:25 226:10	recurring	155:4 156:17	38:14 82:13
226:15 241:22	178:16	165:5 189:24	86:13 98:7
recollection	redirect 209:6	199:20 218:21	168:6,13 183:6
10:20 11:4	reduce 68:6,6	218:25 223:15	183:21 184:22
66:6 103:14	100:16 241:23	referring 17:1	221:22 226:13
recommendat...	241:24	26:5,15,25	regards 92:13
197:20	reduced 45:4	66:6,9 123:9	122:7 205:10
record 1:24 5:4	133:18 134:2	132:20 143:1	regeneron 1:8
5:11,13 6:6 7:2	134:17 240:5	168:10,12	5:15 6:14,17
14:8 53:15,19	262:18	184:16 214:9	7:9 16:22 20:6
107:1,5 108:14	reduction	217:1 218:5	25:4,7 32:8,11
108:15,19	108:4,5,23,24	239:4,17 258:3	35:5 36:16
139:16,20	247:20 260:21	263:5	38:6 44:5
180:23 181:2	reductions	refers 170:11	97:24 130:18
184:22 185:24	152:12 172:8	182:2 217:14	159:22 161:8
186:23 187:4	248:1 261:3		167:6 184:21

[regeneron - repeated]

185:14,17,23 187:12,16 188:9,15,24 189:9,16 190:12 202:10 202:16 203:9 203:16,20 204:15 205:10 209:24 211:17 211:21 226:5 234:16,19 236:15 237:16 257:17 259:3,5 regeneron's 24:13,19 25:17 31:19 117:8 130:12 185:1 226:20 234:3 regillo 215:6 262:7,9 regimen 20:5 20:10,16,21 23:8 24:9,12 24:14,21,24 25:18 27:14 30:8 32:3 33:22 35:4,8 35:13,18 36:1 36:15,20 37:1 37:6,14 38:5 38:10,15,20 39:3 44:8,11 44:17 85:25 97:5,23 98:3,8 98:14 99:20	101:10,19 102:3,7,11,17 103:15 104:14 104:20 105:7 105:18 124:6 126:22 132:21 136:2,3 154:15 156:11 158:12 178:3 185:9 196:13 226:4,9 226:14,19 232:11 234:1 234:11 246:9 249:15 257:16 regimens 32:8 46:11 47:6 69:25 97:20 101:17 106:1 116:8 122:25 123:20 185:14 190:19 234:16 247:23 260:22 260:24 regimented 148:18 registration 269:7 regular 132:24 133:3 134:7 136:11,17 regularly 135:1 reinjected 157:3 reinjections 263:19	reiterate 18:8 related 3:15,22 4:2 5:24 59:12 61:19 87:21 141:20 192:14 219:23 220:1 227:22 231:15 238:12 262:13 268:21 relates 19:17 19:21 40:8 209:21 210:5 212:23 225:25 259:13 260:14 relating 202:18 203:9,16,21 204:4,8 205:1 relative 193:23 268:23 relatively 7:12 10:2 relevant 233:3 relied 36:5 39:22 40:2 86:15 relies 245:25 remain 169:13 remaining 148:8 remains 116:7 remember 9:21 10:8,15 12:10 12:19 44:9 63:23 64:12 66:11 83:7,21	211:16,23 218:20 219:1,2 230:3 237:13 remind 15:4 remotely 6:12 remove 13:4 repeat 14:14 17:15 19:19 21:20,22 22:3 23:17 26:12,22 28:25 40:12,20 41:10 42:9 46:22 48:2 49:20 54:19 55:19 58:6 60:25 63:12,15 64:21 69:6 73:18 82:10 83:13 86:4 102:5 104:25 109:6 115:6,18 123:24 127:12 131:18 136:9 136:15 137:1 145:18 171:2 200:8 203:12 217:21 220:11 220:15,15 225:5 231:19 236:12,23 239:14 244:2 258:8,10 260:7 repeated 159:25 178:11 247:24 261:1
--	---	---	--

[rephrase - retina]

rephrase 62:5 report 8:16 17:11 32:16 95:23 127:1 133:15 240:14 241:2,3 242:19 reported 1:20 24:17 100:2 145:8 157:19 159:22 160:13 185:24 188:14 reporter 5:22 6:19 7:15,22 46:5 51:2 64:5 73:17,20 102:4 108:9,13 118:8 137:24 217:21 259:20 268:7 reporter's 3:3 268:4 reporting 32:9 158:7 185:15 234:17 reports 103:18 245:23 represent 237:15 representation 236:9,14 represented 132:22 representing 5:20 reproduced 17:11 45:22	125:19 167:20 168:17 require 22:18 29:18 31:1 82:19 105:17 116:9 121:10 130:22 required 22:19 28:20 29:3,11 34:12 85:24 86:9 88:5,11 95:25 112:21 117:13 128:3 201:9 265:9 requirements 32:16 33:4 34:3 requires 21:18 21:24 22:4,7 24:1 26:7,17 27:2 28:12 31:4 32:22 33:14 44:12 81:7,13,20 85:1,9 88:17 92:12,13 requiring 201:8 research 35:22 70:17 researchers 30:5 reserve 264:5 reset 120:11	resident 9:5 resolution 151:13 respect 33:24 251:22 257:19 respectfully 97:16 respectively 262:24 respondent 2:7 responding 88:20 responds 171:22 response 76:23 111:19 112:14 253:16 responsibility 211:1 responsible 210:21,25 213:16 214:2,7 responsive 23:19 251:23 252:2 rest 139:2 restate 29:7 98:17 results 3:17,20 20:17,18 23:6 24:6,16 25:15 25:21 35:15 37:2,3,18 38:16,17 39:6 56:10,24 57:10	98:9,12 100:2 100:5,23 117:15 124:17 125:21,22 126:14,14 134:11 135:7 135:19,25 137:19 140:3 141:18 150:23 155:8,19,20 158:19 168:8 171:13 180:16 193:8 194:3 197:5,16,17 222:21 226:15 226:16 230:10 235:23 245:24 246:2 249:12 261:7 262:17 263:2,20 retained 188:24 189:15 203:8,15 265:4 rethink 208:25 209:11 retina 9:6,22 44:10 67:16 76:19 80:4,5 118:11 137:9 137:16 138:5,6 138:12,20 142:8 151:8,22 152:14 171:23 197:11 230:18 233:14 237:8
---	--	---	--

[retinal - rights]

retinal 31:25 62:25 63:10,20 67:5,20 78:21 78:24,25 79:10 79:15,16 87:5 87:6,7,19,20 151:18,21 157:5 171:18 171:19 172:9 175:21 185:6 201:10 230:13 230:14 234:8 241:13 247:21 248:1 260:21 261:3,6 retinopathy 60:13 63:1 66:15,19,23 67:6,21,22 76:13,15,17,20 76:22 77:1,5 77:21 78:5,17 87:10,11 114:23 148:7 241:14,15 retrain 12:14 retreatment 151:23 156:12 156:22,24 157:12 171:24 230:19 retreatments 201:17 return 255:13 268:14	revealed 94:3 195:3 review 66:1,25 70:9 117:16 181:15 reviewed 14:20 55:9,25 58:22 60:17 81:10 83:6,20,20 105:7 112:20 113:25 115:21 143:8,12 181:11 219:17 237:9 259:2 reviewing 83:21 135:18 revised 60:18 rhu 10:22 11:1 rid 151:9 ride 73:12,13 113:3,4 120:15 211:19 213:1,2 right 15:24 19:6 23:9 30:13 32:23 43:7 44:9 49:8 50:11 52:1,22 61:24 63:2 66:4 67:8 75:12 81:25 82:22 84:6 85:20 87:3 89:1,10,23,25 90:12,22 91:25 92:16 93:17	101:12 102:1,3 103:9 107:21 108:25 109:18 109:22 110:23 112:12,15 119:6 120:18 121:21 124:15 124:20 126:24 130:7,11 131:10,14,20 131:24 133:8 136:12 141:17 142:23,24 146:3,22 147:13,20 150:1,19 151:3 151:25 153:21 154:8,18 155:12 156:19 158:12 160:8 161:19 162:4 163:17 164:8 165:12,22 166:1 167:24 168:9 170:10 170:11,24 171:12 173:17 173:17,24 174:6 175:20 175:25 176:18 178:24 179:9 180:3 181:25 182:4 183:22 184:10 187:5 188:21 192:11	194:13 199:14 199:24 201:24 202:7,15 203:1 204:6 206:12 208:16 215:7,9 215:16 219:18 220:22 221:24 222:4,14,17,20 222:22 223:14 223:17 224:11 224:18 226:1 226:24 228:4 228:19 231:11 232:10,10,23 233:6,8,16,21 234:1 238:4 239:11 242:23 243:15 244:1 244:11 246:15 247:1,15 248:10,21 249:7,10 250:1 250:8,25 251:8 255:5,20 256:16 257:20 257:25 258:5 258:15 259:15 259:25 260:16 262:14 263:1 263:19 264:5 rightmost 158:17,21 163:4 rights 130:25 131:4,15,23
---	---	--	--

[rise - second]

rise 31:24 73:12,13 113:3 113:4 120:15 185:5 211:19 213:1,2 234:7 risk 45:3 67:16 135:17 197:14 241:9 risks 211:4 robust 177:4 263:21 role 68:1 141:2 141:4 209:21 210:4 212:22 214:1 238:9 240:24 241:18 rolled 134:10 134:10 rolling 198:22 rollover 199:1 199:13 rosenfeld 71:2 127:19 129:17 129:18 223:20 224:10 roughly 144:17 route 65:22 68:25 69:8 routinely 178:12 row 223:22 rules 1:23 run 124:10,11 124:13 129:10 130:23 131:7	131:16 132:14 209:2 212:9 213:20 214:11 running 124:11 rvo 63:24 s s 2:1,4 3:5,8 5:1 79:2 205:25 safety 103:21 197:20 210:22 245:13,22 252:23 sample 144:17 samsung 1:4 5:14 6:9 53:22 189:8 satisfaction 44:18 47:15 satisfied 45:2 47:24 48:10,15 48:21 satisfies 48:4 49:15 51:18 satisfy 51:8 sauce 166:9 sausage 16:19 save 25:7 102:24 saw 19:5,7 37:17 39:6 71:18 94:14,21 108:5 120:14 153:25 176:16 177:3 195:6,16 195:17,21,23	197:5,16,16,25 198:10 211:24 224:23 257:9 saying 128:21 152:25 186:19 222:25 248:15 262:6 says 43:10 51:15 100:19 104:8 105:14 119:10,19 128:5 133:17 134:1 158:15 160:11 163:21 164:13,13 165:1,21 182:6 182:12 183:3 184:2,7,14 196:8 232:8,10 232:21 235:22 238:1,2,7 scare 227:25 schedule 44:4 136:12 193:9 233:5 scheduled 169:12 scholer 1:21 2:9 school 18:12,13 scientific 76:7 90:2 188:20 205:3 258:24 scientists 161:6	scleritis 217:15 scope 9:20,20 12:17,17 13:15 13:15,22,22 14:19,19 15:10 15:10,19,20 16:8,8,16,16 17:22 18:7,23 19:12 41:8,15 46:4,8 51:22 52:6,17 53:3 58:5,17 59:24 60:24 61:6 120:8,24 121:14 159:12 160:17 206:10 206:16,25 207:9,19,24 208:8,18 212:5 212:17 213:10 213:19 214:5 215:25 216:17 216:19 217:3 217:10 218:8 218:14 219:20 221:6,16 225:4 225:11,20 227:16 229:10 229:24 237:21 239:13,22 240:7,13 264:11 scratch 40:14 second 8:23 70:8 71:4
---	---	--	---

[second - set]

103:5 104:10 108:12 128:5 140:25 142:17 158:2,2,3 162:23 163:4,6 169:12 182:6 192:24 197:15 199:15 215:8 228:9 235:6,11 239:4 secondary 46:19 117:21 155:20 210:19 211:21 253:11 secret 166:9 section 20:8 25:24 31:11 33:9 34:9 35:1 36:11,17 38:1 38:8 43:19 85:6,12 86:7 86:12 98:1 103:9 121:19 135:5 157:15 158:2 193:3 226:7 235:9,21 241:4 253:10 263:20 sections 44:7 242:20,21 see 13:23 17:10 17:19,25 19:7 28:2 42:19 43:1,2 45:22 45:24 47:17	54:20 57:22,23 58:7,10,11 70:8,14 85:13 86:22,22 88:20 90:17 95:13 102:8,13 103:12,18 106:15 108:7 109:1,15 110:12 111:19 114:25 119:24 119:25 120:3 124:5,18 125:10,20,24 130:15 133:1 133:16,21 134:5 143:1,6 144:7,8 147:17 151:3,7 152:1 153:4,19 158:6 161:2 164:2 169:7,8 172:7 177:12 178:18 178:23 179:25 182:10,18,19 190:2 193:18 193:19,25 194:1 196:20 196:21 197:2 197:22,23 198:3,3,9,11,15 200:2 206:1 212:7 215:11 215:17 216:15 216:25 217:13	217:17 219:2,4 219:13,14 221:4,12,14,17 228:9,15,16 232:16,19 233:1 235:9,14 235:19 236:6 238:18 239:3,5 239:16,23 249:18,21 250:16,19 255:6,11,12,23 256:8 257:4 259:19,23 seeing 30:20,21 113:10 228:23 seek 25:5 264:6 seeks 116:16 seem 166:9 179:1 180:4 seemed 56:25 147:3 seems 22:17,21 57:11,25 147:4 seen 54:1 128:3 173:13 213:12 235:4,22 237:12,22,23 243:22 246:22 249:1 256:19 select 224:25 225:7,16 235:24 selected 222:16 236:2,10 237:3	237:18 self 158:5 sell 130:25 selling 131:15 131:23 sense 203:19 204:14 236:5 248:13 sensitive 5:6 sent 88:24 sentence 70:8 114:15 115:19 115:25 116:6 119:9 122:22 123:8 130:15 143:25 149:4 158:2,3 179:14 182:7 193:7,20 194:10 228:10 232:21 239:4,5 sentences 250:4 250:8 sequence 130:9 sequences 41:19 sequential 163:15 179:1,8 180:4 245:11 sequentially 155:23 serious 193:15 served 9:5 254:13 set 55:21 86:17 117:15
--	--	---	---

[setting - slow]

setting 211:12 211:14	shots 132:15	268:14 269:5	182:16 245:1,7
seven 110:14 183:15 198:12 246:19 261:21 265:3	show 34:5,13 39:16 85:24 86:8,9 87:22 87:23 88:12 89:11,13,16 96:23 97:12 98:21 100:12 101:18 104:20 105:7 116:16 128:10 150:24 171:14 230:10 241:2,3	significance 58:23 165:19 221:19 significant 67:16 128:13 157:20 158:9 163:1 166:17 166:19 193:11 194:4,12 241:9 247:25 261:3 262:12 263:8 263:17	245:20 sir 8:21 17:3 54:3 181:18 site 141:5 210:7 214:8 sitting 18:4 37:19 50:11,17 65:7 120:4 187:3 203:19 217:7
several 12:21 13:8,16 141:7 189:20	showed 36:8 37:22 101:23 113:3,4,5 117:22 167:5	similar 116:24 144:3,11 149:2 182:14,23	six 25:23 32:1 142:20 185:7 202:5 234:9 245:2,9,13,25 261:13
severe 197:14	showing 87:16 187:18	similarly 172:16 200:21	size 130:12 146:20,22,23
shake 7:23	shown 87:2,4,9 87:18 101:20 151:24,25 171:25 230:20	simple 10:6 84:17 221:10 243:19	skeptical 39:17 161:10
sham 4:1 118:18 190:24 192:13 193:23 194:8,23 197:7 197:12,25 198:17 199:6	shows 135:6,9 135:12 152:10 188:23 189:15 230:13	simpler 80:9 simplify 202:1 simply 112:13 118:12	skepticism 20:14 32:2 35:12 36:25 38:14 98:7 185:8 226:12 226:19 233:25 234:10
shape 167:3	shrug 7:24	simultaneous 66:4	skill 30:19 56:4 135:21
share 8:16 208:5,15	shy 188:18,19	single 59:14 61:18 99:13 127:17 140:13 144:1,10 148:25 182:14	skip 8:22
shared 67:24 241:16	sic 215:12		slide 151:24 171:17,25 230:12,20
sharks 205:6	side 170:10 174:20 177:6,6 177:11 205:19		slow 118:7
shift 70:25	signature 3:3 265:9 266:1		
shortage 264:12			
shorthand 268:6			
shortly 11:24 128:18			
shot 32:7 185:13 190:1,5 191:11,23 231:6 234:15			

[slower - standard]

slower 70:21 small 144:17 165:15 167:5 246:4 smaller 64:11 86:17 150:16 153:18 177:23 society 142:8 solely 121:20 solutions 5:21 5:23 265:4 269:7 solved 178:22 somebody 107:22 sorry 7:6 36:19 41:10 42:9 45:18 46:6 50:16 52:7 63:13 64:22 73:17 83:7 102:4 108:12 113:3 114:11 123:4,5,25 129:4 130:5,6 137:24 141:15 141:25 142:21 142:24 145:17 146:9 149:23 162:14 167:9 167:25 168:18 175:11 177:8 183:11 198:1,2 199:3 201:2,25 203:11,13	217:22 218:1 227:9 233:11 236:19,25 238:25 244:2 251:16 259:21 262:4 263:10 sort 104:10 143:16 147:18 163:22 sounds 8:11 73:6 space 173:11 span 77:11 speak 126:18 176:21 227:9 256:7 257:3 speaking 188:19 speaks 28:7 43:9 51:14 82:2 99:5 103:17 121:23 157:24 158:14 159:6 160:10 161:21 163:19 165:14 170:17 171:1,8 174:1 174:10,14 176:2,9 179:11 180:7 183:2,9 183:24 184:12 194:7,15 200:1 221:16 232:18 232:25 237:6 239:13,22	240:7 242:25 244:14 247:17 248:12 249:20 250:3,18 251:2 251:10 255:10 255:22 258:2 262:16 specialist 80:7 118:12 233:14 specialists 175:21 specific 47:13 50:7 53:5 60:2 72:4,6 73:3,6 77:8 80:5 88:3 96:8 121:8 145:1 207:4,14 211:13 245:10 252:15 specifically 24:22 52:8 82:20 83:23 86:13 100:3,11 114:11 140:3 143:19 149:12 149:15 156:1 164:24 218:21 224:10 specification 115:2,9 specifications 118:1 specified 140:22 212:15	spectrum 76:18 speculate 232:9 speculation 22:2,9,16 23:4 28:24 29:6 90:14 93:12 97:1,15 98:24 124:9,22 191:13,25 231:23 232:6 256:7 spell 10:23 spelling 205:23 spend 15:21 224:4 spent 58:19 216:18 253:21 264:9 sponsor 197:4 sponsored 64:11 129:9,10 squint 125:20 st 2:4 stable 128:18 stainable 240:4 stand 177:16 standard 29:21 30:3,10,22 31:6 36:6 37:20 39:11,23 70:12,16 71:9 71:23 72:1,7 72:21,25,25 73:8,14,22 74:10,22,25
---	---	--	--

[standard - struthers]

75:2,10,18,24 76:15,21 77:2 77:5,17,19,22 78:1,16,20,23 79:14,19 80:15 81:8,16,23 85:2,18 88:6,7 88:11,22,24 89:6 91:7 95:17,25 107:10,11 108:8,22 109:3 109:4,8,10,20 110:1,9,21 111:5,10,24 112:4,9,13,18 112:22,23 113:1 117:18 118:5 179:25 242:14 246:23 standards 27:20,23 32:25 107:17 stanwood 2:13 5:20 staph 178:14 start 8:12 45:20 49:22 70:5 132:16 141:11 146:24 153:14 158:23 227:10 249:2 started 9:4 138:17 164:3 188:6 189:6	starting 56:2 114:16 119:9 142:18 196:2 219:4 starts 8:24 45:21 96:13 126:1 151:4 182:1 218:23 249:12 state 1:19 6:2,5 7:1 20:2 23:5 24:5,10 25:14 26:2 35:2 36:13 38:3 48:5 67:12 81:10 82:3,23 101:14 117:14 125:14 132:3 134:14 150:23 172:11 177:16 184:25 185:20 195:8 226:2 241:4 264:8 267:5,13 268:2 268:7 stated 1:24 44:15 196:2 statement 123:2 130:3 144:15 148:25 149:11,19 150:8 237:2 264:3 statements 56:12 166:21	states 1:1 5:16 74:20 85:21 100:8,14 107:15 132:6 245:11 statistical 32:9 75:21 144:20 165:18 185:15 234:17 statistically 166:17,19 stayed 71:7 steering 141:6 188:11,12 254:13 stenographic 1:20 step 108:11 211:2 218:24 stepping 136:23 137:2 138:13 steps 13:19 14:16 15:6,15 16:1,5 stick 76:10 87:25 stipulations 3:2 stock 202:11,16 stood 180:11 stop 70:13 147:5 stopping 254:9 straightforward 63:6 150:6	strategies 240:9 stratus 128:19 street 1:22 2:9 5:19 269:8 strike 14:3 20:25 59:18 72:22 187:14 205:7 231:6 243:18 253:7 255:2 strong 184:8 strongest 184:6 strongly 172:13 172:25 177:19 184:17,23 187:14,19 189:1,17 243:6 243:14 structure 243:2 243:3 struggle 216:9 struthers 2:8 6:10,11 8:18 9:19 12:16 13:14,21 14:18 15:9,18 16:7 16:15 17:21 18:6,22 19:11 21:5,21 22:1,8 22:15 23:2,15 23:21 24:2 26:9,19 27:4 28:6,22 29:5 29:13,25 30:14
---	--	---	---

[struthers - study]

31:8 32:19	110:24 111:12	187:6,23 188:1	248:22 249:19
33:7 34:6,16	111:25 112:5	189:4,19 190:6	250:2,17 251:1
34:24 36:9	112:16 119:17	191:12,24	251:9,21,25
37:24 39:14	120:7,23	192:10 194:6	252:4 253:8,14
40:1,10,19,24	121:13,22	194:14 196:24	254:24 255:9
41:7,14 42:5,8	122:5 123:4,13	199:25 200:7	255:21 256:6
43:8 46:3,7,20	123:23 124:8	200:13 201:1	256:17 257:2
47:3 48:1,16	124:21,25	203:11,23	258:1,8 259:16
49:1,9,18 50:2	127:11 131:17	204:22 206:9	259:22 260:2
50:14,21 51:13	133:5,7,12	206:15,24	261:10,15,18
51:21 52:5,16	136:13,19	207:8,18 208:7	261:24 262:15
53:2,25 54:16	138:4 143:10	208:17 209:2	263:25 264:7
55:7 56:17	145:13,17,23	209:13 212:4	264:18,21,23
57:6 58:4,16	146:7 147:10	212:16 213:9	268:18
59:5,23 60:23	149:20 150:10	213:18 214:4	studied 123:11
61:5 62:4,11	153:9 154:24	214:15 215:24	179:7 227:8,14
63:11,22 64:20	155:5 156:7	216:5,16 217:2	studies 24:16
65:2,9,25	157:23 158:13	217:9 218:2,7	25:3,13 44:17
66:17,24 67:9	159:5,11 160:9	218:12 219:19	62:15 65:4,5
69:5,13,20	160:16 161:20	220:3,11 221:5	65:11 69:24
72:15 73:2	162:12,14	221:15 222:5	87:17 88:9,13
74:12 75:13	163:18 165:13	222:23 223:18	106:4 117:2,3
77:24 82:1	166:2,13 167:9	224:12,19	169:10,18
83:18 84:23	167:13,25	225:3,10,19	170:11 182:2
86:3,11 88:1	168:3,10,18,22	227:15 229:9	190:12 222:3
88:15 90:13,23	169:3 170:16	229:23 231:22	223:6,12 224:2
91:3,21 92:7	170:25 171:7	232:4,17,24	227:20 238:10
92:20 93:5,11	173:4,25 174:9	233:9 234:24	238:21 240:1
93:22 96:6,25	174:13 175:8	236:16,22	245:21 252:22
97:14 98:23	175:12 176:1,8	237:5,20	257:10
99:4 101:4	176:19 178:8	239:12,21	study 3:18,21
102:12,19	179:10 180:6	240:6,17	4:3 24:19,22
103:16 104:24	180:22 183:1,8	242:24 243:16	25:1,9,22 34:9
105:11 106:22	183:23 184:11	244:12 246:16	35:20 38:22,23
109:5,11,23	186:12,17,25	247:16 248:11	38:25 56:9

[study - suggesting]

79:1,3 93:25 94:3,9,21 95:13 99:13 100:4 103:21 114:23 116:16 116:19,24,25 116:25 117:5 122:7 127:14 128:1 135:5,7 135:11,13 140:8 141:18 142:19 143:2 148:7 152:11 153:18 155:9 155:22,23 156:25 157:3 158:19 167:5 169:14 170:23 190:17 192:15 192:21 193:8 194:2,25 195:2 195:11,23 197:3,4 200:4 200:6,10,12,19 200:21 201:4 210:8 211:9 213:16 214:2 214:10 215:2 215:20 216:13 216:14 221:22 222:9,11,12,15 222:17,19 223:1,3,7,17,20 223:25 224:8 224:10,17	225:1,7,17 226:21 244:22 245:12,19 246:1 249:13 256:1 257:10 258:7 262:1,9 studying 9:2 stuff 252:20 styled 1:17 subfoveal 262:13 subject 7:18 190:5 191:11 subjects 118:2 152:11 197:12 210:9,24 245:2 245:8 254:11 submacular 128:18 submitted 8:15 19:2 62:16 135:4 162:19 237:16 268:12 subscribed 267:6 269:2 subsequently 179:4 subset 128:16 substance 181:7 204:10 subtypes 193:12 194:13 succeed 47:7 231:9	succeeding 233:6 success 19:17 19:21,25 20:2 21:4,8,14,18,24 22:6,18 23:1 23:11,14 24:1 25:25 26:7,17 27:2,13 28:3 28:12,21 29:4 29:12,23 31:10 32:16 33:3,10 34:2,10,13,22 35:2 36:8,12 37:23 38:2 39:12,24 40:8 40:14,17,22 44:1 46:11 82:19 85:7,23 86:7,8,15,20 88:6 89:7 95:22 96:11,18 96:22 97:11,17 97:19 98:20 99:3,16,19 101:3,16 104:19,23 105:6,10 106:2 122:2,6 139:23 143:8,24 161:10 170:23 222:4 224:17 224:22 225:25 229:19 230:6,8 230:9 231:4	240:16 242:20 253:12 256:13 257:7 successful 20:16 24:21 25:21 35:14,23 36:1 37:2,12 37:13 38:16 97:5 98:9 106:3 122:9 152:7 161:11 170:2 172:5 198:20 226:14 230:25 successfully 20:4 35:3 36:14 38:4 97:22 226:4 257:15 sufficient 93:20 246:13 248:8 sufficiently 116:24 suggest 118:1 135:20 172:14 172:17 177:19 184:17 196:13 243:6,14 suggested 95:8 161:16 176:15 176:16 187:19 189:17 249:24 suggesting 184:23 186:23 250:22
--	---	--	--

[suggestion - summers]

suggestion	48:3,23 49:7	115:8 119:19	184:1,8,15
165:22 170:22	49:11,21 50:6	120:18 121:7	186:15,22
171:3	50:17 51:10,16	121:18 122:1	187:3,9,25
suggests 158:19	52:1,11,20	122:12 123:6,8	188:21 189:10
172:25 189:2	53:7,12,20	123:16 124:1	189:23 191:21
243:14 249:13	54:1,20 55:12	124:12,24	192:6,11,23
suite 1:22 5:19	55:20 56:20	125:2 126:20	194:10 200:3,9
269:8	57:14 58:7	127:13 131:19	200:16 201:3
sullivan 2:4	59:1,6 60:5,19	133:9,14	203:13 204:2
summary	61:1,8 62:7,18	136:16,23	204:25 206:12
260:19 261:9	63:14 64:2,6	138:1,13	206:21 207:3
262:1	64:23 65:6,21	139:13,21	207:12,22
summers 2:3	66:5,21 67:1	143:7,15	208:13,23
3:7 6:7,8,23	68:22 69:7,15	145:15,19	209:9,18,19
8:20 12:20	70:2 72:17,19	146:3,10	212:12,22
13:18,24 14:8	72:20 73:5	147:17 149:24	213:15,25
14:10,15,23	74:1,23 76:2	153:23 155:1,6	214:17,23
15:14,24 16:13	77:16 78:4	156:16 158:1,7	216:3,8,23,25
16:21 17:15	81:18 82:4	158:16 159:2,9	217:6,13,23
18:3,17 19:1	84:1 85:4 86:5	159:24 160:12	218:3,15,17
19:15 20:24	87:1 88:4 89:1	161:13 162:4	219:7,14 220:2
21:1,17,23	90:19,25 91:11	162:13,18	220:5,13
22:5,13,23	92:5,16,22	163:12 164:14	221:10,21
23:9,18,23	93:7,16 95:20	165:20 166:10	222:14 223:4
26:4,13,23	96:10 97:7	167:8,11,16,19	224:6,15,25
27:15 28:10	98:15 99:1	168:2,5,12,20	225:6,15,23
29:1,9,21 30:9	101:7,8 102:1	168:25 169:5	227:23 229:15
30:25 32:14,23	102:6,14,24	170:7,19 171:3	230:4 231:25
33:24 34:12,18	103:13 104:3	171:10 173:17	232:8,20 233:2
36:4 37:19	105:2 106:6,24	174:3,12 175:2	233:12 235:1
39:8,21 40:4	107:6 108:11	175:19 176:5	235:14 236:18
40:13,21 41:4	108:20 109:7	176:14 178:3	236:24 239:15
41:11,22 42:7	109:18 110:6	178:23 180:2	239:24 240:13
42:10 43:11	111:7,23 112:2	180:10,20	240:21 243:9
46:14,23 47:13	112:12 113:14	181:3 183:4,13	243:18 245:4

[summers - targets]

247:1 248:5,14 248:25 249:22 250:5,20 251:4 251:12,22 252:3 253:6,9 254:22 255:1 255:12,24 256:11,22 257:5 258:4,12 259:23,25 260:5 261:16 261:22,25 262:25 264:2 264:15,17 268:18 super 126:1 superior 179:3 supplemental 215:16,22 217:4 support 44:2 246:13 248:18 256:19 supporting 248:7 supports 240:3 suppose 259:8 supposed 105:4 120:17 212:7 229:1 suppression 250:13 sure 10:24 13:24 14:15 21:15 22:5	26:13,23 29:9 45:17,19 46:23 49:21 54:20 61:1,25 63:14 64:23 65:13,19 69:7 73:5,10 73:12 74:6 83:14 86:5 89:4 96:10 101:7 102:6 105:2,5 109:7 124:12 125:5 126:12 129:25 133:8 136:7 140:25 145:19 146:18 159:21 183:16 189:10 205:3 210:7 211:2,9 212:2 212:13,14 213:14,16 214:2,17 223:22 228:20 236:24 239:15 248:25 258:4 259:5 260:11 263:24 surefire 252:9 surgeon 9:6,22 10:10 surgery 89:21 surgical 10:7 205:14 surgically 89:22	surpassed 71:17 surprising 99:23 100:24 sustained 250:13 sustaining 152:7 172:6 230:25 swear 6:19 switched 156:10 sworn 1:16 6:21 189:21 267:6 268:10 269:2 synced 264:16 synopsis 56:9 56:24 t t 3:5,8 205:25 table 8:17 56:8 56:24 57:10 151:2 215:16 215:22 217:5 take 5:10 8:6,9 13:19 14:16 15:6,16 16:2,5 26:4,13,23 53:13 64:15 88:20 91:6,6 101:6 106:15 106:24 122:15 126:21 132:17 139:15 140:2	153:24 161:5 167:18 180:20 208:25 209:10 209:21 211:6 214:16 218:24 254:16 taken 1:17 5:13 72:19 181:5 268:23 talk 9:1 28:8 44:13 45:8,9 68:10 71:24 72:11 89:5 97:21 99:12,22 124:23 209:20 212:10,18 213:11,20 214:11 219:22 220:18 225:12 229:11,15,25 244:22 261:6 talked 116:15 125:4 172:18 197:1 198:21 talking 33:13 58:20 72:3,6,9 89:8 95:24 123:2 130:8 171:17 240:8 253:10 talks 159:7 244:19 tanked 184:6 targets 229:14 253:19
---	---	--	---

[tell - think]

tell 15:15 27:9 27:10 29:17 37:20 56:1 79:7 89:24 105:20 106:7 125:7,13 147:12 213:25 223:6 247:6 260:10 telling 189:22 252:6 tells 156:21 temperatures 159:20 tempered 173:9 ten 127:5,9,14 180:8 198:13 term 12:25 20:2 25:25 27:8 29:16 41:12 80:24 82:8 107:10 terminology 27:8 terms 21:7 22:20 65:11 66:9 76:9 202:11 203:25 212:2,12 terrible 177:11 test 104:15 116:17 159:19 160:21 190:13 tested 68:21 101:19 160:24	245:21 252:21 257:11 testified 6:21 175:23 205:9 205:12 221:22 237:21 testify 168:21 testimony 15:15,19 23:3 23:16 24:3 26:10,20 27:5 28:23 30:1,10 31:9 32:20,24 50:15,22 54:11 54:17 55:8 57:24 65:10 67:10 69:21 74:13 75:14 83:19 88:16 91:4,22 96:3,7 99:5 109:24 111:13 112:17 120:24 143:11 161:21 166:4 166:14 175:2,9 176:20 178:9 181:8,11,15 184:13 190:7 204:5,9 208:18 213:23 214:5 216:7 222:6,24 223:19 224:20 240:18 246:17 256:18 257:5 260:6 268:9,23	testing 69:17 106:17 127:22 tests 105:21 106:8 texas 1:20,22 5:19 7:7 186:18 267:5 267:13 268:2,7 269:6,8 text 180:18 221:17 texts 181:19 thank 7:8 8:18 12:11 53:24,25 59:5 61:8 62:7 62:7 85:4 104:17 107:6 129:5 133:12 141:15 142:24 146:8 148:19 155:1,5 163:4 181:18 189:23 192:10 216:8 234:24 236:5 252:4 261:15 thanks 123:6 therapeutic 95:9 150:22,24 171:14 230:11 therapies 130:19 228:12 241:6 therapy 70:23 75:18,22,25 76:16 126:7	134:11 151:16 156:20 164:1,7 167:2,2 197:25 232:12 242:6 theses 98:4 thick 14:5 thickness 31:25 95:3,5 151:18 151:21 171:18 171:19 172:9 185:6 198:1 201:10 230:13 230:14 234:8 247:21 248:1 260:21 261:3,6 thing 8:8 30:21 60:17 84:11 88:23,25 89:25 106:12 113:9 131:12 138:7 149:16 176:10 176:11 181:17 202:22 204:1 things 60:3 65:13 69:24 71:25 89:20 125:24 147:12 164:11 177:4 211:7 212:13 221:21 237:25 252:8,9 think 8:14 14:4 21:13,13 22:11 23:19 33:21 35:25 37:13
--	--	--	--

[think - today]

39:1,2,4 59:18 62:19 65:3,15 65:18 66:3 68:18,19 70:3 84:16 86:23 94:11 101:15 121:4 130:20 131:11 140:24 148:22 150:6 152:24 154:24 161:9 164:5 170:13 172:24 174:4 179:13 180:15 195:14 204:20,24 205:15,18 222:19 231:25 233:2,10 236:4 236:20 240:23 242:16 257:8 258:14,16,20 thinking 154:14 thinks 159:16 thinner 151:8 151:10 thinning 153:5 153:25 third 131:7,21 169:3 170:9 181:25 thought 21:9 26:1,1 30:7,11 31:16,25 32:4 33:18 35:23	37:11 118:12 118:14 131:15 131:22 134:12 149:24 174:24 185:6,10 223:23 234:9 234:12 238:14 252:19 256:2 256:10 thousand 12:21 13:1,9 204:21 205:4 threatening 128:9 three 9:24 25:20 44:25 46:12 47:9 48:8,19 49:5 51:6,19 94:15 101:10 103:25 122:8 133:19 134:3,18 139:11 142:20 146:13,19 147:14 154:15 165:25 166:8 166:24 169:25 170:4 178:15 178:19,20,22 179:18 182:21 190:14,23 192:4 193:10 193:22 194:21 195:18 196:10 196:14,14	198:10,13 216:11 221:2 244:8 246:21 253:24 254:2,4 256:2 262:11 262:21 thresholds 77:4 77:7 throckmorton 269:8 tied 42:23 43:4 tight 126:1 tighter 126:3 till 162:16 time 5:8 6:2 8:1 8:1 9:8,12 10:4 10:13,17,21 11:1,13,17,20 15:22 22:3 25:2,4,7 30:6 30:12,24 31:15 31:22 41:9 45:5 49:20 54:19 58:19,20 60:18 64:21 65:12 66:4 69:6 72:2,11 81:8 83:6,13 83:22 85:3,17 85:19 86:4 104:12,25 106:23 108:1,3 112:1,11,23 115:6 116:3 117:21 119:3	119:12,16,18 119:22 120:21 123:24 130:13 130:20,21 137:5,7 148:3 150:7 157:25 160:24 161:4 167:14 183:16 185:1,3 196:22 198:23 203:24 208:1 215:13 216:18 218:14 219:23 224:4,5 225:5 231:12 233:17 234:5 249:5 258:10 260:4 261:11 264:1,6,10,12 268:16 times 7:11 19:4 25:23 44:15,16 111:15 125:15 127:21 129:13 132:2 161:1 172:22 189:20 258:5 tip 151:12 title 14:1 141:18 155:8 235:2 titled 14:11 today 6:12,16 7:8,17 8:6 13:20 14:17,24 15:8,13,15,23
---	---	---	--

[today - treatment]

16:6,20 18:2,4 18:16,18,25 19:8,14 41:21 50:18 51:25 52:10,19 53:6 53:8 58:25 65:7 71:16 121:17 181:6,8 187:3 203:20 204:5 207:2,11 207:21 208:5 208:12,15,22 212:11,21 213:23 214:14 216:18 217:5,7 217:12 218:11 218:20,25 220:21 221:9 221:20 225:14 236:8,13 237:1 249:1 264:10 today's 265:2 together 154:3 told 222:15 247:12 262:9 tolerability 245:14 tolerate 138:25 tolerated 196:12 248:2 261:5 262:14 took 123:16 124:1 181:14 183:15 197:17	top 18:12 54:25 146:24 total 56:1 140:13 145:22 265:2 totalitary 95:12 totality 27:11 35:19 37:7 38:21 40:2 46:12 47:11 52:7,7 53:4 55:9 56:1,22 58:22 86:20 90:15 95:13 99:17 105:21 106:8 114:1 115:22 122:10 143:12 172:19 tough 164:12 towards 165:2 tracer 216:14 trade 76:7,10 trademark 1:1 5:17 traffic 164:20 training 8:23 9:15 transcript 264:16 268:8 268:11 trap 3:14,19,22 4:4 20:19,20 23:6,7 24:7,8 25:12 32:1,5 35:16,17 37:4	37:5 38:18,19 70:11 98:12,13 99:10 100:4,15 100:20 103:22 117:18,24 118:4 132:3,7 140:10 141:19 143:13 150:25 155:10 157:4 159:4,8,10 169:20 171:15 172:14 173:1 177:19 179:6 184:18,23 185:7,11 189:2 189:17 190:13 226:17,18 228:11,25 229:19 230:11 231:8 232:3,21 234:9,13 235:2 235:10,22 236:10 237:3 238:19,21,25 239:1,9,18,19 240:15,20 242:22 243:7 243:12,21,24 244:10 245:1,8 245:15 246:3 248:8,18 249:14,16,25 250:7,9,23 251:7 255:7,17 255:18 256:3	256:24 257:21 257:24 259:14 260:15 261:2 263:7,16 traps 244:20 treat 16:17,18 78:18 84:8,8 97:20 110:1,13 112:8 126:13 128:24 136:1 138:19,23 175:22 treated 69:24 81:12 92:1 165:16 169:10 treating 44:2 68:5 71:13 74:4 80:24 81:6,19 82:8 82:14 83:3,11 83:17 84:3,19 85:8 105:14 109:25 110:16 112:21 114:18 119:1,5,5 128:14 191:15 191:15,16 241:22 treatment 3:14 20:10 35:9 36:21 38:10 44:11,14,22 46:10 48:6 49:3 50:23 51:3 62:6
--	---	---	--

[treatment - tried]

67:17 71:8,10 77:7,20 78:2 79:19 81:14,15 81:21,22 82:20 84:9,13 85:1 85:10,16,17 86:1,1,9,14 92:4,18,21 94:5,6 98:3 100:16 106:11 106:19,20 112:24 113:23 114:21,22 115:4,12 116:4 118:24 119:13 119:16,23 120:22 121:3,5 121:24 127:10 128:2,11,12 129:24 132:21 132:23,24 133:3,18 134:2 134:7,17 136:3 136:11,17 147:25 148:6 152:6,7 158:11 163:22 169:9 172:4 178:10 178:11 195:5 196:19 198:17 199:23 200:4 200:10 210:13 222:13 230:25 231:1 241:5,10 245:15 262:19	treatments 47:5 107:19,20 107:24,25 128:6 165:15 226:9 232:13 242:4,6 trend 152:4 165:2,21,21 166:16,22 230:23 trial 1:2 4:1 20:13 25:3,6 25:15 30:23 31:11,16 33:11 33:12,17 35:10 36:12,23 37:8 37:9 38:2,12 40:3 70:9 73:24 74:17 78:8 86:16,21 86:21,25,25 89:16,21,24 91:6,14,17 92:10,12,13,25 93:14,14,17,18 93:20 94:8 98:5 101:18 103:19 117:17 124:10,11,23 125:22 126:14 126:22 127:15 127:17 129:8,9 130:23 131:2,8 131:16 134:9 140:4,6,9	141:1,3,8,8,9 147:21,24 148:17 149:13 150:11,12,12 150:16 162:17 166:7,18 167:1 169:23 170:24 177:5,23 188:7 188:9 190:4 191:4,11,14,22 192:2,5,13 195:10 196:13 197:18,21 199:16,19 200:22 201:4 209:22,24 210:1,5 211:17 212:9,23,24 213:11 214:8 226:10,24 227:2,3,4,5,12 243:4 253:20 254:10,14 trials 10:21 12:4 20:7 24:22 25:5 27:10 29:17,19 31:1,2,13,20,21 32:18 33:6,12 33:16 34:5 35:6 36:3,17 37:17 38:7 39:7,10 44:6 63:24,25 64:3 64:7,9,9,10,11	64:11 65:15,20 70:20,24 71:15 75:5,7 78:14 87:19,24 88:18 89:2,13 90:1,4 90:6 97:25 99:21 100:6,12 100:24 105:24 106:13 117:8 117:12 118:19 122:24 123:9 123:12,14 124:4,11,14,18 126:5,9 127:2 129:10 130:10 130:14,22 131:22 146:18 160:21 166:18 167:7 185:2,3 188:6 190:10 190:14 191:19 202:19,22,25 203:3 212:10 212:20 213:13 213:21,24 214:11,12 224:24 225:13 226:6 233:5 234:4,5 245:18 246:6,12 247:3 247:13 248:16 250:21 252:22 254:9 257:18 tried 107:19 206:6 224:10
---	---	--	--

[true - unmasked]

true 28:4 92:5 92:9 268:8 truly 125:7 truth 189:22 try 27:15 33:1 33:25 44:17 63:5 74:16 76:9 100:20 109:13 139:4 174:18 208:1 trying 28:10 29:20 37:21 68:22 69:16 72:5 77:18 93:8 109:18 121:8 146:15 174:17,22 175:15 188:6,9 223:11 224:6 231:5 246:20 tuffs 233:14 turn 27:16 80:21 103:8 139:22 142:14 206:2 209:16 215:11 216:21 216:23 218:17 261:16 two 24:24 29:18 31:1 32:17 33:5 34:4 61:9 77:13 103:24 106:16 146:19 147:13,14,15	150:17 190:12 197:4 198:12 201:17 234:17 235:23 252:21 252:23 263:10 type 111:2 typical 111:2 typically 147:24,24 237:8 <tr> <td>u</td><td></td></tr> <tr> <td> u 10:25 11:1 76:6 79:2 u.s. 1:7 3:11 16:22 131:1 uh 115:15,17 157:13 210:2 228:7 unaware 236:8 236:13 237:1 uncertain 100:1 uncertainty 20:20 23:7 24:8,13,20 25:17,25 26:5 26:15,25 35:17 37:5 38:19 98:13 226:18 under 8:23 15:4 133:16,25 186:14 188:13 231:3 238:18 238:24 255:17 </td><td></td></tr>	u		u 10:25 11:1 76:6 79:2 u.s. 1:7 3:11 16:22 131:1 uh 115:15,17 157:13 210:2 228:7 unaware 236:8 236:13 237:1 uncertain 100:1 uncertainty 20:20 23:7 24:8,13,20 25:17,25 26:5 26:15,25 35:17 37:5 38:19 98:13 226:18 under 8:23 15:4 133:16,25 186:14 188:13 231:3 238:18 238:24 255:17	
u					
u 10:25 11:1 76:6 79:2 u.s. 1:7 3:11 16:22 131:1 uh 115:15,17 157:13 210:2 228:7 unaware 236:8 236:13 237:1 uncertain 100:1 uncertainty 20:20 23:7 24:8,13,20 25:17,25 26:5 26:15,25 35:17 37:5 38:19 98:13 226:18 under 8:23 15:4 133:16,25 186:14 188:13 231:3 238:18 238:24 255:17					

 undercuts 175:6 **underlying** 112:9 **undersigned** 267:6 269:2 **understand** 7:16,21 16:25 20:1 21:17,23 22:6 28:15,18 29:1,8,9 30:9 36:4 40:7,13 41:5,12 43:3 46:14 68:23 69:16 71:21 81:4 98:15 101:8 102:2,6 109:12,19 120:1 131:6 146:16 219:9 220:14 237:17 243:4 245:16 248:14 262:2,5 **understanding** 18:4,18 19:9 21:3 22:25 23:10,13,25 26:6,16 27:1 28:11 34:21 40:18,23 41:5 41:12 81:18 82:7,12 104:18 105:3,5 135:2 206:3,4,14,22 207:5,15 208:3 | 208:14 209:12 217:7,18,24 218:1,4 231:17 231:20 250:23 **understatement** 184:4 **understood** 41:3 70:11 81:15 84:12 85:16 108:20 117:17 172:12 172:16 177:17 177:21 189:1 238:9 256:24 **undertreatment** 169:11 **unethical** 134:12 191:19 191:20 203:4 **unexpected** 43:24 **unintelligible** 102:3 125:3 217:20 **unique** 145:25 238:20 239:8 239:17,25 **unit** 5:12 **united** 1:1 5:16 74:20 107:15 **units** 265:3 **university** 8:24 9:3 **unmasked** 12:5 |

[unmet - vein]

unmet 43:23 44:20 45:2 47:25 48:4,10 48:15,21 unquote 101:18 101:19 unreasonable 149:16 150:7 untreatable 107:18 untreated 169:13 unusual 111:22 146:4 uptick 198:16 upwards 152:5 230:23 urquhart 2:4 use 42:24 43:6 43:15 56:5 74:20 76:7 101:16 107:10 117:3 166:16 184:21 187:16 190:13 222:2 242:3 used 10:3 13:1 13:2 30:22,22 31:14 37:7 38:21 57:1,12 57:25 76:8 84:25 100:24 116:15 117:9 187:12 243:21 250:14 251:7	257:22 258:17 265:3 268:16 using 97:19 165:24 169:17 170:14 182:21 usually 12:6 108:3 205:5 v v 11:2 76:6 79:21 v1.c 36:17 38:8 98:1 226:7 v1c 20:8 v2 10:22 11:1 va 196:10,15 262:12,22 vague 88:2 248:23 value 110:7 variable 47:6 175:4,14 various 75:7 112:15 vascular 3:18 3:21 10:3 67:15 68:2,8 111:16 141:19 155:9 241:8,19 241:25 252:25 vascularization 80:2 vaso 111:14 vegf 3:14 4:4 13:13 20:19,20 23:6,7 24:7,8	25:12 30:4 32:1,4 33:16 35:16,17,22 37:4,5 38:18 38:19 67:25 68:5,6 70:11 70:24 71:5 74:19 75:18,22 75:25 76:16,23 77:2,7,20 98:12,13 99:10 100:4,15,20 103:22 108:2 111:14,14,15 117:18,24 118:4 122:24 124:4,14 126:7 128:15 132:3,7 138:17 140:10 143:13 150:24 157:4 159:4,7 159:10 166:7 169:20 171:14 172:14 173:1 177:19 178:11 179:6 184:17 184:23 185:7 185:10 189:2 189:17 190:13 197:25 226:17 226:18 228:11 228:12,13,25 229:18,21 230:11 231:8 232:3,12,21,22	234:9,12 235:2 235:9,22,24,25 236:3,10,11 237:3,4,19 238:3,4,10,18 238:21,24 239:1,8,18,19 240:14,19 241:6,18,23,24 242:3,15,22 243:6,12,21,24 244:9,19 245:1 245:8,15 246:3 248:7,18 249:14,16,25 250:7,9,11,13 250:14,23 251:7 252:12 252:16,18 253:21 255:7 255:17,18 256:3,24 257:21,24 259:13 260:15 261:2 263:7,16 vegfs 107:14 242:10 vein 62:25 63:10,20 67:5 67:20 68:16 78:21,24 79:1 79:10,15,16 87:6,6,7,19,20 241:13
--	---	--	--

[verbal - visual]

verbal 7:23 veritext 5:21,23 265:4 269:7 versed 60:16 versus 5:15 39:3 45:16 60:2,3,3 100:6 191:6 vessels 67:14 67:15 76:22 80:2 241:8,9 video 5:9,12 264:16,19 videographer 2:13 5:3,21 6:18 53:15,18 107:1,4 108:15 108:18 139:16 139:19 180:23 181:1 214:18 214:21 261:11 261:13 264:15 264:18,21 265:1 videotaped 1:11,14 265:2 view 20:6,6 24:16,16,19,22 25:13,16,22 31:20,21 35:5 35:6 36:3,3,16 36:17 37:17,17 38:6,7 39:6,6 47:9 56:9,24 57:10 58:20	62:15 68:24,25 69:7 72:21 81:23 97:11,19 97:24,24 98:21 99:21,21 100:12 105:24 106:3,3,14 110:6 112:14 115:1,8 117:8 117:15 118:22 122:23,24 123:21,21 126:5 130:10 130:10,13,13 131:21,22 136:2 150:7 169:9,10 170:11,11,24 171:4,4 174:23 182:2,2 185:1 185:3 188:6,11 188:12 190:11 190:11,14 191:20 200:4,4 200:10,10,23 200:23 201:5,5 201:23,23,25 201:25 202:3,3 221:23 222:3 222:15 224:9 224:16 225:25 226:1,6,6 227:19 233:5 233:25 234:4,5 257:18,18	viewed 32:6 41:24 113:21 115:3,10 121:1 185:12 189:25 234:14 violated 78:16 violation 76:8 vision 67:17 68:8,9 71:6,7 71:17,17 75:20 84:14 95:17 105:19 107:19 108:4,23 111:4 112:25 120:12 125:24 128:9 128:13 135:17 148:7,12 153:13,15 175:18 179:15 179:25 197:14 197:24 198:9 241:10 242:1,2 242:7,12,13 254:11 263:17 263:22 visit 128:8 199:8 visits 44:12 45:6 126:4 127:22 128:7 190:25 211:5 222:19 vista 65:19 visual 86:23 89:11 91:12	92:24 94:15,19 110:8,20 111:2 113:23 114:23 117:10,22 118:4 121:2 122:3 124:2,2 126:23 127:24 134:23,24 135:13 144:2 144:10,16,23 147:19 149:1 150:15,17 153:7,7,10,12 153:16,20,20 153:22 156:11 157:21 161:24 162:1,4,8 163:1,12 165:2 165:9 166:1 169:15,16 172:16 173:21 174:6 175:13 175:24 176:4,6 176:11,15,25 177:1,11,21,24 179:3 182:16 182:23 183:6 183:21 193:11 194:4,12 195:6 195:18 196:5 198:2 240:4 245:24 246:23 248:2 259:14 260:15 261:4
--	---	--	---

[vitae - weeks]

vitae 3:10 vitrectomies 9:23 12:22 13:3,9 vitreoretinal 9:6 10:10 vivid 65:19 voices 264:20 264:25 vs 1:7	214:25 220:8 224:2 228:3 229:4,15 260:8 261:10 264:16 264:19,22,23 way 21:16 24:5 54:6 76:19 89:15 105:19 105:22 106:1,7 128:1,24 131:13,20 138:23 148:8 148:12,16 164:15 167:3 169:23 202:17 204:6,9 211:11 216:11 224:25 225:6,16 236:4 246:7,7 258:24 ways 8:16 138:21 we've 53:12 101:4 121:19 139:13 164:15 167:21 168:6 169:1 171:17 181:5 183:20 214:15 242:22 243:22 244:5,5 249:1,4 258:4 263:5 wear 150:22,25 171:15 230:12 wearing 173:16	week 3:19 24:24 25:12 27:14 31:17 32:3 33:22 35:4 36:1 37:13 38:5 99:19 100:1,10 100:12,13,14 100:19 101:11 101:24 103:24 103:24,25 122:8 132:5,6 132:25 134:8 136:12,18 137:12,17 138:9 140:12 140:16,18,23 140:23 150:25 151:1,9,11 152:3,3,5,10 154:18 155:11 157:1 158:18 161:9 162:10 163:2 165:8 169:25 170:15 171:6,15,16 172:3,3,13,15 172:17 173:2 175:6 177:18 177:20 182:7 182:17,22,24 184:3,18,24 185:9 187:19 189:3,18 190:25 230:12	230:12,21,21 230:24 234:11 243:6,6,7 249:12 253:25 263:16,18 weeks 24:15 25:19 32:1 44:24 45:2 48:8,10,18,20 49:4,6 50:25 51:5,7,18 104:2 132:12 132:13 133:4 137:11,15 138:9,12 139:8 140:11 142:19 144:4,5,12,14 149:3,6 154:11 157:2,21,22 158:9,10 160:7 161:5,18 165:3 165:10 169:14 170:6 173:23 176:18,25 178:5 182:13 182:15,24 183:7,22 184:9 185:7 190:20 190:21,22 200:6,11 234:9 245:2,9,13,25 246:4,14 247:25 248:9 254:1,4,6 261:2 263:7,23
w			
waffles 179:21 walk 13:18 14:15 15:6 wane 95:9 172:18 182:17 182:24 wanes 184:3 waning 173:16 want 8:12,22 30:9 36:6 45:20 54:10 55:10,12 71:20 71:23 77:8 95:20 107:8 108:9 109:13 124:23 133:7 139:23 140:1 144:25 157:13 164:16 168:23 177:12 181:24 189:10,13 193:1 196:7 206:2 208:24 209:10,10,20			

[weeks - yeah]

263:23 weight 243:1 welcome 107:6 139:21 181:3 214:23 255:4 went 18:13 70:20,21 107:17 164:8 167:1 west 2:9 wet 3:22 20:10 35:9 36:21 38:10 61:19,23 62:3,10 67:22 69:1,9 72:2 87:3,12,13,15 87:25 97:20 98:3 113:6 132:23 135:23 136:1,11,17 141:19 151:20 171:21 226:9 227:22 230:16 238:15 240:24 241:15 244:22 whim 156:21 whispering 5:6 white 10:1 227:21 wide 100:17,18 widely 44:14 186:1 willing 208:4 win 45:7	witness 1:15 6:17,19 14:13 15:21 16:10 17:14,23 24:4 28:5 41:16 42:4 53:14 55:18 58:18 60:11 67:11 73:19 77:14 81:2 93:23 97:2 101:13 102:23 103:11 105:13 115:5 125:17 126:17 133:6 143:5 147:2 158:5,25 163:10,20 168:20 175:9 176:23 183:10 190:9 192:19 194:16 216:17 219:6,12 220:10 235:12 237:21 247:18 251:11 252:1 253:15 266:2 268:9,10,13,13 woo 2:13 6:14 woods 244:17 word 13:2 18:19 19:5 166:16 173:7 186:18 258:17 wording 120:3	words 15:22 17:25 19:7,7 19:10 25:9 89:20 127:18 140:12 150:15 151:13 153:4 153:11 156:13 168:13 177:10 210:24 222:1 235:17 239:23 258:18 work 21:13,19 21:25 22:7,12 24:15 25:11 30:7,11 31:16 32:5 33:19,21 39:2 131:9 171:6 175:7 185:11 187:20 195:15 202:20 203:21 204:15 205:1 234:13 240:11 243:15 246:21 252:9 254:20 258:21 worked 21:9 107:20 211:22 working 109:16 211:25 212:1,25 works 68:13 89:22 130:24 153:19 world 30:5,17 33:16 107:14	107:15 worldwide 35:22 130:25 131:3,15,23 worse 126:11 128:12 worth 131:15 131:22 132:10 172:24 246:20 269:8 wound 238:13 wrap 18:10 wrapping 16:12 write 244:18 writer 238:1 writing 203:3 244:16 written 237:14 244:16,17 259:3,6 wrong 14:4 147:15 198:2 wrote 237:7,11 247:6
			x
			x 3:5,8
			y
			yeah 9:4 10:25 12:18 22:5 32:21 42:7 43:19,21 47:4 48:5 50:23 51:23 52:5

[yeah - zoom]

53:4 54:9	204:2 207:22	140:5 141:15
56:22 59:25	212:18 213:11	143:3,3,3
62:7 63:14	215:16,17	155:16 156:3
65:11 69:23	218:9 219:2,13	156:20 159:7
72:11,14,15,17	220:15 221:7	york 2:10
73:22 81:3	225:6 227:3,5	z
82:11 83:20	227:17 229:11	z 10:25 76:6
84:25 88:4	229:25 232:7	zach 2:3 6:8
90:15 91:11	235:20 236:13	268:18
93:13 96:8,16	237:7 239:5,23	zachsummers
102:9 103:3,4	239:23 240:8	2:5
103:12,18	244:4 247:10	zero 140:12
104:3,5,7,7,15	248:14 249:12	151:4 154:4
106:24 108:11	250:4 251:3,21	254:13
109:12 112:2	253:5,5 256:8	zoom 2:8,13
114:15 115:13	258:12,12	
115:13,14,19	259:9,19 260:7	
115:21 119:19	262:5,8 263:20	
120:9 124:1,1	264:17	
125:2 129:19	year 3:17 74:7	
130:1,6 138:5	94:2,9 104:9	
140:1 141:4	104:10 129:13	
143:15,21,21	134:12 140:19	
144:15 145:3	141:1 142:9	
145:15,24	155:8,19 169:9	
147:9 148:19	169:12 192:20	
150:11 151:6	195:2,11	
152:20 158:1	198:25 199:15	
158:22,22	199:18 210:20	
161:23 170:7	215:2 262:1	
170:18 175:11	years 65:12	
179:13 183:13	70:18 189:8	
189:21 197:1	203:18 216:1	
200:9,16 201:3	yep 55:1 96:14	
202:1,20 203:7	114:9 133:24	

Federal Rules of Civil Procedure

Rule 30

(e) Review By the Witness; Changes.

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

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

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

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

VERITEXT LEGAL SOLUTIONS

COMPANY CERTIFICATE AND DISCLOSURE STATEMENT

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

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

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Errata

Deposition of David M. Brown, MD

December 13, 2023

Samsung Bioepis Co., Ltd. v. Regeneron Pharmaceuticals, Inc.

IPR2023-00442

Page:Line	Change From	Change To	Reason
13:4	individual patients	vitreous	Transcription Error
13:16-17	than an	—	Transcription Error
24:19	1, 2	1/2	Transcription Error
24:24-25	two Q8 arms	2Q8 arm	Transcription Error
25:8	foreign redundant	for and running	Transcription Error
25:22	1, 2	1/2	Transcription Error
31:24	rise and mean	rise in mean	Transcription Error
35:6	VIEW trials	VIEW 2 trials	Transcription Error
44:3	are	on a	Transcription Error
56:24	1, 2	1/2	Transcription Error
66:3	part of	prior to	Transcription Error
71:18	MARINE	MARINA	Transcription Error
97:24	VIEW 1, VIEW	VIEW 1, VIEW 2	Transcription Error
118:16	PTD	PDT	Transcription Error
149:7	doggy	dodgy	Transcription Error
152:10	CR2	CRT	Transcription Error
169:12	scheduled	schedule	Transcription Error
172:1	bravo, and	bravo, in	Transcription Error
174:23	view	VIEW	Transcription Error
200:14	3Q8	2Q8	Correction
205:21	outcome	Alcon	Transcription Error
206:20	yet	today	Transcription Error
223:12	better	better than	Transcription Error
241:15	retinopathy	retinopathy of	Transcription Error
248:3	neovascular...	neovascular AMD.	Transcription Error
248:13	That makes sense.	I see that sentence.	Transcription Error
254:9	Panda	PANDA	Transcription Error
254:14	Panda	PANDA	Transcription Error

January 12, 2023

Date



David M. Brown, MD