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Page 1

1 APPEARANCES	1 I N D E X (continued)
2	2
3 FOR THE PETITIONER:	3 DEPOSITION EXHIBIT: PAGE
4 QUINN EMANUEL URQUHART & SULLIVAN LLP	4 Exhibit 9 - Article, "Crystal Structure at 1.7 A 92
5 BY: SARAH M. CORK, PH.D., ESQ.	5 Resolution of VEGF in Complex with
6 865 South Figueroa Street, 10th Floor	6 Domain 2 of the Flt-1 Receptor";
7 Los Angeles, California 90017	7 Exhibit 2081
8 213.443.3633	8 Exhibit 10 - U.S. Patent No. 7,374,758 B2 92
9 sarahcork@quinnemanuel.com	9 Exhibit 11 - Article, "Identification of the 96
10	10 Residues in the Extracellular Region
11 FOR THE PATENT OWNER:	11 of KDR Important for Interaction with
12 ARNOLD & PORTER KAYE SCHOLER LLP	12 Vascular Endothelial Growth Factor
13 BY: JEREMY COBB, ESQ.	13 and Neutralizing Anti-KDR Antibodies";
14 BY: ALICE HO, PH.D., ESQ. (Appearing Remotely)	14 Exhibit 2082
15 601 Massachusetts Avenue NW	15 Exhibit 12 - Structure Article, "The Structural 96
16 Washington DC 20001	16 Basis for the Function of Two Anti-VEGF
17 202.942.6828	17 Receptor 2 Antibodies"; Exhibit 2083
18 jeremy.cobb@arnoldporter.com	18 Exhibit 13 - Article, "KDR - Vascular endothelial 97
19 alice.ho@arnoldporter.com	19 growth factor receptor 2 - Homo sapiens";
20	20 Exhibit 2084
21 ALSO PRESENT: EILEEN WOO, ESQ. (Appearing Remotely)	21 Exhibit 14 - UNIPROT - 3/7/23 4:30 p.m.; Exhibit 2085 97
22	22 Exhibit 15 - Article, "A signature of the T - R 118
23 THE VIDEOGRAPHER: GREGG EISMAN	23 transition in human hemoglobin";
24	24 Exhibit 2069
25	25 //
Page 2	Page 4
1 I N D E X	1 I N D E X (continued)
2	2
3 EXAMINATION PAGE	3 DEPOSITION EXHIBIT: PAGE
4 By Ms. Cork 7	4 Exhibit 16 - Article, "The molecular structure of 129
5	5 spider dragline silk: Folding and
6 DEPOSITION EXHIBIT: PAGE	6 orientation of the protein backbone";
7 Exhibit 1 - Expert Declaration of Alexander M. 10	7 Exhibit 2070
8 Klibanov, Ph.D.; Exhibit 2057	8 Exhibit 17 - Article, "Relationship of protein 129
9 Exhibit 2 - U.S. Patent No. 10,130,681 B2 23	9 molecular structure to metabolisable
10 Exhibit 3 - U.S. Patent No. 9,254,338 B2 25	10 proteins in different types of dried
11 Exhibit 4 - Textbook excerpt, "Biochemistry - 52	11 distillers grains with solubles: a
12 Fifth Edition"; Jeremy M. Berg, John L.	12 novel approach"; Exhibit 2072
13 Tymoczko, Lubert Stryer; Exhibit 2065	13 Exhibit 18 - Article, "Molecular Dynamics Study of 130
14 Exhibit 5 - "WHO Drug Information"; Volume 20, 68	14 Onset of Water Gelation around the
15 Number 2 - 2006; Exhibit 1107	15 Collagen Triple Helix"; Exhibit 2071
16 Exhibit 6 - Article, "The second immunoglobulin-like 91	16 Exhibit 19 - JMB article, "The Folding of Spectrin 130
17 domain of the VEGF tyrosine kinase	17 Domains I: Wild-type Domains Have
18 receptor Flt-1 determines ligand binding	18 the Same Stability buy very Different
19 and may initiate a signal transduction	19 Kinetic Properties"; Exhibit 2073
20 cascade"; Exhibit 2078	20 Exhibit 20 - Article, "VEGF Trap-Eye for the 156
21 Exhibit 7 - UNIPROT document; 3/7/23; 4:26 p.m.; 92	21 treatment of neovascular age-related
22 Exhibit 2080	22 macular degeneration"; Exhibit 1006
23 Exhibit 8 - UNIPROT document; "FLT1 - Vascular 92	23 Exhibit 21 - Article, "Aflibercept"; Exhibit 1012 192
24 endothelial growth factor receptor 1 -	24
25 Homo Sapiens"; Exhibit 2079	25 //
Page 3	Page 5

1 DECEMBER 20, 2023 8:58 A.M. SAN DIEGO, CALIFORNIA 2 THE VIDEOTAPE OPERATOR: Good morning. We're 08:57:26 3 going on the record at 8:58 a.m. on Wednesday, 08:57:36 4 December 20th, 2023. Please note that the microphones 08:57:40 5 are sensitive and may pick up whispering and private 08:57:44 6 conversations. Please mute your phones at this time. 08:57:47 7 Audio and video recording will continue to take place 08:57:50 8 unless all parties agree to go off the record. This is 08:57:53 9 Media Unit 1 of the video recorded deposition of 08:57:57 10 Alexander Klibanov testifying in the matter of Samsung 08:58:01 11 Biopesis Company Limited vs. Regeneron Pharmaceuticals, 08:58:05 12 Inc., filed in the United States Patent and Trademark 08:58:09 13 Office before the Patent Trial and Appeal Board, Case 08:58:11 14 No. IPR2023-00442. 08:58:15 15 This deposition is being held at Morrison & 08:58:20 16 Foerster, LLP, 125231 High Bluff Drive, Suite 100. My 08:58:21 17 name is Gregg Eisman, representing Veritext, and I'm the 08:58:30 18 videographer. The court reporter today is Rosalie Kramm, 08:58:33 19 also from the firm Veritext. I'm not related to any 08:58:36 20 party in this action, nor am I financially interested in 08:58:39 21 the outcome. 08:58:42 22 If there are any objections to the proceeding, 08:58:43 23 please state them at the time of your appearance. 08:58:45 24 Counsel and all present, including remotely, 08:58:47 25 will now state their appearances and affiliations for the 08:58:50 Page 6	1 Do you understand that? 08:59:58 2 A. Yes. 08:59:59 3 Q. You've been deposed before, right? 09:00:01 4 A. Yes. 09:00:02 5 Q. How many times? 09:00:03 6 A. I mean, I don't remember exactly. 09:00:08 7 Q. Can you give me an estimate? 09:00:10 8 A. I would say that over the last 30, 35 years, 09:00:15 9 maybe four dozen times. 09:00:21 10 Q. So you're familiar with the process, but I'll 09:00:28 11 go over some ground rules for this deposition anyway. 09:00:30 12 Okay? 09:00:32 13 A. Okay. And if you could slow down, please, I 09:00:33 14 would greatly appreciate it, and speak up a little bit. 09:00:35 15 Q. I'll do that. 09:00:39 16 I would ask you to listen carefully to my 09:00:41 17 questions, and if there is something you do not 09:00:44 18 understand, let me know, and I will try to make the 09:00:46 19 question clearer. Okay? 09:00:50 20 A. Yes. 09:00:51 21 Q. If you do answer, I will assume that you 09:00:53 22 understood the question. Is that fair? 09:00:56 23 A. Yes. 09:00:58 24 Q. If you need to correct an answer, please let me 09:01:00 25 know, and I'll let you do that. Okay? 09:01:02 Page 8
1 record, beginning with the noticing attorney. 08:58:53 2 MS. CORK: Sarah Cork from Quinn Emanuel on 08:58:56 3 behalf of Samsung Biopesis. 08:58:58 4 MR. COBB: Jeremy Cobb with Arnold & Porter on 08:59:04 5 behalf of patent owner Regeneron Pharmaceuticals, and I 08:59:06 6 believe with me on the line is Alice Ho from Arnold & 08:59:13 7 Porter on behalf of Regeneron as well as in-house counsel 08:59:16 8 from Regeneron, Eileen Woo. 08:59:20 9 THE VIDEOTAPE OPERATOR: Thank you. 08:59:24 10 Will the reporter please swear in the witness. 08:59:24 11 * * * 08:59:32 12 ALEXANDER M. KLIBANOV, PH.D., 08:59:32 13 having been first duly sworn, testified as follows: 08:59:32 14 08:59:32 15 EXAMINATION 08:59:32 16 BY MS. CORK: 08:59:34 17 Q. Good morning, Dr. Klibanov. 08:59:36 18 A. Good morning. 08:59:37 19 Q. Could you please state your full name for the 08:59:39 20 record. 08:59:40 21 A. Alexander Maxim Klibanov, K-l-i-b-a-n-o-v. 08:59:41 22 Q. You've just taken an oath to tell the truth, 08:59:50 23 the whole truth in response to each question that I ask. 08:59:52 24 It's the same oath that you would be given if you were 08:59:55 25 testifying in court. 08:59:57 Page 7	1 A. All right. 09:01:05 2 Q. I'll ask that you please answer audibly and 09:01:07 3 that you not answer with "uh-huh" or "huh-huh" or nodding 09:01:09 4 or shaking your head, because the court reporter can't 09:01:13 5 capture that. Okay? 09:01:16 6 A. Yes. 09:01:18 7 Q. I'll also ask that you please wait until I 09:01:19 8 finish my question before you answer, because the court 09:01:21 9 reporter can only take down one person speaking at a 09:01:24 10 time. Okay? 09:01:28 11 A. Yes, especially if you extend the same courtesy 09:01:29 12 to me. 09:01:32 13 Q. I will try to do that. 09:01:34 14 Your attorney may object to some of my 09:01:37 15 questions today. Unless your attorney instructs you not 09:01:39 16 to answer, you are required to answer my question 09:01:42 17 truthfully and accurately. Okay? 09:01:46 18 A. Yes. 09:01:50 19 Q. If you need a break today, please let me know, 09:01:50 20 and I'll do my best to accommodate you. Okay? 09:01:52 21 A. Yes. 09:01:56 22 Q. I ask that you do not guess when you answer, 09:01:56 23 but that you provide your best estimate or recollection. 09:01:59 24 Okay? 09:02:01 25 A. Yes. 09:02:02 Page 9

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1 Q. Is there any reason that you feel you would be 09:02:04 2 unable to testify truthfully and accurately today? 09:02:06 3 A. Not that I know of. 09:02:10 4 Q. Will you let me know if that changes? 09:02:12 5 A. Of course. 09:02:14 6 Q. I would like to establish a routine for this 09:02:16 7 deposition, that when I direct you to a certain paragraph 09:02:19 8 of your declaration, that you please read that paragraph 09:02:21 9 and enough of your declaration, as necessary, to orient 09:02:25 10 yourself, and then let me know when you're done. Okay? 09:02:27 11 A. Yes. Thank you. 09:02:30 12 MS. CORK: I'd like to mark as Exhibit 1 the 09:02:42 13 Expert Declaration of Alexander M. Klibanov, Ph.D., 09:02:46 14 Exhibit 257 and IPR2023-00442. I have a copy for 09:02:52 15 counsel. 09:03:10 16 (Exhibit 1 was marked for identification.) 09:03:11 17 THE REPORTER: Exhibit 1. 09:03:12 18 THE WITNESS: Thank you very much. 09:03:14 19 BY MS. CORK: 09:03:19 20 Q. Dr. Klibanov, do you recognize your declaration 09:03:20 21 that is Exhibit 1 to this proceeding? 09:03:24 22 A. Yes, this seems to be my declaration that I've 09:03:26 23 submitted in this case. 09:03:28 24 Q. Are you aware of any errors in Exhibit 1? 09:03:29 25 A. No. 09:03:32 Page 10	1 Q. Thank you for clarifying that. 09:04:38 2 Is English your first language? 09:04:41 3 A. No. 09:04:43 4 Q. Do you understand English fluently? 09:04:45 5 A. I think so. 09:04:48 6 Q. We don't need a translator here today, do we? 09:04:51 7 A. I do not. 09:04:54 8 Q. You understand all the words in your 09:04:56 9 declaration, which is Exhibit 1, even though they are 09:04:59 10 written in English? 09:05:03 11 A. I understand them because they're written in 09:05:05 12 English as opposed to Chinese, for example, or German. 09:05:08 13 Q. If I refer to your declaration throughout this 09:05:20 14 deposition, will you understand that I'm referring to 09:05:22 15 Exhibit 1, the declaration for the '681 Patent in this 09:05:25 16 IPR proceeding filed by Samsung Biopesis, unless I 09:05:29 17 specify otherwise? 09:05:34 18 A. I don't see any other choice. 09:05:36 19 Q. Exhibit 1, your declaration, is not the first 09:05:40 20 declaration that you've submitted in a proceeding with 09:05:43 21 respect to the '681 Patent, is it? 09:05:46 22 A. I think it's the second one. 09:05:51 23 Q. You are aware of another IPR proceeding that 09:05:55 24 involves the '681 Patent, true? 09:05:57 25 A. I'm aware that there is another proceeding, 09:06:03 Page 12
1 Q. Is there anything that you would wish to change 09:03:33 2 in Exhibit 1? 09:03:35 3 A. No. 09:03:38 4 Q. You signed this declaration, did you not? 09:03:41 5 A. I did. 09:03:44 6 Q. And can you please go to the last page of your 09:03:46 7 declaration. Is that your signature? 09:03:49 8 A. Yes. 09:03:52 9 Q. You signed this declaration under penalty of 09:03:54 10 perjury, correct? 09:03:57 11 A. Yes. 09:03:59 12 Q. Do you take that oath seriously? 09:04:01 13 A. I certainly do. 09:04:03 14 Q. Did you prepare Exhibit 1? 09:04:05 15 A. Yes. 09:04:09 16 Q. Did you read every word of Exhibit 1 before you 09:04:10 17 signed it? 09:04:13 18 A. Yes. 09:04:15 19 Q. Do you understand every word in your 09:04:17 20 declaration that is Exhibit 1 in this proceeding? 09:04:19 21 A. I think I do. 09:04:23 22 Q. What does that mean? 09:04:26 23 A. That means that I understand it in -- in my 09:04:29 24 way. You may understand a particular word differently, 09:04:32 25 but I understand, you know, as I read it. 09:04:35 Page 11	1 yeah. I don't know all the details, but I'm aware there 09:06:06 2 is another proceeding. 09:06:09 3 Q. And you've been deposed in that other IPR 09:06:11 4 proceeding involving the '681 Patent, true? 09:06:14 5 A. Yes, quite some time ago. 09:06:17 6 Q. When was the last time you reviewed the 09:06:22 7 declaration that you submitted in that other IPR 09:06:24 8 proceeding involving the '681 Patent? 09:06:27 9 A. Shortly before that deposition in that other 09:06:32 10 case. 09:06:36 11 Q. Was there a clerical error in the declaration 09:06:42 12 that you submitted in the first proceeding involving the 09:06:45 13 '681 Patent? 09:06:48 14 A. There may have been. I don't recall. 09:06:51 15 Q. Sitting here today, is there anything you would 09:06:54 16 wish to change in that declaration that you submitted in 09:06:57 17 the other proceeding involving the '681 Patent? 09:07:00 18 MR. COBB: Objection. Form. 09:07:04 19 THE WITNESS: Well, as I just said, I reviewed 09:07:06 20 that other declaration a number of months ago. I haven't 09:07:09 21 even looked at it since then. So there is no way that I 09:07:16 22 can possibly want to correct anything. 09:07:19 23 BY MS. CORK: 09:07:24 24 Q. So there is nothing that you would want to 09:07:25 25 change in any -- in that declaration that you submitted 09:07:26 Page 13

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1 in the other proceeding involving the '681 Patent? 09:07:29	1 was also another patent, another Regeneron patent that 09:10:44
2 A. I don't remember exactly everything that's in 09:07:33	2 was a member of the same family. 09:10:49
3 that declaration. So there is no way that I can possibly 09:07:37	3 Q. You've been involved in other IPR proceedings 09:10:52
4 want to change anything. 09:07:41	4 involving related patents, which I'll call the '338 and 09:10:55
5 Q. But sitting here today, there is nothing that 09:07:43	5 '069 patents for short. 09:11:00
6 you recall that you would want to change for that 09:07:45	6 A. I mean, I -- I'm not sure I understand the 09:11:05
7 declaration. 09:07:47	7 relevance of the numbers that you just mentioned, but 09:11:09
8 A. That's a correct statement. 09:07:48	8 I -- you know, as I said, I was involved in other 09:11:12
9 Q. And for simplicity we can refer to that -- 09:07:56	9 proceedings related to this general subject matter with 09:11:16
10 A. If you could just slow down, ma'am. I will 09:07:59	10 Regeneron being the patent holder. 09:11:23
11 just keep reminding you, but if you do your best to 09:08:02	11 Q. Are you familiar with a Regeneron patent that 09:11:28
12 remember it, I would greatly appreciate it. 09:08:06	12 ends in the number '338? 09:11:31
13 Q. Would it be okay with you if we can refer to 09:08:10	13 A. It sounds familiar. It may have been the first 09:11:39
14 that other proceeding involving the '681 Patent as the 09:08:14	14 patent that I opined on, but, again, I'm not sure. I'm 09:11:42
15 1225IPR? 09:08:23	15 obviously here trying to be laser-focused on the '681 09:11:46
16 A. I don't know what the "1225" refers to. So 09:08:26	16 Patent. 09:11:50
17 maybe we can just refer to it as the other '681 09:08:31	17 Q. You did submit declarations regarding other 09:11:57
18 proceeding. 09:08:39	18 Regeneron patents that are members of the same family as 09:12:01
19 Q. Fair enough. You understand that there is only 09:08:43	19 the '681 Patent, true? 09:12:04
20 other one proceeding involving the '681 Patent that 09:08:46	20 A. I certainly did submit other declarations. 09:12:09
21 you've submitted a declaration in. 09:08:50	21 You're using the expression "the same family." You know, 09:12:13
22 A. The one that we just discussed, I thought -- 09:08:56	22 I'm not exactly sure about that. But they certainly 09:12:19
23 yeah, that's the only one that I'm aware of. 09:08:58	23 dealt with the same general subject matter, and Regeneron 09:12:24
24 Q. You were deposed on the declaration that you 09:09:03	24 was the patent holder. 09:12:30
25 submitted in that other proceeding involving the '681 09:09:06	25 Q. You submitted declarations regarding other 09:12:33
Page 14	Page 16
1 Patent back in May of 2023, right? 09:09:10	1 Regeneron patents that are related to the '681 Patent; is 09:12:36
2 A. I mean, I remember that was about half a year 09:09:16	2 that fair? 09:12:43
3 ago. I don't remember the date. But I will certainly 09:09:19	3 A. Yes, related, that's correct. 09:12:44
4 take your word for it. 09:09:21	4 Q. Can you tell me the last time you reviewed 09:12:48
5 Q. And you were deposed in that proceeding, 09:09:24	5 those declarations? 09:12:51
6 correct? 09:09:26	6 A. The last time I reviewed those declarations was 09:12:55
7 A. Yes. 09:09:27	7 before my deposition in those cases. 09:13:01
8 Q. Are you familiar with that testimony that you 09:09:29	8 Q. And not since then? 09:13:07
9 gave in that deposition? 09:09:37	9 A. That's correct. 09:13:08
10 A. Could you explain what you mean by, "Are you 09:09:38	10 Q. Sitting here today, are you aware of anything 09:13:10
11 familiar with that testimony"? 09:09:40	11 incorrect or factually inaccurate in those declarations? 09:13:13
12 Q. Have you reviewed your transcript from that 09:09:43	12 A. I mean, I don't know one way or the other. I 09:13:20
13 other proceeding? 09:09:46	13 certainly can tell you that when I submitted those 09:13:23
14 A. When? 09:09:48	14 declarations, I -- it was my view that those declarations 09:13:27
15 Q. At any time. 09:09:49	15 were accurate and correctly reflected my opinions. 09:13:35
16 A. I believe I reviewed it shortly after the 09:09:52	16 Q. So sitting here today, there was -- there is 09:13:43
17 deposition and submitted errata sheets, and that was the 09:09:56	17 nothing you would change in any of those prior 09:13:45
18 last time I saw it, but that again was about half a year 09:10:03	18 declarations for related patents. 09:13:48
19 ago. And I do remember that our court reporter in that 09:10:07	19 MR. COBB: Objection. Asked and answered. 09:13:52
20 case did a superb job. 09:10:14	20 THE WITNESS: I mean, I -- I would have no 09:13:53
21 Q. This other declaration that you submitted 09:10:26	21 basis for either changing or not changing it, because 09:13:55
22 regarding the '681 Patent is not the first declaration 09:10:29	22 I -- I'm not aware of exactly what was stated in those 09:13:59
23 that you submitted with respect to patents in the same 09:10:32	23 declarations. 09:14:04
24 family as the '681 Patent, true? 09:10:36	24 BY MS. CORK: 09:14:06
25 A. Yes, that's a true statement. I believe there 09:10:42	25 Q. You were deposed on those declarations nearly 09:14:08
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1 two years ago, true? 09:14:11	1 review. 09:18:54
2 A. I mean, that sounds right. Again, I will 09:14:15	2 A. Thank you. Yes, ma'am. 09:18:55
3 certainly take your word for it, because you seem to be 09:14:18	3 Q. You state: "I am being paid for my time spent 09:19:19
4 much more aware of the specific dates than I am. 09:14:21	4 working on this matter at my usual and customary hourly 09:19:22
5 Q. Did you review your transcripts or testimony 09:14:26	5 rate." 09:19:26
6 from those depositions? 09:14:29	6 Do you see that? 09:19:28
7 A. Reviewed when? 09:14:32	7 A. Yes. 09:19:28
8 Q. At any time. 09:14:34	8 Q. What is your usual and customary hourly rate? 09:19:30
9 A. Again, shortly after the deposition itself I 09:14:36	9 A. I believe it is -- in this case, it's \$975 an 09:19:38
10 reviewed the transcript for correctness, and I may have 09:14:43	10 hour. 09:19:43
11 submitted errata sheets. But since that time, I haven't 09:14:50	11 Q. What did you mean that that is your "customary 09:19:50
12 even looked at it. 09:14:56	12 rate"? 09:19:52
13 Q. How long did you prepare for today's 09:15:04	13 A. It means that's what I charge others, as well. 09:19:57
14 deposition? 09:15:06	14 It sort of varies depending on when I started working on 09:20:04
15 A. And when you say "prepared," what exactly do 09:15:12	15 the particular case, but, generally, that means that 09:20:08
16 you mean by that? 09:15:15	16 that's -- that's what I charge others, too. 09:20:13
17 Q. I don't want to invade the province of your 09:15:21	17 Q. Over the past 30 years, you've charged \$975 an 09:20:23
18 counsel's preparation with you, but perhaps you can give 09:15:24	18 hour working on similar matters as an expert witness? 09:20:30
19 me an estimate of the time that you spent doing things 09:15:27	19 A. No. 09:20:33
20 that you would consider preparation for today's 09:15:33	20 Q. When did you start charging \$975 an hour 09:20:41
21 deposition. 09:15:36	21 working on similar matters as an expert witness? 09:20:45
22 A. Sure. Well, I -- I re-reviewed my declaration, 09:15:38	22 A. I mean, I don't know. I started several years 09:20:48
23 which is Klibanov Exhibit 1. I re-reviewed some of the 09:15:51	23 ago. Obviously, when I started out many years ago, 09:20:51
24 key documents cited in this declaration, not necessarily 09:16:04	24 whether it was 30 or 35 years, I charged less, but then 09:20:57
25 the entirety of those documents, but some main points, 09:16:11	25 the cost of living has increased, inflation has taken its 09:21:02
Page 18	Page 20
1 particularly those that are cited in my declaration. 09:16:18	1 toll. So I gradually increased my consulting rate, my 09:21:07
2 And also yesterday I met with counsel for 09:16:25	2 hourly rate. 09:21:15
3 Regeneron for several hours. 09:16:34	3 Q. Are you able to estimate how much time you 09:21:18
4 Q. Can you give me an estimate of the total time 09:16:38	4 spent working on your declarations for the '681 Patent 09:21:21
5 that you've spent preparing for today's deposition? 09:16:41	5 and related patents? 09:21:27
6 A. I mean, I don't know. 10, 15 hours, something 09:16:57	6 A. No. 09:21:31
7 like that. Maybe a little more. 09:17:01	7 Q. You can't provide any estimate at all? 09:21:34
8 Q. You said that you met with counsel for 09:17:10	8 A. I cannot. 09:21:37
9 Regeneron to prepare. Could you identify the counsel for 09:17:11	9 Q. You don't know if it's more than 50 hours? 09:21:40
10 Regeneron who you met with? 09:17:16	10 A. I -- I do not know, and remembering that you 09:21:45
11 A. Sure. So it was Jeremy Cobb who is sitting 09:17:18	11 specifically cautioned me in the beginning of this 09:21:49
12 here. It was his colleague Alice Ho, H-o, and for some 09:17:22	12 declaration (sic) not to guess, I certainly don't want to 09:21:53
13 of that preparation a Regeneron attorney, Eileen Woo, 09:17:34	13 speculate. I have no idea. 09:21:57
14 W-o-o, was also present. 09:17:42	14 Q. But you're refusing to provide an estimate of 09:22:02
15 If you sneeze, then bless you. 09:17:53	15 the amount of time you spent working on your declarations 09:22:06
16 Q. Thank you. 09:18:03	16 in this matter and related matters? 09:22:09
17 How many times have you served as an expert 09:18:10	17 MR. COBB: Objection. Argumentative. 09:22:11
18 witness before? 09:18:12	18 THE WITNESS: I disagree with the way you 09:22:13
19 A. I mean, again, over the last 30, 35 years, 09:18:22	19 phrased your question, in particular using the word 09:22:15
20 maybe close to three dozen times, something like that. 09:18:29	20 "refusing." I'm just unable to do so. I just have no 09:22:19
21 Q. Nearly 40 times? 09:18:35	21 idea. I don't view it as a refusal. 09:22:23
22 A. I mean, that sort of seems about right, over 09:18:39	22 BY MS. CORK: 09:22:30
23 that period of time. 09:18:43	23 Q. Have you served as an expert witness for 09:22:34
24 Q. Could you please turn to paragraph 2 of 09:18:47	24 Regeneron with respect to any other patents than the '681 09:22:37
25 Exhibit 1, and let me know when you've had a chance to 09:18:50	25 Patent and its related patents? 09:22:41
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1 A. Well, you previously mentioned the patent where 09:22:50 2 the last three digits starts with a 3, '338 or something 09:22:54 3 like that. Are you including it in the related family 09:22:58 4 group? 09:23:02 5 Q. Yes. 09:23:03 6 A. Well, then, I don't think that I ever consulted 09:23:07 7 for Regeneron on anything else. Not that I recall, at 09:23:11 8 least. 09:23:21 9 Q. Can you estimate how much Regeneron has paid 09:23:21 10 you for your services as an expert witness? 09:23:26 11 A. I have no idea. Again, the same answer. 09:23:30 12 Q. Can you provide an estimate of how much 09:23:42 13 Regeneron has paid you for your services as an expert 09:23:45 14 witness? 09:23:49 15 MR. COBB: Objection. Asked and answered. 09:23:51 16 THE WITNESS: I'm not able to do so, and I 09:23:52 17 certainly don't want to speculate. 09:23:54 18 BY MS. CORK: 09:23:58 19 Q. So you don't know if Regeneron has paid you 09:24:02 20 more than a million dollars. 09:24:04 21 A. I -- I cannot imagine that it will be more 09:24:09 22 than -- or anything even close to a million dollars, but 09:24:12 23 I -- I have no idea. 09:24:15 24 Q. Do you know if Regeneron has paid you \$100,000? 09:24:17 25 A. I really don't want to speculate. 09:24:20 Page 22	1 THE REPORTER: Exhibit 2. 09:27:41 2 THE WITNESS: Thank you. 09:27:44 3 BY MS. CORK: 09:27:46 4 Q. Dr. Klibanov, do you recognize Exhibit 2? 09:27:47 5 A. Yes. 09:27:55 6 Q. Exhibit 2 is the patent that is the subject of 09:27:56 7 your declaration in this proceeding; isn't that right? 09:28:00 8 A. That's correct. 09:28:04 9 Q. I'm going to refer to this patent as the '681 09:28:06 10 Patent. Okay? 09:28:07 11 A. That's fine with me. 09:28:09 12 Q. Let's turn to the last page and look at the 09:28:13 13 claims, and let me know when you're there. 09:28:16 14 A. Did you say the last page? 09:28:21 15 Q. Pages where the claims are. 09:28:24 16 A. Okay. Yes, ma'am. 09:28:26 17 Q. You recognize these claims, true? 09:28:35 18 A. I mean, I recognize these claims as the 09:28:39 19 concluding portion of the '681 Patent, yes. 09:28:46 20 Q. The claims of the '681 Patent recite a 09:28:51 21 therapeutic dosing regimen involving a VEGF antagonist, 09:28:55 22 true? 09:29:00 23 MR. COBB: Objection. The document speaks for 09:29:01 24 itself. 09:29:03 25 THE WITNESS: Again, you paraphrased what the 09:29:04 Page 24
1 Q. So you're -- you won't provide me an estimate 09:24:29 2 of how much Regeneron has paid you; is that right? 09:24:32 3 MR. COBB: Objection. Form. 09:24:35 4 THE WITNESS: I'm unable to provide you with an 09:24:39 5 estimate. I have no idea. 09:24:41 6 BY MS. CORK: 09:24:43 7 Q. You can't say if it's more or less than 09:24:44 8 \$100,000. 09:24:49 9 A. Again, I'm unable to provide you with an 09:24:50 10 estimate. So I don't want to speculate, in particular 09:24:52 11 given your explicit instructions in the beginning of this 09:24:57 12 deposition. 09:25:00 13 MS. CORK: Could I ask the court reporter to 09:25:43 14 read back your testimony at page 4, lines 19 to 22. 09:25:44 15 (Record was read.) 09:26:19 16 BY MS. CORK: 09:26:20 17 Q. Do you recall that you agreed to provide your 09:26:21 18 best estimate to my questions, sir? 09:26:23 19 A. I do if I have it; but you also instructed me 09:26:24 20 not to guess, and if I were to offer any -- any 09:26:28 21 definitive or semi-definitive response, it will be a 09:26:37 22 sheer guess. 09:26:45 23 MS. CORK: I'd like to mark as Exhibit 2 U.S. 09:27:21 24 Patent No. 10,130,681. 09:27:24 25 (Exhibit 2 was marked for identification.) 09:27:30 Page 23	1 claim says. The claims -- and there are two independent 09:29:06 2 claims, but they both start with the phrase, "A method 09:29:11 3 for treating." But it's not an unreasonable way to 09:29:16 4 characterize them. 09:29:23 5 BY MS. CORK: 09:29:24 6 Q. Do you disagree that the claims of the '681 09:29:31 7 Patent recite a therapeutic dosing regimen involving a 09:29:33 8 VEGF antagonist? 09:29:39 9 A. No. As I just said, it's not an unreasonable 09:29:41 10 way of characterizing the claims. So I do not disagree. 09:29:45 11 I'm not an ophthalmologist, though, or a doctor, even. 09:29:49 12 So my task in this case has been much more limited, and 09:29:56 13 specifically it -- it is limited to the subject matter 09:30:00 14 under the third "WHEREIN" in the independent claims. 09:30:07 15 MS. CORK: I'd like to mark as Exhibit 3 U.S. 09:30:26 16 Patent No. 9,254,338, with a copy to counsel. 09:30:28 17 (Exhibit 3 was marked for identification.) 09:30:34 18 THE REPORTER: Exhibit 3. 09:30:45 19 THE WITNESS: Thank you. 09:30:47 20 BY MS. CORK: 09:30:48 21 Q. Dr. Klibanov, do you recognize Exhibit 3? 09:30:49 22 A. Well, I see that the last three digits, patent 09:30:55 23 number '338. So that appears to be a patent that was the 09:30:59 24 subject matter of my previous testimony. So that's what 09:31:08 25 I can tell you. 09:31:13 Page 25

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1 Q. Please take a moment to flip through the '338 09:31:16 2 Patent, which is Exhibit 3. 09:31:19 3 A. For what purpose? 09:31:24 4 Q. Well, I would like to see if you recognize it 09:31:27 5 once you've had a chance to review it. 09:31:30 6 A. I mean, I don't know what you mean by, do you 09:31:57 7 recognize it? It appears to be the '338 Patent. That's 09:31:59 8 all I can tell you. 09:32:03 9 Q. You've previously offered opinions with respect 09:32:04 10 to Exhibit 3, the '338 Patent, correct? 09:32:06 11 A. That's my recollection. And I think we 09:32:13 12 discussed that issue a few minutes ago. 09:32:15 13 Q. And you're comfortable if I refer to Exhibit 3 09:32:17 14 as the '338 Patent, right? 09:32:22 15 A. That's fine. 09:32:24 16 Q. Let's turn to the end of the '338 Patent and 09:32:27 17 look at the claims. 09:32:30 18 A. Okay. 09:32:34 19 Q. Do you recognize the claims of the '338 Patent? 09:32:35 20 A. I mean, I don't understand the question. 09:32:41 21 Q. Are the claims of the '338 Patent familiar to 09:32:44 22 you? 09:32:46 23 A. I would say vaguely at best. I -- I have not 09:32:51 24 reviewed them recently, certainly not in preparation 09:32:56 25 for -- for this deposition. 09:33:02 Page 26	1 MR. COBB: Objection. Form; scope. 09:35:10 2 THE WITNESS: Let me review the corresponding 09:35:12 3 limitation of the '338 Patent. 09:35:14 4 Yes, it appears to be what that corresponding 09:35:50 5 claim limitation in 3 -- in the '338 Patent is. 09:35:54 6 BY MS. CORK: 09:36:03 7 Q. Do you understand SEQ. ID No: 2 to refer to an 09:36:03 8 amino acid sequence described in these patents? 09:36:07 9 MR. COBB: Objection. Form. 09:36:13 10 THE WITNESS: I understand that the term, the 09:36:28 11 claim term, SEQ. ID No. 2, corresponds to the amino acid 09:36:30 12 sequence provided in each of these two patents, the '681 09:36:38 13 Patent and the '338 Patent. 09:36:43 14 BY MS. CORK: 09:36:48 15 Q. Do you agree that Sequence ID No: 2 is the same 09:36:48 16 sequence for both the '681 Patent and the '338 Patent? 09:36:52 17 A. I did not compare them side by side. 09:37:00 18 Q. Do you have any reason to dispute that Sequence 09:37:05 19 ID No: 2 is identical for both the '681 and the '338 09:37:09 20 Patents? 09:37:14 21 MR. COBB: Objection. Scope. 09:37:17 22 THE WITNESS: I mean, I have no reason to 09:37:20 23 dispute or not to dispute that. As I said, I have not 09:37:25 24 compared the amino acid sequences in these two patents 09:37:28 25 side by side. 09:37:34 Page 28
1 Q. Could you turn back to Exhibit 2, the '681 09:33:16 2 Patent. 09:33:18 3 A. Okay. 09:33:21 4 Q. And go to Claim 1. 09:33:23 5 A. Yes, ma'am. 09:33:31 6 Q. Among other things, Claim 1 of the '681 patent 09:33:35 7 recites that the VEGF antagonist -- 09:33:38 8 A. Excuse me, ma'am. Could you just direct me to 09:33:42 9 a particular line and column? 09:33:46 10 Q. So we're in Exhibit 2, column 21. 09:33:48 11 A. Yeah. 09:33:52 12 Q. Beginning line 51. Are you with me? 09:33:52 13 A. Yes. 09:33:56 14 Q. Claim 1 of the '681 Patent recites, among other 09:34:00 15 things, that: "The VEGF antagonist is a VEGF 09:34:06 16 receptor-based chimeric molecule comprising (1) a VEGFR1 09:34:09 17 component comprising amino acids 27 to 129 of SEQ. ID No: 09:34:16 18 2; (2) a VEGFR2 component comprising amino acids 130 to 09:34:24 19 231 of SEQ. ID No: 2; and (3) a multimerization component 09:34:32 20 comprising amino acids 232 through 457 of SEQ. ID No: 2." 09:34:41 21 Do you see that? 09:34:49 22 A. Yes. 09:34:50 23 Q. Do you agree that the '338 Patent, that's 09:34:55 24 Exhibit 3, that its claims recite the identical 09:35:00 25 limitation that I just read? 09:35:04 Page 27	1 My goal in preparing for this deposition was, 09:37:37 2 as I mentioned earlier, to focus on the '681 Patent, not 09:37:43 3 the '338 Patent. 09:37:47 4 BY MS. CORK: 09:37:51 5 Q. You previously testified that you prepared your 09:37:52 6 declaration with respect to the '681 Patent, true? 09:37:54 7 A. Yes. 09:38:00 8 Q. In preparing your declaration for the '681 09:38:01 9 Patent, which is Exhibit 1, do you recall that there were 09:38:04 10 any differences between the amino acid sequence recited 09:38:09 11 in Claim 1 of the '681 Patent and Claim 1 of the '338 09:38:13 12 Patent recited -- reciting that sequence? 09:38:19 13 A. I -- I don't recall one way or the other. As I 09:38:27 14 said, I haven't really focused on the '338 Patent. I 09:38:30 15 have focused on the '681 Patent. 09:38:36 16 Q. In preparing your declaration for the '681 09:38:42 17 Patent, did you base it upon your declaration for the 09:38:45 18 '338 Patent? 09:38:49 19 A. I'm sorry. Could you repeat it and speak up if 09:38:52 20 at all possible? 09:38:56 21 MR. COBB: And, Dr. Klibanov, you are certainly 09:38:58 22 able to answer her questions, but just be cautious that 09:39:02 23 you do not reveal any privileged communications between 09:39:05 24 yourself and counsel. 09:39:09 25 // Page 29

1 BY MS. CORK: 09:39:19	1 answered. 09:43:43
2 Q. When you were preparing your declaration for 09:39:19	2 THE WITNESS: I mean, I -- I don't see how you 09:43:46
3 the '681 Patent, did you base that declaration upon your 09:39:21	3 can reasonably say that my previous response didn't 09:43:48
4 previous declaration for the '338 Patent? 09:39:26	4 address your question. As I said, they both refer to 09:43:53
5 A. I mean, there was some portions of my '681 09:39:30	5 SEQ. ID No: 2. Whether SEQ. ID No: 2 in the 09:43:58
6 declaration that were taken, as I recall, directly from 09:39:36	6 specification of the '681 Patent is the same as SEQ. ID 09:44:07
7 my declaration on the '338 Patent, in particular 09:39:43	7 No: 2 in the specification of the '338 Patent, I don't 09:44:12
8 discussing some prior art references and things of this 09:39:49	8 know for sure, because I have not compared them side by 09:44:17
9 sort. 09:39:52	9 side. 09:44:20
10 Q. Do you recall changing your analysis with 09:39:56	10 BY MS. CORK: 09:44:22
11 respect to this claim limitation in the '681 Patent 09:39:59	11 Q. Sitting here today, you're not aware of a 09:44:25
12 claims when you were modifying your declaration with 09:40:06	12 difference in the amino acid sequences between this 09:44:28
13 respect to the '338 Patent? 09:40:13	13 limitation recited in the '681 Patent and the 09:44:35
14 MR. COBB: Objection. Vague; form. 09:40:17	14 corresponding limitation recited in Claim 1 of the '338 09:44:39
15 THE WITNESS: Well, I submitted my '681 Patent 09:40:20	15 Patent, correct? 09:44:42
16 declaration in response to Dr. Chaum's, and for our court 09:40:26	16 MR. COBB: Objection. Vague; form. 09:44:44
17 reporter it's C-h-a-u-m, Dr. Edward Chaum, who was a 09:40:33	17 THE WITNESS: I mean, you asked me that 09:44:46
18 declarant for -- who is a declarant for Samsung Biopesis. 09:40:42	18 question before, and, you know, I said to you then, and I 09:44:47
19 In the case of the '338 Patent, I don't believe 09:40:59	19 will say to you now, that I do not know one way or the 09:44:51
20 it was Dr. Chaum who was the declarant. 09:41:04	20 other, because I have not compared them. 09:44:56
21 So, you know, I don't specifically recall one 09:41:14	21 BY MS. CORK: 09:45:01
22 way or the other, but, again, the thrust of my 09:41:16	22 Q. You've testified that an amino acid sequence 09:45:02
23 declaration is to respond to the allegations made by the 09:41:20	23 can have different three-dimensional structures, correct? 09:45:05
24 declarant for the patent challenger. 09:41:26	24 A. I wouldn't put it quite that way. 09:45:12
25 //	25 Q. An amino acid sequence cannot have different 09:45:16
Page 30	Page 32
1 BY MS. CORK: 09:41:33	1 three-dimensional structures? 09:45:19
2 Q. Just looking at the claims of the '681 Patent 09:41:56	2 A. I presume that you're referring to the fact 09:45:26
3 and the '338 Patent, would you agree that they recite the 09:41:58	3 that an amino acid -- that a polypeptide chain with a 09:45:29
4 same amino acid sequence? 09:42:02	4 given amino acid sequence can acquire or can have 09:45:36
5 MR. COBB: Objection. Form; the document 09:42:05	5 different three-dimensional structures. If that is what 09:45:44
6 speaks for itself. 09:42:07	6 you mean by your question, then the answer is yes. 09:45:49
7 THE WITNESS: They both refer to SEQ. ID No: 2, 09:42:13	7 Q. Do the claims of the '681 Patent recite a 09:45:58
8 but, as I already testified repeatedly today, I did not 09:42:20	8 three-dimensional structure? 09:46:01
9 compare SEQ. ID No. 2 in the specification of the '681 09:42:24	9 A. No. They talk about the -- the VEGF antagonist 09:46:09
10 Patent with that in the specification of the '338 Patent. 09:42:35	10 with a certain amino acid -- with a certain amino acid 09:46:28
11 And by the way, for our court reporter, SEQ. 09:42:43	11 sequence. 09:46:34
12 ID, the first word is S-E-Q, so it stands for sequence, 09:42:46	12 Q. Claim 1 of the '681 Patent also recites 09:46:40
13 and "ID" stands for ID. 09:42:51	13 exclusion criteria. 09:46:43
14 BY MS. CORK: 09:42:55	14 Do you see that? 09:46:45
15 Q. That didn't respond to my question, so I'm 09:42:59	15 MR. COBB: Objection. Scope. 09:46:46
16 going to ask it again. Okay? Okay? 09:43:01	16 THE WITNESS: There are some exclusion criteria 09:46:50
17 A. I don't know what "Okay" means. You don't need 09:43:10	17 that follow the third "WHEREIN." It's not something that 09:46:52
18 my permission to repeat your question. So if you wish 09:43:16	18 I have focused on, because that relates to ophthalmology, 09:46:59
19 that you -- if you wish to repeat it, I mean, please do 09:43:20	19 and I'm certainly not an ophthalmologist, or even a 09:47:06
20 so. 09:43:23	20 physician. 09:47:10
21 Q. Just looking at the claims of the '681 Patent 09:43:24	21 BY MS. CORK: 09:47:12
22 and the '338 Patent, and specifically Claim 1 for each, 09:43:28	22 Q. So you don't have any opinions about those 09:47:12
23 would you agree that these claims recite the same amino 09:43:35	23 exclusion criteria recited in the '681 Patent claims? 09:47:14
24 acid sequence? 09:43:39	24 A. That's correct. I do not have any opinions. I 09:47:21
25 MR. COBB: Objection. Form; asked and 09:43:41	25 mean, that's outside of my area of expertise or the scope 09:47:23
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1 of my '681 declaration. 09:47:28	1 to treat angiogenic eye disorders? 09:51:24
2 Q. Your curriculum vitae is attached as 09:47:35	2 A. I'm -- I'm not sure. 09:51:38
3 Exhibit 261 to your declaration, true? 09:47:38	3 Q. What do you mean by that? 09:51:45
4 A. Not to the declaration that you introduced 09:47:43	4 A. Exactly that. I don't specifically recall one 09:51:47
5 today as Klibanov Exhibit 1. 09:47:47	5 way or the other. 09:51:51
6 Q. Would you please go to paragraph 12 of 09:48:03	6 Q. Sitting here today, you're not able to identify 09:51:53
7 Exhibit 1. 09:48:06	7 any drugs to treat angiogenic eye disorders that you 09:51:57
8 A. Yes, ma'am. 09:48:18	8 personally have worked on? 09:52:02
9 Q. You state that: "My curriculum vitae attached, 09:48:20	9 A. Sitting here today, I'm not sure one way or the 09:52:05
10 as Exhibit 261, summarizes my education and academic 09:48:23	10 other whether I have worked on any such biologic drugs. 09:52:09
11 experience." 09:48:28	11 Q. It's fair to say you were not involved in the 09:52:20
12 Do you see that? 09:48:29	12 development of aflibercept. 09:52:23
13 A. I do. 09:48:29	13 A. That's a correct statement. 09:52:30
14 Q. Did you prepare the CV that is attached as 09:48:32	14 Q. Your knowledge of aflibercept comes from 09:52:31
15 Exhibit 261 to your declaration? 09:48:34	15 outside sources, rather than your personal knowledge? 09:52:34
16 A. Yes, that's something I prepared. It's my 09:48:47	16 MR. COBB: Objection. Vague. 09:52:41
17 academic curriculum vitae. I prepared it, correct. 09:48:49	17 THE WITNESS: I would not put it this way. I 09:52:43
18 Q. And Exhibit 261 is accurate, to the best of 09:48:55	18 have reviewed literature on aflibercept, and as a result 09:52:46
19 your knowledge? 09:48:59	19 of this review, the information in those references has 09:52:53
20 A. It was certainly accurate as of the time when I 09:49:00	20 become my personal knowledge. 09:52:58
21 submitted it. 09:49:03	21 BY MS. CORK: 09:53:11
22 Q. Sitting here today, can you tell me how many 09:49:15	22 Q. Have you ever personally worked on the 09:53:11
23 biologic drugs you have invented? 09:49:17	23 development of a therapeutic dosing regimen? 09:53:13
24 MR. COBB: Objection. Form. It is not a 09:49:20	24 A. Yes, as a part of a larger team that included 09:53:21
25 memory test. You have his CV. You can share it with 09:49:25	25 physicians, I have worked on such subject matters. 09:53:26
Page 34	Page 36
1 him. 09:49:28	1 Q. Did any of those therapeutic dosing regimens 09:53:33
2 MS. CORK: I'll ask counsel not to make 09:49:30	2 that you worked on involve treatments for angiogenic eye 09:53:37
3 speaking objections. 09:49:32	3 disorders? 09:53:43
4 THE WITNESS: I have worked on a number of 09:49:42	4 A. Not that I specifically recall. 09:53:48
5 biologic drugs. I -- I don't know what you mean by 09:49:44	5 Q. Exhibit 1, Section 2, sets forth your 09:53:55
6 "invented." 09:49:47	6 qualifications and experience, beginning at paragraph 3. 09:54:01
7 BY MS. CORK: 09:49:51	7 Would you agree? 09:54:04
8 Q. Sitting here today, can you give me an estimate 09:49:52	8 A. Yes. 09:54:18
9 of how many biologic drugs you have invented? 09:49:55	9 Q. Does Section 2 of your declaration accurately 09:54:18
10 MR. COBB: Objection. Form. 09:49:59	10 summarize your professional education and training? 09:54:21
11 THE WITNESS: What do you mean by "have 09:50:01	11 A. I mean, I would say yes, with summarizing -- or 09:54:29
12 invented"? 09:50:04	12 summarizes being the keyword. This is a summary. It's 09:54:34
13 BY MS. CORK: 09:50:08	13 obviously not a detailed description of my qualifications 09:54:38
14 Q. In your own opinion, have you invented any 09:50:12	14 and experience. It's a summary. 09:54:46
15 biologic drugs? 09:50:15	15 Q. Do you have any formal medical training? 09:54:50
16 MR. COBB: Objection. Form. 09:50:17	16 A. I'm not a physician, if that's what you mean. 09:54:54
17 THE WITNESS: I have worked on a number of 09:50:20	17 Q. So the answer to my question is, no, you don't 09:54:58
18 biologic drugs as a part of a team. Some of these drugs 09:50:23	18 have any formal medical training. 09:55:00
19 have become commercial products. So in my mind I have 09:50:37	19 A. I took my -- during my undergraduate and 09:55:17
20 contributed to inventing these drugs, not necessarily as 09:50:46	20 graduate years, I actually took some medical courses. I 09:55:20
21 a named inventor, but I have contributed to the 09:50:54	21 don't necessarily view it as formal medical training. I 09:55:26
22 development and ultimately their introduction as 09:51:00	22 certainly don't have any degrees, nor do I consider 09:55:31
23 commercial products to treat people. 09:51:10	23 myself a physician. 09:55:34
24 BY MS. CORK: 09:51:14	24 But I did take some courses in medicine. 09:55:35
25 Q. Have you worked on the development of any drugs 09:51:17	25 Q. But you didn't go to medical school. 09:55:41
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1 A. I did not go to medical school. Yes. 09:55:43	1 Q. Paragraph 20 of your declaration reads: "I 09:58:39
2 Q. You've never been licensed as a medical doctor 09:55:46	2 understand that Patent Owner contends that a POSA is an 09:58:45
3 of any kind. 09:55:48	3 ophthalmologist with experience in treating angiogenic 09:58:50
4 A. Certainly not. 09:55:50	4 eye disorders, including through its use of VEGF Trap-Eye 09:58:54
5 Q. Including as an ophthalmologist. 09:55:51	5 antagonists." 09:58:58
6 A. Correct. 09:55:53	6 Do you see that? 09:58:58
7 Q. If someone had an eye problem, would you know 09:55:55	7 A. I do. 09:59:00
8 how to diagnose if that person has an angiogenic eye 09:55:58	8 Q. And "Patent Owner" is Regeneron, correct? 09:59:00
9 disorder? 09:56:02	9 A. Yes. 09:59:03
10 A. I don't think so. 09:56:10	10 Q. "POSA" is shorthand for a person of ordinary 09:59:03
11 Q. So you don't have any idea what kind of tests a 09:56:11	11 skill in the art, true? 09:59:07
12 doctor would use for diagnosing angiogenic eye disorders? 09:56:13	12 A. Yes, and actually to be more specific, as of 09:59:09
13 MR. COBB: Objection. Form. 09:56:19	13 the time of the invention. 09:59:12
14 THE WITNESS: I do not specifically know. 09:56:21	14 Q. And paragraph 19, the preceding paragraph, 09:59:19
15 Again, I may have read about it, but I am certainly 09:56:22	15 would you agree that you set forth the definition of a 09:59:25
16 not -- I don't have any firsthand knowledge of that. 09:56:26	16 person of ordinary skill in the art that is offered by 09:59:29
17 BY MS. CORK: 09:56:30	17 the Petitioner Samsung Bioepsis? 09:59:32
18 Q. If someone had an eye problem, would you know 09:56:30	18 A. I would not put it that way. 09:59:38
19 what an appropriate treatment would be for that person? 09:56:33	19 Q. How would you explain what is in paragraph 19 09:59:47
20 A. I think an appropriate treatment would be to 09:56:39	20 of your declaration? 09:59:50
21 see an ophthalmologist. 09:56:42	21 A. What I state in paragraph 19 is how the 09:59:54
22 Q. You do not have any experience prescribing 09:56:47	22 Petitioner, which is Samsung Bioepsis, defined a POSA in 09:59:59
23 treatments to people with eye problems, correct? 09:56:50	23 the case of the '681 Patent, as I understand it. 10:00:15
24 A. I do not prescribe any medicines for eye 09:56:55	24 Q. In paragraph 19, you state that: "Petitioner," 10:00:22
25 problems or anything else. 09:56:59	25 which is Samsung, "further contends that a POSA would not 10:00:26
Page 38	Page 40
1 Q. You have no experience treating angiogenic eye 09:57:02	1 necessarily be an ophthalmologist, but would have similar 10:00:31
2 disorders. 09:57:04	2 knowledge regarding the diagnosis and treatment of 10:00:34
3 MR. COBB: Objection. Asked and answered; 09:57:06	3 angiogenic eye disorders, including the administration of 10:00:37
4 form. 09:57:08	4 therapies to treat said disorders." 10:00:40
5 THE WITNESS: That's correct. 09:57:08	5 Do you see that? 10:00:43
6 BY MS. CORK: 09:57:10	6 A. I do. 10:00:44
7 Q. You have no experience administering 09:57:17	7 Q. It's true that there are two competing 10:00:49
8 aflibercept to a patient with an angiogenic eye disorder? 09:57:20	8 definitions of a person of ordinary skill in the art in 10:00:53
9 A. Correct, nothing beyond what I have read in the 09:57:25	9 this proceeding, correct? 10:00:56
10 literature, including the literature that I have reviewed 09:57:29	10 A. I think that's a reasonable way to characterize 10:01:04
11 in working on this case. 09:57:33	11 it. 10:01:06
12 Q. Go to Section 4 of your declaration, Exhibit 1, 09:57:47	12 Q. Do you have any opinions on which is the 10:01:08
13 beginning at paragraph 17. Please let me know when 09:57:51	13 correct definition of a person of ordinary skill in the 10:01:10
14 you're there. 09:57:56	14 art for the '681 Patent? 10:01:13
15 A. Yes, ma'am. I'm there. 09:58:03	15 A. I do not have any specific opinions, but, as I 10:01:22
16 Q. Have you had a chance to look through Section 4 09:58:07	16 say in paragraph 21, my opinions that are set forth in my 10:01:27
17 of your declaration? 09:58:09	17 '681 declaration remain the same under either of those 10:01:34
18 A. You mean just now? 09:58:11	18 definitions of a POSA. 10:01:40
19 Q. Are you familiar with Section 4 of your 09:58:16	19 Q. Understanding that your opinions don't change 10:01:43
20 declaration, or do you need a moment to review it? 09:58:18	20 regardless of which definition is adopted, you don't have 10:01:46
21 A. I mean, I'm generally familiar with it, because 09:58:22	21 an opinion on which definition is the correct one to 10:01:51
22 I wrote it, but I certainly -- if you're going to ask me 09:58:25	22 choose to adopt. 10:01:56
23 questions about it, then, again, pursuant to the 09:58:28	23 MR. COBB: Objection. Form. 10:01:58
24 expressed instructions that you gave me in the beginning 09:58:30	24 THE WITNESS: Yeah, I personally do not have an 10:02:02
25 of this deposition, I would want to review it. 09:58:34	25 opinion with respect to this matter. 10:02:05
Page 39	Page 41

1 BY MS. CORK: 10:02:09 2 Q. You would not dispute, for example, that the 10:02:10 3 Petitioner's definition is correct? 10:02:12 4 MR. COBB: Objection. Misstates his testimony; 10:02:16 5 form. 10:02:19 6 THE WITNESS: Well, as you correctly read a 10:02:27 7 moment ago in paragraph 20, I say that I understand that 10:02:31 8 the Patent Owner, which is Regeneron, contends that a 10:02:36 9 POSA is an ophthalmologist with experience in treating 10:02:40 10 angiogenic eye disorders, including through the use of 10:02:47 11 VEGF antagonist. 10:02:53 12 So if the Patent Owner, which is Regeneron, is 10:02:58 13 correct, then I would dispute the Petitioner's POSA 10:03:01 14 definition. 10:03:10 15 But I have no personal view as I mentioned 10:03:11 16 earlier of which definition is correct. 10:03:17 17 BY MS. CORK: 10:03:24 18 Q. Do you have any opinions on the correct level 10:03:25 19 of ordinary skill with respect to the '681 Patent? 10:03:26 20 MR. COBB: Objection. Vague. 10:03:38 21 THE WITNESS: My opinion is limited to the fact 10:03:42 22 that either way, a POSA would have an understanding of 10:03:45 23 basic principles of biochemistry that I discuss in some 10:03:57 24 detail in my '681 declaration. So that's the extent of 10:04:01 25 my personal opinion. 10:04:09 Page 42	1 Q. Do you have expertise in developing treatments 10:06:20 2 for angiogenic eye disorders? 10:06:24 3 A. I don't consider myself an expert in this area 10:06:29 4 if -- if that's what you mean, but I may have some 10:06:32 5 knowledge through studying the literature. 10:06:35 6 Q. Have you ever developed a treatment for an 10:06:39 7 angiogenic eye disorder? 10:06:41 8 A. I don't think so. 10:06:47 9 Q. Would you agree that your opinions regarding 10:06:57 10 the prior art to the '681 Patent are not the opinions of 10:06:59 11 a person of ordinary skill in the art for that patent? 10:07:04 12 MR. COBB: Objection. Form; calls for a legal 10:07:08 13 conclusion. 10:07:11 14 THE WITNESS: Well, you know, as I just said, 10:07:17 15 I -- it may be that I -- I have not spent a lot of time 10:07:20 16 analyzing it. I -- it may be that I am a POSA according 10:07:27 17 to Petitioner's definition with respect to the '681 10:07:34 18 Patent. 10:07:38 19 But, regardless, I'm certainly an expert in the 10:07:39 20 areas of protein chemistry and biochemistry that I have 10:07:47 21 opined on in my '681 Patent declaration. 10:07:52 22 BY MS. CORK: 10:08:00 23 Q. Do you meet every aspect of Samsung Biopesis's 10:08:01 24 definition of a person of ordinary skill in the art for 10:08:05 25 the '681 Patent? 10:08:08 Page 44
1 BY MS. CORK: 10:04:13 2 Q. Do you meet either definition of a person of 10:04:18 3 ordinary skill in the art for the '681 Patent? 10:04:21 4 A. I do not meet Patent Owner's definition, 10:04:31 5 because I'm not an ophthalmologist. 10:04:37 6 I may or may not meet the Petitioner's 10:04:41 7 definition. 10:04:48 8 But I most certainly meet the -- the aspect 10:04:50 9 that specifically deals with protein chemistry and 10:04:58 10 biochemistry, which are the opinions that I'm offering in 10:05:05 11 my '681 declaration. 10:05:11 12 Q. Is it your testimony that you have knowledge 10:05:21 13 regarding the diagnosis of angiogenic eye disorders? 10:05:26 14 A. I mean, I read some papers dealing with this 10:05:36 15 subject matter. I certainly don't consider myself an 10:05:39 16 expert, but I may have some knowledge of that, correct. 10:05:43 17 Q. You are not an expert in the diagnosis of 10:05:48 18 angiogenic eye disorders. 10:05:51 19 A. That's correct. I'm not an expert in this 10:05:53 20 area. 10:05:56 21 Q. And you're not an expert in the treatment of 10:05:58 22 angiogenic eye disorders. 10:06:01 23 A. That's correct, as well. I'm not an expert in 10:06:02 24 this area. I may have the knowledge that will be similar 10:06:06 25 to knowledge of a POSA, but I'm certainly not an expert. 10:06:11 Page 43	1 A. I have not conducted this analysis. I have not 10:08:09 2 compared myself with what is provided in every aspect, as 10:08:13 3 you put it, of Samsung's definition of a POSA. 10:08:21 4 Q. Looking at paragraph 19 of your declaration, 10:08:28 5 Exhibit 1, what is your opinion regarding whether you 10:08:32 6 satisfy Samsung Biopesis's definition of a person of 10:08:38 7 ordinary skill in the art for the '681 Patent? 10:08:42 8 MR. COBB: Objection. Scope. 10:08:46 9 THE WITNESS: I have no opinion. I -- as I 10:08:49 10 said, I have not conducted a thorough comparison of my 10:08:51 11 experience and qualifications with what's described in 10:08:58 12 the excerpt provided in paragraph 19, and subsequently of 10:09:05 13 my '681 Patent declaration. 10:09:18 14 BY MS. CORK: 10:09:24 15 Q. Are you unwilling to make that comparison now? 10:09:25 16 MR. COBB: Objection. Vague; scope; asked and 10:09:29 17 answered; form. 10:09:31 18 THE WITNESS: It's not a question of being 10:09:34 19 unwilling, but, I mean, I would have to think about it, 10:09:35 20 and we'd have to maybe go back to some of my experience 10:09:42 21 that I may have some documents related to. 10:09:50 22 So I'm just not able to do it right now. 10:09:55 23 It wasn't relevant to -- to my opinions 10:09:58 24 expressed in the '681 Patent declaration, because, you 10:10:05 25 know, even if I'm not a POSA, according to Petitioner's 10:10:17 Page 45

1 definition, I probably would be a -- an ordinary -- at 10:10:21 2 least an ordinarily skilled protein chemist or biochemist 10:10:35 3 with whom such a POSA would have consulted. 10:10:41 4 BY MS. CORK: 10:11:09 5 Q. I just want to make sure that I understand you. 10:11:09 6 If in a later proceeding you are asked to state 10:11:12 7 whether you are a person of ordinary skill for the '681 10:11:15 8 Patent, you're not going to give a different answer than 10:11:18 9 you just gave, correct? 10:11:22 10 MR. COBB: Objection. Vague; calls for 10:11:23 11 speculation; form. 10:11:24 12 THE WITNESS: If I'm specifically asked by 10:11:29 13 counsel to review in detail my prior professional 10:11:32 14 experience, various aspects of it, and based on that 10:11:40 15 determine whether I am a POSA under Petitioner's 10:11:47 16 definition, I will conduct that exercise. 10:11:54 17 And as a result of conducting this exercise, I 10:12:01 18 may arrive at a different answer than the one I just gave 10:12:07 19 you now, simply because, as of now, I have not been asked 10:12:11 20 to conduct this exercise, and I have not conducted it. 10:12:17 21 BY MS. CORK: 10:12:25 22 Q. Then it's fair to say that your opinions in 10:12:28 23 your declaration, Exhibit 1, are not offered from the 10:12:31 24 perspective of a person of ordinary skill in the art. 10:12:35 25 MR. COBB: Objection. Form. 10:12:38 Page 46	1 used. 10:14:15 2 BY MS. CORK: 10:14:18 3 Q. At this point in time, are you a person of 10:14:19 4 ordinary skill in the art for the '681 Patent? 10:14:22 5 MR. COBB: Objection. Form. 10:14:27 6 THE WITNESS: I may be, according to the 10:14:29 7 Petitioner. I mean, I am who I am, and the Petitioner 10:14:32 8 provided the definition. I just have not ascertained, 10:14:39 9 based on my -- all my prior relevant experience whether I 10:14:47 10 am such a person. 10:14:51 11 BY MS. CORK: 10:14:54 12 Q. Sitting -- 10:14:55 13 A. But I may very well be this person. I just 10:14:56 14 don't know. 10:14:59 15 Q. Sitting here today, you have not ascertained 10:14:59 16 whether you are a person of ordinary skill in the art 10:15:03 17 with respect to the '681 Patent, true? 10:15:06 18 A. I would not put it that way. 10:15:11 19 Q. I'm trying to understand whether you believe 10:15:17 20 that you are a person of ordinary skill in the art with 10:15:19 21 respect to the '681 Patent. Do you understand that? 10:15:22 22 A. I hear what you are saying. I already told you 10:15:28 23 that I'm not a person of ordinary skill in the art 10:15:31 24 according to the Patent Holder's definition. Full stop. 10:15:36 25 So, obviously, I've looked into this matter. 10:15:42 Page 48
1 THE WITNESS: Well, my opinions are with 10:12:44 2 respect to protein chemistry and biochemistry, and with 10:12:48 3 respect to those aspects, in my opinion, that's how a 10:12:52 4 person of ordinary skill in the art would see those 10:13:00 5 aspects. 10:13:07 6 BY MS. CORK: 10:13:15 7 Q. That didn't answer my question, sir, so I'm 10:13:16 8 going to ask it again. 10:13:17 9 Is it fair to say that your opinions in your 10:13:19 10 declaration, Exhibit 1, are not offered from the 10:13:22 11 perspective of a person of ordinary skill in the art? 10:13:26 12 MR. COBB: Objection. Argumentative; asked and 10:13:30 13 answered. 10:13:31 14 THE WITNESS: I would not necessarily agree 10:13:36 15 with that. I mean, they may be. I -- I may turn out to 10:13:38 16 be somebody who is a POSA, according to the Petitioner's 10:13:42 17 definition. So I disagree with your characterization of 10:13:48 18 my previous answer. 10:13:54 19 BY MS. CORK: 10:13:55 20 Q. At this point in time, in your deposition, you 10:13:56 21 have not been defined as a person of ordinary skill in 10:13:59 22 the art for the '681 Patent, true? 10:14:04 23 MR. COBB: Objection. Form. 10:14:07 24 THE WITNESS: I'm sorry. You said I have not 10:14:09 25 been designed? I didn't get -- catch the verb that you 10:14:10 Page 47	1 I have not determined whether I am a person of 10:15:45 2 ordinary skill in the art, according to the Petitioner's 10:15:52 3 definition. I, at this time, do not know that. I may be 10:15:56 4 such a person, but I just don't know that one way or the 10:16:02 5 other. 10:16:06 6 But certainly my opinions with respect to 10:16:08 7 protein chemistry and biochemistry expressed in my '681 10:16:12 8 declaration would be those that a POSA would hold, in my 10:16:19 9 judgment. 10:16:28 10 Q. If you don't know whether you're a person of 10:16:58 11 skill in the art for the '681 Patent, how can you be sure 10:17:02 12 that a person of skill in the art for the patent would 10:17:07 13 hold your opinions with respect to protein chemistry and 10:17:10 14 biochemistry? 10:17:13 15 MR. COBB: Objection. Form. 10:17:16 16 THE WITNESS: Because I'm certainly at least a 10:17:18 17 POSA, and indeed in my judgment an expert in the area of 10:17:20 18 protein chemistry and biochemistry, and I stand by the 10:17:28 19 opinions related to this subject matter that I expressed 10:17:37 20 in my declaration; and therefore, I believe that the POSA 10:17:41 21 would hold those views, because those are the correct 10:17:49 22 views, in my judgment. 10:17:53 23 BY MS. CORK: 10:17:57 24 Q. Would you please go to paragraph 8 of your 10:18:21 25 declaration, and let me know when you've had a chance to 10:18:23 Page 49

13 (Pages 46 - 49)

1 review. 10:18:26	1 THE VIDEOTAPE OPERATOR: Back on the record 10:36:10
2 A. Sure. 10:18:26	2 beginning with Media Unit 2 at 10:37 a.m. 10:36:11
3 MR. COBB: Counsel, if we are moving to a 10:18:27	3 MS. CORK: I'd like to mark as Exhibit 4 a 10:36:20
4 different topic, we have been going about an hour and 20, 10:18:30	4 document titled, "Biochemistry. Fifth Edition," by 10:36:25
5 if you have ten or so minutes left on this one, we can 10:18:33	5 Jeremy Berg and others, which is Exhibit 2065 in 10:36:30
6 continue. 10:18:38	6 IPR2023-00442, with a copy to counsel. 10:36:36
7 MS. CORK: Just one more question, and then we 10:18:45	7 (Exhibit 4 was marked for identification.) 10:36:42
8 can take a break. 10:18:47	8 THE WITNESS: Thank you. 10:37:04
9 MR. COBB: Sure. 10:18:48	9 BY MS. CORK: 10:37:06
10 THE WITNESS: Yes, ma'am, I've reviewed briefly 10:19:28	10 Q. Dr. Klivanov, do you recognize Exhibit 4? 10:37:06
11 that paragraph, paragraph 8. 10:19:31	11 A. Yes, that is one of the prior art publications 10:37:09
12 BY MS. CORK: 10:19:33	12 that I discuss in my '681 Patent declaration. 10:37:13
13 Q. You state you have numerous publications 10:19:33	13 Q. Specifically, you discuss Exhibit 2056 to your 10:37:22
14 relating to therapeutic proteins in the treatment of 10:19:35	14 declaration, which is Exhibit 4 here, at paragraphs 51 to 10:37:27
15 ophthalmologic disorders. 10:19:40	15 56 of your declaration? 10:37:32
16 Do you see that? 10:19:44	16 A. You said paragraphs what? I'm sorry. I missed 10:37:50
17 A. I do. 10:19:44	17 that. 10:37:53
18 Q. Do you analyze any of those publications in 10:19:47	18 Q. Paragraphs 51 to 56. 10:37:54
19 your declaration, Exhibit 1? 10:19:49	19 A. Yes. 10:37:58
20 A. I mean, I don't specifically refer to those 10:19:59	20 Q. Why did you choose Exhibit 2065 to your 10:38:03
21 publications, but clearly my opinions expressed in the 10:20:01	21 declaration for use in your declaration? 10:38:07
22 declaration, the '681 Patent declaration, are formed with 10:20:09	22 MR. COBB: Objection. Form. 10:38:17
23 those publications and others being a part of my 10:20:17	23 Dr. Klivanov, I'll just caution you not to 10:38:21
24 background, my knowledge base. 10:20:22	24 disclose any privileged conversations between yourself 10:38:24
25 Q. Are any of those publications relevant? 10:20:30	25 and counsel. To the extent you can answer the question 10:38:29
Page 50	Page 52
1 A. Ma'am, you would have to speak up and speak 10:20:33	1 without revealing privilege, go ahead. 10:38:33
2 slower. 10:20:35	2 THE WITNESS: Well, this biochemistry textbook, 10:38:41
3 Q. Are any of those publications relevant to the 10:20:36	3 in my considered opinion, is one of several very credible 10:38:49
4 claims of the '681 Patent? 10:20:40	4 and good textbooks, and I believe that it may have come 10:38:59
5 MR. COBB: Objection. Vague. 10:20:46	5 up. Klivanov Exhibit 4 may have come up in some of the 10:39:06
6 THE WITNESS: To the correct interpretation of 10:20:56	6 prior declarations of mine with respect to that family of 10:39:14
7 those claim elements, because I have done a lot of work 10:20:58	7 Regeneron patents. 10:39:24
8 on protein chemistry and biochemistry, protein structure, 10:21:01	8 BY MS. CORK: 10:39:30
9 the relationship between, for example, the primary 10:21:09	9 Q. So Exhibit 4 to your deposition here, which is 10:39:31
10 structure of proteins, which is the amino acid sequence, 10:21:15	10 Exhibit 2065 to your declaration, is accurate, based on 10:39:34
11 and their secondary, tertiary, domain, and quaternary 10:21:19	11 your review of that exhibit? 10:39:41
12 structures, so I think that they are relevant. 10:21:27	12 MR. COBB: Objection. Form; the document 10:39:44
13 BY MS. CORK: 10:21:35	13 speaks for itself. 10:39:45
14 Q. Is there a reason you did not include them in 10:21:35	14 THE WITNESS: It's accurate as far as textbooks 10:39:52
15 your declaration, Exhibit 1? 10:21:37	15 go. I mean, obviously, the purpose of a textbook, and 10:39:55
16 A. I have included what I felt was necessary to 10:21:44	16 this is an undergraduate biochemistry textbook, and I 10:39:59
17 respond to Dr. Chaum's opinions. I -- it was not my goal 10:21:51	17 used to teach undergraduate as well as graduate 10:40:04
18 to provide an encyclopedic coverage of the relevant 10:22:00	18 biochemistry at MIT, obviously it's written with a 10:40:09
19 subject matter. So I have included what I considered 10:22:08	19 specific audience in mind, and in the context of that 10:40:15
20 necessary. 10:22:14	20 audience, yes, it's a fine textbook. 10:40:19
21 MS. CORK: Okay. Why don't we take a little 10:22:17	21 BY MS. CORK: 10:40:27
22 break. 10:22:19	22 Q. Does Exhibit 4, which is Exhibit 2065 to your 10:40:29
23 THE VIDEOTAPE OPERATOR: Off the record at 10:22:20	23 declaration, contain principles of biochemistry that 10:40:33
24 10:23 a.m. 10:22:21	24 would be familiar to a person of ordinary skill in the 10:40:36
25 (Recess was taken.) 10:22:22	25 art for the '681 Patent? 10:40:38
Page 51	Page 53

1 A. Yes. It summarizes those principles. 10:40:44 2 Q. And do you agree with the principles set forth 10:40:51 3 in Exhibit 2065 to your declaration? 10:40:55 4 MR. COBB: Objection. Vague; scope. 10:40:59 5 THE WITNESS: Again, in the context of 10:41:04 6 conveying biochemistry principles to undergraduate 10:41:06 7 students, I do agree with it, yes. I mean, it obviously, 10:41:11 8 like any other undergraduate textbook, it doesn't have a 10:41:16 9 luxury to go into, you know, a great deal of detail on 10:41:20 10 some of the things, but, in general, in this context that 10:41:31 11 I just outlined, the answer is yes. 10:41:34 12 BY MS. CORK: 10:41:36 13 Q. And paragraph 52 of your declaration, 10:41:46 14 Exhibit 1, you state that: "Each protein has a unique, 10:41:48 15 precisely defined amino acid sequence." 10:41:51 16 Do you see that? 10:41:53 17 A. Okay. Let me just again, pursuant to your 10:41:58 18 instructions at the beginning of the deposition, let me 10:42:00 19 just read paragraph 52 to myself. 10:42:03 20 Would you be good enough to repeat your 10:42:55 21 question, ma'am? 10:42:58 22 BY MS. CORK: 10:43:00 23 Q. Do you agree with Exhibit 2065 to your 10:43:01 24 declaration, that each protein has a unique, precisely 10:43:04 25 defined amino acid sequence? 10:43:08 Page 54	1 A. I'm sorry. You'll have to repeat the question 10:45:05 2 and speaking slowly and louder, if possible. 10:45:06 3 Q. You can tell what a protein's identity is from 10:45:11 4 its amino acid sequence, true? 10:45:14 5 MR. COBB: Objection. Form; vague. 10:45:20 6 THE WITNESS: Yeah, the amino acid sequence is 10:45:22 7 one of the features of protein identity or one of the 10:45:24 8 manifestations of protein identity. 10:45:33 9 BY MS. CORK: 10:45:37 10 Q. And you can tell what a protein's identity is 10:45:44 11 just from its amino acid sequence, true? 10:45:47 12 MR. COBB: Objection. Vague. 10:45:52 13 THE WITNESS: Not the entire protein identity, 10:45:53 14 but one aspect of protein identity. 10:45:56 15 BY MS. CORK: 10:46:00 16 Q. And what aspect is that? 10:46:01 17 A. What the order of amino acid residues is along 10:46:07 18 the polypeptide chain. 10:46:13 19 Q. If you have a string of amino acid residues, 10:46:34 20 can you use that information to determine what a protein 10:46:37 21 is? 10:46:39 22 MR. COBB: Objection. Vague. 10:46:45 23 MS. CORK: Withdrawn. 10:46:46 24 Q. If you have a string of amino acid residues, 10:46:47 25 can you use that information to determine what that 10:46:51 Page 56
1 MR. COBB: Objection. Form. 10:43:12 2 THE WITNESS: Yes, I do. Again, in the context 10:43:14 3 of conveying the biochemistry principles to undergrad 10:43:16 4 students, yes. 10:43:24 5 BY MS. CORK: 10:43:28 6 Q. Do you agree that a protein's unique, precisely 10:43:29 7 defined amino acid sequence defines that protein? 10:43:33 8 MR. COBB: Objection. Vague; form. 10:43:41 9 THE WITNESS: What do you mean, "defines this 10:43:43 10 protein"? 10:43:44 11 BY MS. CORK: 10:43:46 12 Q. Are you not able to answer my question? 10:43:58 13 A. I would like you to clarify what you mean by 10:44:03 14 that. What do you mean, "defines this protein"? 10:44:05 15 If you mean that the -- the amino acid sequence 10:44:08 16 defines every aspect of protein structure and behavior, 10:44:15 17 the answer is no. 10:44:22 18 Q. Can you tell what the protein is from its amino 10:44:28 19 acid sequence? 10:44:31 20 MR. COBB: Objection. Vague. 10:44:36 21 THE WITNESS: You can tell what the protein 10:44:37 22 identity is, meaning what its amino acid sequence is. 10:44:43 23 BY MS. CORK: 10:44:52 24 Q. You can tell what a protein's identity is from 10:44:59 25 its amino acid sequence, true? 10:45:02 Page 55	1 protein is? 10:46:54 2 A. I don't understand what the question means. I 10:47:02 3 heard it, I just don't understand what it means. 10:47:04 4 Q. Can you determine a protein's identity from its 10:47:07 5 amino acid sequence? 10:47:10 6 MR. COBB: Objection. Asked and answered. 10:47:12 7 THE WITNESS: Some aspects of protein identity, 10:47:18 8 not all aspects of protein identity. 10:47:20 9 BY MS. CORK: 10:47:22 10 Q. Can you determine aflibercept from its amino 10:47:39 11 acid sequence? 10:47:43 12 MR. COBB: Objection. Vague. 10:47:45 13 THE WITNESS: Again, I -- I don't understand 10:47:50 14 what the question means. 10:47:51 15 BY MS. CORK: 10:47:55 16 Q. If you have a series of amino acids, would you 10:47:56 17 be able to tell whether that series of amino acids is 10:47:59 18 aflibercept or not? 10:48:04 19 MR. COBB: Objection. Vague as to time; form. 10:48:06 20 THE WITNESS: At some point in time the amino 10:48:29 21 acid sequence of aflibercept was determined. It was 10:48:31 22 before the priority date of the '681 Patent. So it 10:48:34 23 depends on when -- we know today that a certain amino 10:48:52 24 acid sequence corresponds to aflibercept. 10:48:55 25 // Page 57

1 BY MS. CORK: 10:49:23	1 factor. But it's not the determinant or the factor. 10:54:04
2 Q. Would you please go to paragraph 58 of your 10:49:24	2 BY MS. CORK: 10:54:23
3 declaration. 10:49:26	3 Q. Could you please go to Exhibit 4, which is 10:54:24
4 A. Let me read it to myself. Yes, ma'am. 10:49:30	4 Exhibit 2065, to your declaration. 10:54:27
5 Q. You state: "I disagree with the Board's 10:50:13	5 A. You know the font here is very small, right? 10:54:42
6 conclusion that the 'primary structure necessarily 10:50:15	6 Well, you shrug your shoulders, but unless you have a 10:54:45
7 drives' the final three-dimensional shape of the protein, 10:50:18	7 magnifying glass, which unfortunately, I have forgotten 10:54:48
8 including its overall 'tertiary structure.'" 10:50:22	8 mine, I may or may not be able to read some of it. 10:54:53
9 Do you see that? 10:50:26	9 Q. Are you saying that you cannot read Exhibit 4 10:54:57
10 A. Yes. 10:50:26	10 to your deposition? 10:55:01
11 Q. Would you please go to paragraph 60 of your 10:50:39	11 A. I am saying that some of the text in Exhibit 4, 10:55:04
12 declaration. 10:50:42	12 as you produced it, and I very much am in favor of trying 10:55:09
13 A. Okay. I'll read it to myself. Okay. 10:50:46	13 to save paper, but here you chose to place two pages on 10:55:16
14 Q. You state that you do not find any statement in 10:51:17	14 one sheet of paper on the same side, and as a result of 10:55:22
15 the Brown textbook that supports the Board's conclusion 10:51:21	15 that, the text is very small. So I may not be able to 10:55:28
16 that primary structure necessarily drives or 10:51:24	16 read some of the text. But I will do my very best. 10:55:31
17 unambiguously defines the final three-dimensional shape 10:51:29	17 Q. I'll just represent that this exhibit was 10:55:36
18 of the protein, true? 10:51:33	18 prepared in the way that it was submitted by your 10:55:38
19 A. You didn't read the entirety of the sentence, 10:51:35	19 counsel. Can you accept that representation? 10:55:41
20 but what you read, indeed, reflects what I say in the 10:51:37	20 A. I mean, I can -- I don't know. I can tell you 10:55:46
21 first sentence in paragraph 60. 10:51:41	21 that that's not what I looked at. I looked at the 10:55:49
22 Q. So it's true that you, when you reviewed the 10:51:48	22 electronic copy, obviously, but that's not what I looked 10:55:55
23 Brown textbook described here, that you did not find any 10:51:51	23 at. But anyway, I mean, let's -- I will give it my best 10:55:58
24 statement supporting the Board's conclusion that primary 10:51:54	24 try. 10:56:02
25 structure necessarily drives or unambiguously defines the 10:51:59	25 Q. Could you, please, go to the page of Exhibit 4 10:56:04
Page 58	Page 60
1 final three-dimensional shape of the protein. 10:52:03	1 that is stamped page 20 of 08. It is at the back of the 10:56:11
2 A. That's correct. In fact, what I say in the 10:52:06	2 document. 10:56:20
3 last sentence in that paragraph, the Brown textbook 10:52:17	3 A. Okay. 10:56:33
4 actually shows the opposite, as I then illustrate in the 10:52:21	4 Q. And, as you mentioned, this is a scan of two 10:56:33
5 subsequent paragraphs. 10:52:25	5 book pages together. Do you see the page down on the 10:56:39
6 Q. And you disagree with the Board, at least in 10:52:34	6 bottom, the red header, that reads "The amino acid 10:56:42
7 part, because you did not find any statement in the Brown 10:52:36	7 sequence --" 10:56:45
8 textbook that the primary structure necessarily drives or 10:52:39	8 A. I'm sorry. We're talking about page 70 of the 10:56:46
9 unambiguously defines the final three-dimensional shape 10:52:43	9 textbook? 10:56:50
10 of the protein, right? 10:52:46	10 Q. Page 20. 10:56:51
11 A. I would not put it quite that way. I would say 10:52:51	11 MR. COBB: Page 20 of the stamped page 72 of 10:56:55
12 that I disagree with the Board on that issue, full stop, 10:52:54	12 the document, of the original. It should be the next 10:56:57
13 based on my more than half a century experience in the 10:52:59	13 page, Dr. Klibanov. 10:57:01
14 areas of protein chemistry and biochemistry; and 10:53:05	14 THE WITNESS: Just a second. I don't have page 10:57:04
15 furthermore it is incorrect to say that the Brown 10:53:09	15 20. I have page 19. Page 20, presumably follows it. 10:57:06
16 textbook somehow supports these statements. 10:53:17	16 So -- but I don't have a stamp that says, page 20. 10:57:10
17 Q. Does the primary structure of a protein drive 10:53:31	17 BY MS. CORK: 10:57:15
18 or define the three-dimensional shape of the protein, in 10:53:33	18 Q. Can you turn the page? 10:57:16
19 your experience? 10:53:38	19 A. Oh, that one? Okay. Sorry. 10:57:20
20 MR. COBB: Objection. Asked and answered; 10:53:40	20 Q. So now you're looking at the page that is Bates 10:57:24
21 form. 10:53:41	21 stamped 20 of 08 in Exhibit 4 to your deposition. 10:57:27
22 THE WITNESS: It's a contributing factor, but 10:53:45	22 A. Yes. 10:57:31
23 by itself it does not define the final three-dimensional 10:53:48	23 Q. Do you see the header that says, "The amino 10:57:34
24 structure of the protein, as I illustrate in paragraphs 10:53:56	24 acid sequence of a protein determines its 10:57:37
25 subsequent to paragraph 60. So it is a contributing 10:54:00	25 three-dimensional structure"? 10:57:40
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16 (Pages 58 - 61)

1 A. I see that header. 10:57:46	1 A. Just a second. Hold on a second. Yes, ma'am, 11:02:03
2 Q. Underneath that header, Exhibit 2065 to your 10:57:52	2 please continue. 11:02:12
3 declaration states: "The amino acid sequence completely 10:57:58	3 Q. Do you see the sentence that is italicized that 11:02:12
4 determines the three-dimensional structure, and hence all 10:58:03	4 begins, "Proteins are linear polymers built of monomer 11:02:15
5 other properties of a protein." 10:58:07	5 units called amino acids"? 11:02:20
6 Do you see that? 10:58:11	6 A. Yes, I do see it. 11:02:22
7 A. I do. 10:58:14	7 Q. Do you agree with that sentence? 11:02:23
8 Q. Do you dispute that Exhibit 2065 to your 10:58:18	8 A. Well, again, in the context of discussing the 11:02:39
9 declaration teaches one of ordinary skill in the art that 10:58:22	9 protein structure, as to be conveyed to undergraduate 11:02:44
10 the amino acid sequence completely determines the 10:58:27	10 students studying biochemistry, there is nothing wrong 11:02:54
11 three-dimensional structure and all other properties of a 10:58:30	11 with this statement. 11:02:58
12 protein? 10:58:33	12 But, again, it has to be understood obviously 11:03:00
13 A. I do dispute that. It teaches undergraduate 10:58:36	13 in the context of -- of the entirety of the chapter and, 11:03:03
14 students that that is the case. Furthermore, it teaches 10:58:41	14 indeed, the entirety of the textbook. 11:03:13
15 it in the portion of the chapter that's entitled, 10:58:50	15 But it's not a wrong statement in the context 11:03:16
16 "Summary," so this, by definition, is a summary. And 10:58:55	16 of conveying this sort of basic principle to 11:03:18
17 therefore, a person of ordinary skill in the art would 10:59:03	17 undergraduate students studying biochemistry. 11:03:23
18 understand that this is just a summary, and the summary 10:59:06	18 Q. Would a person of ordinary skill in the art for 11:03:27
19 that was conveyed to undergraduate students in 10:59:12	19 the '681 Patent understand that proteins are linear 11:03:30
20 biochemistry. 10:59:18	20 polymers built of monomer units called amino acids? 11:03:33
21 And that is what I meant when I previously 10:59:21	21 A. Again, the -- the statement -- a person of 11:03:44
22 answered your question repeatedly by saying that it is 10:59:23	22 ordinary skill in the art would understand that in the 11:03:46
23 accurate within the context of being a text directed to 10:59:27	23 context of a broader area of biochemistry, because this 11:03:50
24 undergraduate students, and here it is even more 10:59:37	24 says linear polymers that some people may erroneously 11:03:55
25 condensed than that, because this is actually a summary 10:59:42	25 interpret as sort of a linear -- as a line, okay, which 11:04:04
Page 62	Page 64
1 of the chapter in question here. 10:59:45	1 has a certain sequence. Okay? 11:04:16
2 Q. Would a person of ordinary skill in the art for 10:59:58	2 So to the extent that the idea here is to 11:04:22
3 the '681 Patent rely on this document that is 11:00:01	3 convey -- if you read this in the context of at least 11:04:27
4 Exhibit 2056 to your declaration? 11:00:07	4 this entire subsection, and there is a -- a reference 11:04:31
5 A. Would not blindly rely on it. In other words, 11:00:13	5 here to Figure 31 and so forth, so it's -- this statement 11:04:38
6 would not say, well, okay, I'm going to ignore everything 11:00:16	6 is certainly not an incorrect statement. 11:04:43
7 else I know, and the person of ordinary skill in the art, 11:00:19	7 But, again, it has to be read in the context, 11:04:47
8 of course, by definition knows everything that was 11:00:23	8 and a person of ordinary skill in the art certainly 11:04:50
9 published, so this person would not blindly rely on that; 11:00:25	9 wouldn't -- would not turn a blind eye to everything else 11:04:54
10 and in particular, on the part of the chapter that is 11:00:30	10 that biochemistry teaches. 11:04:59
11 expressly entitled, "Summary." 11:00:38	11 And with that understanding, as I said, there 11:05:03
12 Q. Could you please go back a few pages to the 11:01:13	12 is nothing wrong with this statement. 11:05:05
13 page that is stamped page 04 of 08 in Exhibit 4 to your 11:01:15	13 Q. A few sentences below, Exhibit 2065 to your 11:05:09
14 deposition. 11:01:23	14 declaration states: "Remarkably, proteins spontaneously 11:05:15
15 A. Okay. I'm there. 11:01:26	15 fold up into three-dimensional structures that are 11:05:20
16 Q. On the right side of the page, do you see the 11:01:29	16 determined by the sequence of amino acids in the protein 11:05:23
17 paragraph that begins with the sentence, "Proteins are 11:01:33	17 polymer." 11:05:26
18 linear polymers built of monomer units called --" 11:01:37	18 Do you see that? 11:05:27
19 A. I'm sorry. Where is that? I mean, I -- I'm 11:01:42	19 A. I do see that. Yes. 11:05:27
20 not sure I understand where you're reading. 11:01:45	20 Q. Did I read it correctly? 11:05:29
21 Q. At the top of the page, does it say "Protein 11:01:47	21 A. You read it correctly. 11:05:31
22 structure and function"? 11:01:51	22 Q. Do you agree with that statement? 11:05:34
23 A. Yes. 11:01:52	23 A. I agree with this statement, again, in the 11:05:38
24 Q. Now, go down just under halfway in that page. 11:01:52	24 context of a broader biochemistry, you know, sort of 11:05:40
25 Do you see the sentence that is italicized? 11:02:00	25 teaching. I mean, obviously, it is not necessarily the 11:05:48
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17 (Pages 62 - 65)

1 case, because in order for a protein to fold up into a 11:05:53 2 three-dimensional structure, in its unique 11:05:59 3 three-dimensional structure, it has to be done under 11:06:04 4 native conditions, including temperature and pH and other 11:06:07 5 things, so, again, this statement is not an incorrect 11:06:13 6 statement, as long as it is read by a POSA in a broader 11:06:16 7 context, which a POSA would necessarily do. 11:06:26 8 But, again, this is an attempt -- a successful 11:06:30 9 attempt -- excuse me -- on the part of the authors to 11:06:34 10 teach basic principles of biochemistry to undergraduate 11:06:38 11 students. 11:06:42 12 And when you do that, and I'm speaking from 11:06:43 13 experience, because, as I said earlier, for many years I 11:06:45 14 taught both undergraduate and graduate biochemistry at 11:06:49 15 MIT, you have to simplify things. And that's exactly 11:06:53 16 what the authors are doing here, and correctly. 11:06:58 17 But, you know, certainly one should not do it 11:07:01 18 with blinders on. 11:07:06 19 Q. You just referred to the folding of proteins 11:07:11 20 under native conditions. 11:07:13 21 A. Yes. 11:07:15 22 Q. What did you mean by "native conditions"? 11:07:15 23 A. I actually specifically added to it that we're 11:07:19 24 talking about the native temperature, pH, other 11:07:23 25 conditions; so, basically, whatever that protein 11:07:31 Page 66	1 membranes, where the vast majority of their micro 11:09:42 2 environment is, in fact, not aqueous. 11:09:48 3 Q. Is it true that changing even a single amino 11:10:23 4 acid in a protein can affect its structure? 11:10:25 5 A. It may affect its structure, yes, in fact, 11:10:34 6 several levels of structure. I presume that when you say 11:10:40 7 "structure," you don't mean the primary structure. The 11:10:44 8 primary structure will be necessarily altered. Higher 11:10:47 9 levels of structure may be affected. 11:10:54 10 MS. CORK: I'd like to mark as Exhibit 5 a 11:11:27 11 document titled, "WHO Drug Information, Volume 20, No. 2, 11:11:28 12 2006," which was Exhibit 1107 in IPR 2021-00881, with a 11:11:35 13 copy to counsel. 11:11:45 14 (Exhibit 5 was marked for identification.) 11:11:45 15 THE REPORTER: Exhibit 5. 11:12:01 16 THE WITNESS: Thank you. 11:12:02 17 BY MS. CORK: 11:12:08 18 Q. We have just marked what was previously marked 11:12:09 19 as Exhibit 22 in your deposition in the IPR proceeding 11:12:11 20 concerning the '338 Patent. Do you agree? 11:12:14 21 A. I have no recollection of it, but I'll take 11:12:25 22 your word for it. 11:12:27 23 Q. You don't remember ever seeing this document 11:12:28 24 that is Exhibit 5 to your current deposition before? 11:12:30 25 A. I don't specifically remember it, no. I -- 11:12:34 Page 68
1 encounters in its natural environment. 11:07:38 2 Q. What is the natural environment of a protein? 11:07:45 3 A. Well, the protein is produced by a cell, and 11:07:49 4 then is either excreted or retained within the cell, and 11:07:58 5 whatever that environment is, we're talking about 11:08:04 6 temperature, we are talking about pH, we're talking about 11:08:08 7 other components that actually may change as the cells' 11:08:13 8 situation changes. 11:08:23 9 So those are the part of that natural 11:08:25 10 environment. 11:08:29 11 Q. Would you consider the cell an aqueous 11:08:36 12 environment? 11:08:41 13 A. I would, indeed, if you mean by aqueous 11:08:42 14 water-based. 11:08:46 15 Q. And, ordinarily, the extra cellular milieu of a 11:08:48 16 cell is also aqueous, true? 11:08:52 17 A. That's true, again, as long as you mean 11:08:57 18 water-based by "aqueous." 11:09:00 19 Q. So the native conditions for a protein are 11:09:13 20 typically aqueous, in your experience. 11:09:16 21 A. For most proteins, that is the case, and, 11:09:22 22 again, "aqueous" means water-based. It doesn't mean 11:09:25 23 water. It means that it's water-based for most proteins. 11:09:29 24 There are some proteins that are called 11:09:34 25 membrane proteins that operate within biological 11:09:37 Page 67	1 but, again, as I showed, if you represent to me that 11:12:38 2 that's what it is, I will take your word for it. 11:12:41 3 Q. Suffice to say your declaration does not 11:12:47 4 discuss this document that is Exhibit 5 to your 11:12:49 5 deposition. 11:12:53 6 A. My '681 declaration does not discuss this 11:12:56 7 document, correct. 11:13:00 8 Q. Would you agree that Exhibit 5 relates to drug 11:13:05 9 information from the World Health Organization? 11:13:09 10 A. Well, it's entitled, "WHO Drug Information." 11:13:14 11 "WHO" stands for the World Health Organization. 11:13:20 12 So just looking at the title page of this document, I -- 11:13:24 13 I would have to reason to disagree with what you just 11:13:29 14 said. 11:13:32 15 Q. The publication date on the first page of 11:13:35 16 Exhibit 5 is 2006, correct? 11:13:37 17 A. Yes. 11:13:47 18 Q. Do you have any reason to dispute that the 11:13:47 19 document reflected in Exhibit 5 was publicly available in 11:13:49 20 2006? 11:13:54 21 A. I mean, I -- I just don't know one way or the 11:13:58 22 other. You know, I have no specific reasons to -- to 11:14:00 23 dispute that or to acquiesce to that proposition. But, 11:14:05 24 you know, it does say "2006" on the cover page. 11:14:11 25 Q. So, as far as you know, the information that is 11:14:17 Page 69

1 reflected in Exhibit 5 was publicly available in 2006. 11:14:20	1 A. Yes. 11:18:51
2 MR. COBB: Objection. Asked and answered; 11:14:27	2 Q. Do you agree this is the next sequential page 11:18:51
3 form. 11:14:29	3 of Exhibit 5? 11:18:54
4 THE WITNESS: I would -- I would not put it 11:14:29	4 A. It seems to be, yes. 11:19:03
5 that way. I have not examined whether this document was 11:14:31	5 Q. At the top of this page, 119, there is an amino 11:19:04
6 publicly available in 2006. So I don't know. 11:14:35	6 acid sequence, true? 11:19:09
7 BY MS. CORK: 11:14:41	7 A. Among other things, yes. 11:19:16
8 Q. Turn to page 5 of Exhibit 5. Do you see the 11:15:01	8 Q. Do you understand that amino acid sequence to 11:19:18
9 notation, "Aflibercept"? 11:15:05	9 refer to aflibercept? 11:19:22
10 A. I do. 11:15:19	10 A. I mean, it -- it may. I -- I have not reviewed 11:19:29
11 Q. Would it be fair to say that page 5 of 11:15:21	11 this document recently, but it's certainly possible. 11:19:33
12 Exhibit 5 discusses general features relating to the 11:15:24	12 Q. Do you have any reason to dispute that that 11:19:38
13 aflibercept molecule? 11:15:36	13 amino acid sequence refers to aflibercept? 11:19:40
14 A. The only thing I can tell you right now, 11:15:41	14 A. I have no reason to definitively state that 11:19:45
15 without reading what it says, there are two entries at 11:15:43	15 that is the case. As I said, I have not seen this 11:19:49
16 the end of the table, both -- both saying, "aflibercept." 11:15:47	16 document in a long time. You know, it says what it says, 11:19:54
17 That's the only thing I can tell you just looking at this 11:16:00	17 but I have not even read the brief description that's 11:20:00
18 page. 11:16:02	18 found, for example, in English on page 118 of 11:20:07
19 Q. What do you mean, "there are two entries"? 11:16:05	19 aflibercept. So, I mean, I cannot tell you that that is 11:20:17
20 A. Well, I mean there are certain things that are 11:16:10	20 necessarily the case. It may be. 11:20:22
21 listed in the left column. Again, the font is very 11:16:14	21 Q. That didn't answer my question, so I'm going to 11:20:28
22 small, but -- well, but as I can see, the last entry in 11:16:20	22 ask it again. 11:20:32
23 the left column says, "Aflibercept." The previous entry 11:16:28	23 Do you have any reason to dispute that that 11:20:33
24 also seems to say "Aflibercept." And, in fact, the one 11:16:35	24 amino acid sequence refers to aflibercept? 11:20:34
25 above that first says something else with an asterisk, 11:16:41	25 MR. COBB: Objection. Asked and answered; 11:20:39
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1 and then also says, "Aflibercept." 11:16:47	1 form. 11:20:40
2 So that's what I mean. 11:16:50	2 THE WITNESS: I have no reason to dispute it, 11:20:42
3 Q. Each of those three entries that say 11:16:52	3 and I have no reason to unequivocally agree with it. I 11:20:44
4 "Aflibercept" have next to them a description of some 11:16:54	4 have not reviewed this document in quite some time, as I 11:20:48
5 kind relating to that entry. Would you agree? 11:17:00	5 just indicated. 11:20:56
6 A. I would. 11:17:05	6 BY MS. CORK: 11:21:05
7 Q. And the top one is in English, and the two that 11:17:07	7 Q. Do you have any reason to dispute that the 11:21:58
8 are below it are in a different language that is 11:17:12	8 amino acid sequence of aflibercept was publicly available 11:22:00
9 different from each other, true? 11:17:16	9 for persons of skill in the art for the '681 Patent by 11:22:04
10 A. Yes, that appears to be the case. 11:17:27	10 2006? 11:22:09
11 Q. Would you agree that this page refers to 11:17:32	11 MR. COBB: Objection to form. 11:22:10
12 aflibercept, but described in three different languages? 11:17:36	12 THE WITNESS: I have not specifically looked 11:22:16
13 A. I think that's probably reasonable. Again, I 11:17:51	13 into that issue, so I have no specific reason to dispute 11:22:17
14 haven't read these descriptions, or at least the one in 11:17:54	14 or to unequivocally agree with that statement. 11:22:24
15 English, but, I mean, that seems like a reasonable -- a 11:17:56	15 BY MS. CORK: 11:22:31
16 reasonable way of interpreting it. 11:18:02	16 Q. Do you have any opinions regarding whether the 11:22:31
17 Q. Continuing on to the next page, which is the 11:18:09	17 amino acid sequence of aflibercept was available to a 11:22:34
18 next sequential page of the document -- withdrawn. 11:18:17	18 person of ordinary skill in the art for the '681 Patent 11:22:38
19 The page we were just looking at is marked page 11:18:24	19 before January 2011? 11:22:42
20 118. Do you see that at the bottom left? 11:18:28	20 A. No, I have no reason to dispute that. It was 11:22:45
21 A. It's marked what? 11:18:34	21 available to a person of ordinary skill in the art prior 11:22:49
22 Q. 118 at the bottom left. 11:18:40	22 to specifically January 13, 2011. 11:22:54
23 A. Yes. 11:18:42	23 Q. Do you have an opinion regarding whether the 11:23:05
24 Q. If you turn the page, the next page is marked 11:18:44	24 amino acid sequence of a molecule known as VEGF Trap-Eye 11:23:07
25 119 in the bottom right. Do you see that? 11:18:48	25 was available to a person of ordinary skill in the art 11:23:12
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1 nor the '681 Patent before January of 2011? 11:23:16	1 that's for sure, but I have some familiarity with that 11:27:05
2 MR. COBB: Objection. Form. 11:23:25	2 subject matter. 11:27:08
3 THE WITNESS: Not necessarily. There were -- 11:23:29	3 BY MS. CORK: 11:27:09
4 as I describe in detail in my declaration, there were 11:23:31	4 Q. Are you familiar with different clinical trial 11:27:09
5 actually several sequences that -- that could have been 11:23:36	5 phases? 11:27:12
6 that. So today we know that aflibercept and VEGF 11:23:46	6 A. Yes, that's what I just said. 11:27:13
7 Trap-Eye have the same amino acid sequence, but that was 11:23:56	7 Q. What's your understanding of what happens in a 11:27:19
8 not known prior to January 13, 2011. 11:24:00	8 Phase I clinical trial? 11:27:21
9 BY MS. CORK: 11:24:09	9 MR. COBB: Objection. Scope; form. 11:27:25
10 Q. Are you familiar with the process of bringing 11:24:43	10 THE WITNESS: It is focused on safety. Phase I 11:27:27
11 new drugs to market? 11:24:45	11 clinical trial -- trials solely focus on the safety of 11:27:32
12 MR. COBB: Objection. Vague; scope. 11:24:51	12 the drug. 11:27:37
13 THE WITNESS: I'm somewhat familiar with this 11:24:55	13 BY MS. CORK: 11:27:39
14 process, because I've been involved in some aspects of 11:24:57	14 Q. What's your understanding of what happens in a 11:27:40
15 this process over the years. 11:25:03	15 Phase II clinical trial? 11:27:41
16 BY MS. CORK: 11:25:06	16 MR. COBB: Objection. Scope. 11:27:43
17 Q. Are you familiar with the term, Investigational 11:25:07	17 THE WITNESS: Phase II clinical trials, the 11:27:46
18 New Drug Application? 11:25:09	18 safety is evaluated using a larger population. Phase I 11:27:49
19 A. Yes, I've heard this term previously 11:25:18	19 is done -- typically done with volunteers. Phase II is a 11:27:57
20 abbreviated as IND Application. 11:25:21	20 much larger population, and sometimes these days there is 11:28:03
21 Q. Are you familiar with the term Biologics Access 11:25:23	21 sort of a hybrid Phase II where safety continues to be 11:28:15
22 Application? 11:25:28	22 assessed, and also efficacy begins to be assessed. 11:28:19
23 A. I have heard this term before. 11:25:29	23 BY MS. CORK: 11:28:28
24 Q. Would you agree that these applications are 11:25:32	24 Q. What is your understanding of what happens in a 11:28:29
25 filed with the FDA to seek approval of a drug? 11:25:34	25 Phase III clinical trial? 11:28:30
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1 MR. COBB: Objection. Scope. 11:25:39	1 MR. COBB: Objection. Scope. 11:28:34
2 THE WITNESS: Generally speaking, that's my 11:25:49	2 THE WITNESS: Again, that obviously -- you 11:28:35
3 understanding, yes. 11:25:50	3 know, that's not something that I opine on in my 11:28:38
4 BY MS. CORK: 11:25:51	4 declaration, but, in general, Phase III clinical trials 11:28:42
5 Q. Do you have an understanding of what is 11:25:51	5 is a category of clinical trials, from my prior 11:28:52
6 involved in preparing these applications? 11:25:53	6 experience, even though I'm not opining on that in the 11:28:57
7 MR. COBB: Objection. Vague; form. 11:25:57	7 context of the '681 Patent, where both safety and 11:29:00
8 THE WITNESS: In general, certainly not 11:26:03	8 efficacy are evaluated using larger patient populations, 11:29:05
9 specifically, but I've seen some of these applications, 11:26:06	9 and typically multicenter patient populations. 11:29:15
10 and there is a lot of information that goes into them. 11:26:11	10 BY MS. CORK: 11:29:21
11 BY MS. CORK: 11:26:17	11 Q. Do you agree that, in general, a drug 11:29:22
12 Q. It takes a lot of effort to prepare these 11:26:20	12 progresses from Phase I to Phase II to Phase III clinical 11:29:25
13 applications. 11:26:22	13 studies? 11:29:30
14 A. That's for sure. 11:26:24	14 MR. COBB: Objection. Scope. 11:29:31
15 Q. And they're expensive. 11:26:26	15 THE WITNESS: Not necessarily. 11:29:34
16 A. I beg your pardon? 11:26:28	16 BY MS. CORK: 11:29:37
17 Q. They're expensive to prepare. 11:26:29	17 Q. What do you mean by that? 11:29:38
18 A. Sure. It takes a lot of effort and money to 11:26:33	18 A. What I mean by that is if in Phase I you find 11:29:40
19 prepare them. Yes. 11:26:36	19 that the drug is unsafe, there will be no progression to 11:29:43
20 Q. Are you familiar with clinical trials? 11:26:39	20 Phase II and Phase III. Again, it's not something that 11:29:47
21 MR. COBB: Objection. Vague. 11:26:46	21 I'm opining on in my declaration. And I don't hold 11:29:50
22 THE WITNESS: I've been involved in creating 11:26:47	22 myself out as an expert in clinical trials. 11:29:55
23 documentation for various clinical trials, and, you know, 11:26:49	23 So, likewise, if you -- if something is not 11:29:59
24 I'm obviously aware of several phases of clinical trials. 11:26:55	24 found safe in Phase II, there will be no progression to 11:30:03
25 So, in general, I'm not a regulatory expert, 11:27:01	25 Phase III. 11:30:09
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1 BY MS. CORK: 11:30:11	1 the art, that person of skill in the art has some 11:33:52
2 Q. Would you agree that, in general, a drug 11:30:15	2 knowledge relating to the diagnosis and treatment of 11:33:55
3 doesn't get to Phase III unless that drug is tested in 11:30:17	3 angiogenic eye disorders, true? 11:33:58
4 Phase I and Phase II? 11:30:20	4 MR. COBB: Objection. Form. 11:34:06
5 MR. COBB: Objection. Scope. 11:30:22	5 THE WITNESS: That's probably true, yes. 11:34:10
6 THE WITNESS: Again, it's -- you know, I'm not 11:30:30	6 Again, as I already explained to you, I'm not offering 11:34:16
7 an expert in this area. It's not something that I'm 11:30:32	7 opinions as to which -- or -- or opinions with respect to 11:34:19
8 opining on in my declaration or have been asked to form 11:30:35	8 the various aspects of who a person of ordinary skill in 11:34:25
9 any opinions in my declaration. 11:30:39	9 the art would be in the context of the '681 Patent. 11:34:30
10 But, in general, from my prior experience, 11:30:41	10 BY MS. CORK: 11:34:37
11 that -- that is the case. There are sometimes clinical 11:30:46	11 Q. To the extent a person of skill in the art for 11:35:09
12 trials, you know, like Phase II-A, II-B, II-C, so 11:30:51	12 the '681 Patent is interested in the diagnosis or 11:35:11
13 sometimes there is a more differentiated structure of 11:30:57	13 treatment of angiogenic eye disorders, would that person 11:35:16
14 clinical trials. 11:31:01	14 be interested in structural differences between similar 11:35:23
15 But, again, not -- just not relevant to what 11:31:03	15 drugs that could be used for that purpose? 11:35:26
16 I've been asked to form opinions on in the context of 11:31:07	16 MR. COBB: Objection. Incomplete hypothetical; 11:35:29
17 this case. 11:31:12	17 scope; form. 11:35:31
18 BY MS. CORK: 11:31:13	18 THE WITNESS: I'm not entirely sure what the 11:35:39
19 Q. Do you have an understanding of whether 11:31:18	19 question means, but I would certainly say that I -- I 11:35:41
20 changing the structure of a drug can change its safety? 11:31:20	20 don't see any reason why a POSA would turn a blind eye to 11:35:45
21 MR. COBB: Objection. Vague; scope. 11:31:25	21 such potential differences. 11:35:51
22 THE WITNESS: What do you mean "the structure 11:31:31	22 BY MS. CORK: 11:35:54
23 of the drug"? What structure are you talking about? 11:31:33	23 Q. Do you agree that such potential differences 11:35:55
24 BY MS. CORK: 11:31:38	24 could impact the different drugs' safety, for example? 11:35:57
25 Q. Any aspect of the structure of a drug. 11:31:38	25 MR. COBB: Objection. Form; incomplete 11:36:03
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1 MR. COBB: Same objections. Form; vague; 11:31:41	1 hypothetical; scope. 11:36:04
2 scope. 11:31:43	2 THE WITNESS: Well, as I already said, if you 11:36:08
3 THE WITNESS: Well, if you change the -- for 11:31:54	3 change the primary structure of a protein drug, for 11:36:09
4 example, the primary structure of a protein drug, it's 11:31:56	4 example, that's not the same drug. So it may not be as 11:36:13
5 not going to be the same active pharmaceutical ingredient 11:32:01	5 safe as the other, or one drug may not be as safe as the 11:36:19
6 or API anymore. 11:32:05	6 other, because they are different molecules. 11:36:23
7 BY MS. CORK: 11:32:12	7 BY MS. CORK: 11:36:27
8 Q. And changing the primary structure of a protein 11:32:34	8 Q. Let's go to paragraph 61 of your Exhibit 1 to 11:36:39
9 drug could affects its safety or efficacy, true? 11:32:36	9 the deposition. 11:36:44
10 MR. COBB: Objection. Scope. 11:32:40	10 A. Just a second. Let me read it to myself. Yes, 11:36:45
11 THE WITNESS: In general, that's certainly a 11:32:44	11 ma'am. 11:38:02
12 possibility, although, again, it -- it's -- it has -- 11:32:47	12 Q. Denaturing a protein changes its 11:38:04
13 it's way beyond what I've been asked to opine on in -- to 11:32:52	13 three-dimensional structure, true? 11:38:07
14 form opinions on for the purposes of my '681 Patent 11:32:57	14 A. Yes, that's correct. 11:38:13
15 declaration. 11:33:02	15 Q. But even if you denature a protein, its 11:38:16
16 BY MS. CORK: 11:33:05	16 underlying primary structure, i.e., it's amino acid 11:38:19
17 Q. Would it be important to a person of skill in 11:33:24	17 sequence, remains exactly the same, true? 11:38:24
18 the art for the '681 Patent to understand structural 11:33:27	18 MR. COBB: Objection. Form. 11:38:27
19 differences between similar drugs? 11:33:30	19 THE WITNESS: Yes, if you don't change the 11:38:28
20 MR. COBB: Objection. Form; scope; calls for 11:33:32	20 covalent structure, meaning the primary structure, it 11:38:30
21 speculation. 11:33:36	21 will remain the same. 11:38:34
22 THE WITNESS: I don't understand the question. 11:33:41	22 BY MS. CORK: 11:38:35
23 I heard it. I just don't understand what it means. 11:33:42	23 Q. So denaturing a protein doesn't change the 11:38:35
24 BY MS. CORK: 11:33:45	24 protein's amino acid sequence. 11:38:38
25 Q. Under either definition of a person of skill in 11:33:49	25 A. Yes, that is -- strictly speaking, that is the 11:38:45
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1 case, yes. 11:38:48	1 protein, or confirmation of aflibercept in this case, may 11:41:45
2 Q. If a protein is denatured, is it still 11:38:49	2 preserve its ability to bind VEGF. 11:41:52
3 identifiable as that protein? 11:38:52	3 BY MS. CORK: 11:41:59
4 MR. COBB: Objection. Vague; form. 11:38:55	4 Q. Are you aware of any therapeutic formation of 11:41:59
5 THE WITNESS: It is identifiable with respect 11:38:59	5 aflibercept in which aflibercept is denatured? 11:42:03
6 to its primary structure or its amino acid sequence. 11:39:01	6 MR. COBB: Objection. Scope. 11:42:08
7 BY MS. CORK: 11:39:07	7 THE WITNESS: I have not looked into it, but 11:42:09
8 Q. Is denatured aflibercept still identifiable as 11:39:10	8 certainly, again, if you use different -- if one were to 11:42:12
9 aflibercept? 11:39:15	9 use different formulation of aflibercept, there certainly 11:42:18
10 MR. COBB: Objection. Incomplete hypothetical; 11:39:18	10 could be minor changes in the structure of aflibercept. 11:42:24
11 form. 11:39:19	11 BY MS. CORK: 11:42:33
12 THE WITNESS: It will still be identifiable 11:39:22	12 Q. Do you have any reason to believe that when 11:42:37
13 with respect to its primary structure or the amino acid 11:39:24	13 aflibercept was administered in any clinical trial, that 11:42:41
14 sequence, not with respect to other aspects. 11:39:28	14 it was administered in a denatured form? 11:42:44
15 BY MS. CORK: 11:39:31	15 MR. COBB: Objection. Scope; form. 11:42:47
16 Q. Are you familiar with aflibercept's mechanism 11:39:32	16 THE WITNESS: Again, it's not something I've 11:42:59
17 of action? 11:39:34	17 been asked to form opinions on, but, as I said, if we're 11:43:00
18 MR. COBB: Objection. Scope. 11:39:36	18 talking about if by denaturation we're referring to a 11:43:04
19 THE WITNESS: To the extent that I describe it 11:39:40	19 minor change in the confirmation, this minor change could 11:43:08
20 in my declaration. 11:39:43	20 have occurred just as a result of changing a formulation 11:43:12
21 BY MS. CORK: 11:39:45	21 that is -- that was used in such clinical trials. 11:43:17
22 Q. Do you agree that aflibercept binds VEGF? 11:39:48	22 BY MS. CORK: 11:43:24
23 MR. COBB: Objection. Form. 11:39:56	23 Q. Sitting here today, do you have any reason to 11:43:25
24 THE WITNESS: Aflibercept can bind VEGF. 11:40:00	24 believe that when aflibercept was administered in 11:43:28
25 //	25 clinical trials, that it was administered in a denatured 11:43:31
Page 82	Page 84
1 BY MS. CORK: 11:40:07	1 form? 11:43:35
2 Q. In binding VEGF, aflibercept can interfere with 11:40:08	2 MR. COBB: Objection. Form; scope. 11:43:36
3 the VEGF's angiogenic activity, true? 11:40:15	3 THE WITNESS: I haven't looked into it, and, 11:43:41
4 MR. COBB: Objection. Scope. 11:40:19	4 again, would depend on what the denatured form is. The 11:43:43
5 THE WITNESS: That's -- that's not something, 11:40:24	5 word "denaturation" or "denatured form" are broad terms, 11:43:49
6 again, that I have been asked to form opinions on, but, 11:40:25	6 and denaturation is defined as a significant 11:43:53
7 in general, that is my understanding. 11:40:28	7 confirmational change in the structure of a protein. 11:43:58
8 BY MS. CORK: 11:40:32	8 So -- which begs the question, okay, what's 11:44:02
9 Q. If aflibercept is denatured, can it bind VEGF? 11:40:33	9 significant? 11:44:06
10 MR. COBB: Objection. Scope. 11:40:38	10 But as I already repeatedly testified, minor 11:44:07
11 THE WITNESS: Again, it is not something I've 11:40:46	11 changes in the confirmation of aflibercept, that some 11:44:12
12 opined -- I've been asked to form opinions on, but it 11:40:48	12 people may call denaturation, because it's a significant 11:44:20
13 depends on the extent of denaturation. Some minor extent 11:40:51	13 confirmational change brought about by changes in pH, for 11:44:24
14 of denaturation may preserve its ability to do so. 11:40:57	14 example, or other excipients in the formulation, may 11:44:29
15 BY MS. CORK: 11:41:03	15 result in a significant confirmational change. 11:44:38
16 Q. Would denatured aflibercept be useful as a 11:41:05	16 BY MS. CORK: 11:44:54
17 therapeutic? 11:41:08	17 Q. My question just related to aflibercept was 11:44:54
18 MR. COBB: Objection. Calls for speculation; 11:41:10	18 administered in clinical trials. Did you understand 11:44:56
19 form; scope. 11:41:12	19 that? 11:44:59
20 THE WITNESS: Again, not something that I have 11:41:17	20 A. I do, and in response to that portion of your 11:45:00
21 been asked to form opinions on, but, again, it will 11:41:19	21 question, I said I haven't looked into it. I haven't 11:45:03
22 depend on the extent of denaturation. The definition of 11:41:23	22 looked into the way that aflibercept is administered in 11:45:06
23 denaturation is a little vague and varies from one 11:41:28	23 clinical trials. That's not something that I've been 11:45:15
24 textbook to another. 11:41:36	24 asked to form opinions on. 11:45:18
25 But a minor change in the confirmation of a 11:41:38	25 Q. Does your declaration, Exhibit 1, discuss the 11:45:58
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1 composition of the formulation of aflibercept? 11:46:01 2 A. My recollection is that I provide some aspects 11:46:14 3 of that discussion in the context of analyzing the Dixon 11:46:17 4 paper, D-i-x-o-n, this is obviously for our court 11:46:24 5 reporter, and I'll be happy to go there and point you to 11:46:28 6 that. 11:46:35 7 Q. Would you, please? 11:46:36 8 A. Well, for example, I do see in paragraph 37 of 11:47:02 9 my declaration, and specifically the first sentence on 11:47:06 10 page 12 where I say, "Dixon also reports that 'VEGF 11:47:13 11 Trap-Eye and {Regeneron's} aflibercept (the oncology 11:47:26 12 product) have the same molecular structure, but there are 11:47:37 13 substantial differences between the preparation of the 11:47:43 14 purified drug product and their formulations.'" Full 11:47:49 15 stop. 11:47:55 16 And there is a then direct citation to the 11:47:57 17 Dixon paper. 11:48:04 18 Q. Does your declaration set forth the compilation 11:48:14 19 of the formulation of aflibercept? 11:48:18 20 A. I don't think it specifically does that. I 11:48:27 21 mean, obviously, my declaration speaks for itself. It 11:48:29 22 says what it says. It doesn't say what it doesn't say. 11:48:31 23 I don't specifically go into that. 11:48:34 24 But in the very next sentence, right after the 11:48:39 25 one that I read to you, it says my paragraph 37 says, in 11:48:46 Page 86	1 be able to identify any specific excipient of any 11:50:55 2 aflibercept formulation? 11:50:59 3 A. Well, buffers are excipients. So I already 11:51:02 4 answered your question with respect to buffers, which are 11:51:08 5 excipients. 11:51:11 6 Q. Are there other kinds of excipients, besides 11:51:14 7 buffers? 11:51:17 8 A. Yes. 11:51:20 9 Q. Can you identify any other kind of excipient 11:51:20 10 that is a component of any aflibercept formulation? 11:51:24 11 MR. COBB: Objection. Scope; form. 11:51:28 12 THE WITNESS: Well, I already mentioned water, 11:51:33 13 components of water, such as protons, which is hydrogen 11:51:39 14 ions, also will be such components, sometimes referred to 11:51:44 15 as excipients. 11:51:56 16 My recollection is, again, I haven't been asked 11:52:01 17 to form opinions on that, but my recollection is that 11:52:04 18 there are also some detergents that may be present; also 11:52:07 19 some tonicity agents, but, again, this is just something 11:52:17 20 that I have learned through studying the literature in 11:52:21 21 preparing my '681 declaration. 11:52:26 22 BY MS. CORK: 11:52:33 23 Q. Sitting here today, you can't identify any 11:52:33 24 excipient such as detergents or tonicity agents that are 11:52:35 25 part of any aflibercept formation, true? 11:52:40 Page 88
1 the same paragraph, "Dixon subsequently states that 'VEGF 11:48:54 2 Trap-Eye undergoes further purification steps during 11:49:01 3 manufacturing' and 'is also formulated with different 11:49:07 4 buffers and at different concentrations (for buffers in 11:49:14 5 common)' compared to the oncology product aflibercept." 11:49:26 6 And, again, there is a direct reference to the 11:49:34 7 Dixon paper. 11:49:39 8 Q. Sitting here today, can you identify any 11:49:42 9 specific component of any aflibercept formulation? 11:49:45 10 MR. COBB: Objection. Scope. 11:49:55 11 THE WITNESS: I have not been asked to form 11:49:58 12 opinions, but I can -- I -- I can. For example, I can 11:50:01 13 identify water as one of the components, because my 11:50:07 14 understanding is that those formulations are aqueous 11:50:10 15 solutions, meaning water-based solutions. 11:50:16 16 BY MS. CORK: 11:50:22 17 Q. Can you identify any specific buffer that is 11:50:24 18 part of any aflibercept formulation? 11:50:27 19 MR. COBB: Objection. Scope. 11:50:30 20 THE WITNESS: I may have seen it in some of the 11:50:36 21 literature that I have reviewed, but sitting here right 11:50:38 22 now, I do not recall. It's not something that I have 11:50:41 23 been asked to form opinions on. 11:50:46 24 BY MS. CORK: 11:50:49 25 Q. Is that also true for excipients? You wouldn't 11:50:51 Page 87	1 MR. COBB: Objection. Scope; form. 11:52:45 2 THE WITNESS: I don't specifically recall. As 11:52:47 3 I said, I may have seen them, but I just don't recall at 11:52:49 4 the moment. 11:52:54 5 BY MS. CORK: 11:52:55 6 Q. Is the composition of the formulation of 11:52:56 7 aflibercept relevant to the opinions that you offer in 11:52:59 8 your declaration? 11:53:03 9 A. What is relevant is what I recite in my 11:53:14 10 declaration. So that is what's relevant. So what I -- 11:53:17 11 what I have in my declaration, since I don't specifically 11:53:23 12 discuss buffers, other excipients, that therefore I have 11:53:26 13 not viewed them to be directly relevant to the opinions 11:53:36 14 that I expressed in response to Dr. Chaum's opinions. 11:53:42 15 Q. Sitting here today, can you identify any 11:53:50 16 specific component of any formulation for VEGF Trap-Eye? 11:53:54 17 MR. COBB: Objection. Scope. 11:53:59 18 THE WITNESS: Yes. 11:54:04 19 BY MS. CORK: 11:54:05 20 Q. And what are those components? 11:54:08 21 MR. COBB: Objection. Scope. 11:54:11 22 THE WITNESS: Water, for example. Again, I 11:54:12 23 have not been asked to form opinions, but from what I've 11:54:14 24 seen, my recollection is that those are all aqueous -- 11:54:17 25 aqueous formulations, meaning water-based formulations. 11:54:24 Page 89

1 BY MS. CORK: 11:54:29 2 Q. Can you identify any specific components of any 11:54:30 3 VEGF Trap-Eye formulation, besides water? 11:54:33 4 MR. COBB: Objection. Scope. 11:54:36 5 THE WITNESS: And you don't mean the active 11:54:45 6 pharmaceutical ingredient, and besides the active 11:54:47 7 pharmaceutical ingredient itself? 11:54:51 8 BY MS. CORK: 11:54:54 9 Q. That's right. 11:54:54 10 A. Again, I know I may have seen some of them in 11:54:55 11 reviewing documents in preparation of my declaration, but 11:55:01 12 I do not recall them right now, because they were not 11:55:05 13 directly relevant to the opinions that I have expressed 11:55:14 14 in my '681 Patent declaration. 11:55:16 15 MR. COBB: Counsel, if you are done with this, 11:55:46 16 we are at another hour and 25 minutes. 11:55:48 17 MS. CORK: Should we take a five-minute break? 11:55:51 18 MR. COBB: Sure. 11:55:53 19 THE VIDEOTAPE OPERATOR: Off the record at 11:55:54 20 11:56 a.m. 11:55:55 21 (Recess was taken.) 11:55:57 22 THE VIDEOTAPE OPERATOR: Back on the record 12:11:59 23 beginning Media Unit 3 at 12:12 p.m. 12:12:00 24 BY MS. CORK: 12:12:06 25 Q. Dr. Klivanov, would you please go to paragraph 12:12:14 Page 90	1 MS. CORK: I'd like to mark as Exhibit 7 a 12:16:10 2 UNIPROT sequence that is designated Exhibit 2080, with a 12:16:12 3 copy to counsel. 12:16:34 4 (Exhibit 7 was marked for identification.) 12:16:34 5 THE REPORTER: Exhibit 7. 12:16:35 6 THE WITNESS: Thank you. 12:16:37 7 MS. CORK: I'd like to mark as Exhibit 8 12:16:37 8 another UNIPROT document, titled, "PI17948," marked as 12:16:43 9 Exhibit 2079, with a copy to counsel. 12:16:51 10 (Exhibit 8 was marked for identification.) 12:16:57 11 THE REPORTER: Exhibit 8. 12:17:10 12 THE WITNESS: Thank you. 12:17:11 13 MS. CORK: I'd like to mark as Exhibit 9 an 12:17:18 14 article titled, "Crystal Structure at 1.7 angstroms 12:17:21 15 Resolution of VEGF in Complex with Domain 2 of the Flt-1 12:17:22 16 Receptor," designated Exhibit 2081, with a copy to 12:17:26 17 counsel. 12:17:32 18 (Exhibit 9 was marked for identification.) 12:17:32 19 THE REPORTER: Exhibit 9. 12:17:43 20 THE WITNESS: Thank you. 12:17:45 21 MS. CORK: And I'd like to mark as Exhibit 10 12:17:54 22 U.S. Patent No. 7,374,758, to Papadopoulos et al., 12:17:56 23 stamped Samsung Bioepis Exhibit 1036. Copy to counsel. 12:18:04 24 THE REPORTER: Exhibit 10. 12:18:29 25 (Exhibit 10 was marked for identification.) 12:18:30 Page 92
1 85, paragraph 85 of your declaration, which is Exhibit 1. 12:12:17 2 A. Let me read it to myself. Yes, ma'am. 12:12:36 3 Q. Between paragraphs 86 and 91 of your 12:13:07 4 declaration, you analyzed prior art that describes, in 12:13:12 5 your view, more than one amino acid sequence for VEGFR1 12:13:17 6 Domain 2. 12:13:22 7 Do you see that? 12:13:26 8 A. I do. 12:13:27 9 Q. Do you see the table in paragraph 86 of your 12:14:28 10 declaration that summarizes certain literature sources? 12:14:31 11 A. Yes, I do. 12:14:36 12 Q. These literature sources are Davis-Smyth et 12:14:39 13 al., which is Exhibit 2078 to your declaration; a UNIPROT 12:14:43 14 PI17948 sequence, which is reflected in Exhibits 2079 and 12:14:47 15 2080 to your declaration; a Wiesmann et al., 1997 article 12:14:58 16 that is Exhibit 2081 to your declaration; and a 12:15:05 17 Papadopoulos reference that is Exhibit 1036 to your 12:15:10 18 declaration. 12:15:16 19 Do you see that? 12:15:16 20 A. Yes. 12:15:17 21 MS. CORK: I'm going to mark as Exhibit 6 an 12:15:36 22 article by Davis-Smyth, which is Exhibit 2078. 12:15:42 23 (Exhibit 6 was marked for identification.) 12:15:48 24 THE REPORTER: Exhibit 6. 12:16:00 25 THE WITNESS: Thank you. 12:16:02 Page 91	1 THE WITNESS: Thank you. 12:18:30 2 BY MS. CORK: 12:18:40 3 Q. Exhibits 6 to 10 that you've just been handed, 12:18:41 4 Dr. Klivanov, are the references that are discussed in 12:18:43 5 paragraph 86 of your declaration? 12:18:47 6 A. I wouldn't say discussed. I mean, they are 12:18:49 7 listed there. They're discussed subsequently. 12:18:51 8 Q. They're discussed between paragraphs 86 and 91 12:19:14 9 of your declaration? 12:19:17 10 A. Yes, that's correct. 12:19:36 11 Q. And you're familiar with Exhibits 6 through 10? 12:19:37 12 A. Well, I'm not sure what you mean by familiar. 12:19:42 13 I mean, obviously, at some point I -- I reviewed those. 12:19:44 14 As you know, these are the same sections that were 12:19:51 15 present in my prior declaration. So I basically 12:19:54 16 transferred these sections from -- from there to this 12:20:00 17 particular declaration. I have not re-reviewed these 12:20:07 18 papers since that time. 12:20:13 19 Q. In paragraphs 86 to 91 of your declaration, you 12:20:26 20 analyzed the starting and amino acids for VEGFR Domain 2, 12:20:31 21 as set forth in these references, Exhibits 6 to 10, 12:20:38 22 correct? 12:20:43 23 A. The starting amino acid residue, the ending 12:20:45 24 amino acid residue, and the domain length. 12:20:49 25 Q. Do you analyze the domain amino acid sequences 12:20:56 Page 93

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1 in these references side by side to show any differences 12:21:01	1 literature searches -- sources pertaining to VG -- 12:25:07
2 in their overlapping regions? 12:21:06	2 VEGFR2, Domain 3, and their amino acid composition. 12:25:17
3 A. I mean, I -- there is obviously some analysis 12:21:14	3 Q. These references are Davis-Smyth et al., which 12:25:30
4 of the amino acid sequences. I mean, the paragraphs 86 12:21:19	4 is Exhibit 2078 to your declaration; Lu et al., 2000, 12:25:33
5 through 91, you know, speak for themselves. 12:21:23	5 which is Exhibit 2082 to your declaration; Franklin et 12:25:38
6 Q. Are there any differences in the overlapping 12:21:31	6 al., which is Exhibit 2083 to your declaration; and two 12:25:42
7 regions of the VEGFR1 Domain 2 as set forth in these 12:21:34	7 UNIPROT entries which are Exhibit 2084 and 2058 to your 12:25:47
8 references that are Exhibits 6 to 10? 12:21:41	8 declaration, true? 12:25:53
9 MR. COBB: Objection. Form. 12:21:45	9 A. Yes. 12:25:54
10 THE WITNESS: I mean, I -- I can analyze them 12:21:46	10 MS. CORK: I'd like to mark as Exhibit 11 a 12:26:05
11 one reference at a time. You know, I don't want to make 12:21:49	11 document titled, "Identification of the Residues in the 12:26:09
12 any blanket statements. As I just indicated, you know, 12:21:51	12 Extracellular Region of KDR Important for Interaction 12:26:12
13 my opinions are laid out in some detail in paragraphs 12:21:55	13 with Vascular Endothelial Growth Factor and Neutralizing 12:26:15
14 86 -- 86 through 91 of my '681 declaration. 12:22:02	14 Anti-KDR Antibodies," Lu et al., which is designated 12:26:20
15 BY MS. CORK: 12:22:10	15 Exhibit 2082, with a copy to counsel. 12:26:25
16 Q. Sitting here today, can you identify any 12:22:12	16 (Exhibit 11 was marked for identification.) 12:26:31
17 differences in the overlapping regions of the VEGFR1 12:22:15	17 THE REPORTER: Exhibit 11. 12:26:47
18 Domain 2 as set forth in these references that are 12:22:18	18 MS. CORK: I'd like to mark an article titled, 12:26:49
19 Exhibits 6 through 10? 12:22:25	19 "The Structural Basis for the Function of Two Anti-VEGF 12:26:50
20 MR. COBB: Objection. Form. 12:22:28	20 Receptor 2 Antibodies," Lu et al., which is designated 12:26:53
21 THE WITNESS: I mean, I'll be glad to re-review 12:22:29	21 Exhibit 2083. This is Exhibit 12 with a copy to counsel. 12:26:59
22 paragraphs 86 through 91 to myself, and then I may be 12:22:32	22 (Exhibit 12 was marked for identification.) 12:27:20
23 able to do it. So that's what I would need to -- to do 12:22:39	23 THE WITNESS: Thank you. 12:27:21
24 to carefully analyze these paragraphs and what I referred 12:22:44	24 MS. CORK: Let's mark as Exhibit 13 a UNIPROT 12:27:21
25 to in these paragraphs, and I'll be glad to do it. 12:22:48	25 entry titled, "P35968 VGFR2_HUMAN," designated 12:27:24
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1 BY MS. CORK: 12:22:52	1 Exhibit 2084, a copy to counsel. That's Exhibit 13? 12:27:30
2 Q. So it's fair to say that the answer to my 12:22:53	2 (Exhibit 13 was marked for identification.) 12:27:52
3 question is, no, sitting here at this moment, you are not 12:23:13	3 THE REPORTER: Exactly. Yes. Exhibit 13. 12:27:53
4 able to identify any differences in the overlapping 12:23:15	4 THE WITNESS: Thank you. 12:27:54
5 regions of the VEGFR1 Domain 2 as set forth in these 12:23:19	5 MS. CORK: Let's mark as Exhibit 14 a UNIPROT 12:27:57
6 references that are Exhibits 6 to 10? 12:23:25	6 document, designated as Exhibit 2085. A copy to counsel. 12:28:03
7 MR. COBB: Objection. Form. 12:23:27	7 (Exhibit 14 was marked for identification.) 12:28:09
8 THE WITNESS: I think that would be unfair to 12:23:29	8 THE REPORTER: Exhibit 14. 12:28:24
9 say that. I'm -- what I'm telling you is that I have not 12:23:30	9 THE WITNESS: Thank you. 12:28:28
10 committed those particular aspects that you're inquiring 12:23:34	10 BY MS. CORK: 12:28:37
11 about to memory. I have provided -- specifically 12:23:38	11 Q. These references, which are Exhibits 11 to 14, 12:28:37
12 provided a detailed description of each of these 12:23:45	12 as well as Exhibit 6, are discussed in paragraphs 92 to 12:28:42
13 references with respect to the issues that I analyzed; 12:23:48	13 97 of your declaration, true? 12:28:48
14 and I'll be happy to do it right now, sitting here, and 12:23:50	14 A. And also paragraph 98 of my declaration. 12:29:03
15 try to answer your question. 12:23:55	15 Q. In paragraphs 92 to 98 of your declaration, you 12:29:11
16 BY MS. CORK: 12:24:02	16 discuss the starting and ending amino acid sequences for 12:29:15
17 Q. In paragraph 92 of your declaration, you 12:24:02	17 VEGFR Domain 3 as set forth in these Exhibits 6 and 14 -- 12:29:20
18 discuss -- 12:24:10	18 11 through 14? 12:29:26
19 A. Just a second. Yes, ma'am. 12:24:14	19 A. Yes, and then I summarize my findings in the 12:29:29
20 Q. Have you reviewed paragraph 92 to your 12:24:17	20 subsequent paragraphs. So it actually goes all the way 12:29:33
21 declaration? 12:24:20	21 through paragraph 1 of 2. 12:29:36
22 A. No. Just a second. I have reviewed it now. 12:24:21	22 Q. For these exhibits, 6 and 11 through 14, do you 12:29:41
23 Q. Paragraph 92 to your declaration summarizes 12:24:53	23 analyze the domain sequences for VEGFR2, Domain 3, side 12:29:46
24 certain literature sources, true? 12:24:57	24 by side to show any differences in the overlapping 12:29:53
25 A. That's correct. Yes. Certainly -- certainly 12:25:04	25 regions as set forth in these exhibits? 12:29:56
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1 A. Well, I -- what I analyze is the domain length, 12:30:03 2 specifically, because, obviously, if the domain length 12:30:08 3 differs, then by definition the amino acid sequence 12:30:12 4 differs. So that's what I'm doing in these paragraphs 12:30:16 5 with respect to VEGFR2, Domain 3, and that's the same 12:30:20 6 thing that I was doing with respect to VEGFR1 Domain 2. 12:30:27 7 Q. But you don't align the domain sequences for 12:30:34 8 VEGFR Domain 3 from each of these references with each 12:30:38 9 other, do you? 12:30:42 10 A. No. There was no reason for me to do that, 12:30:43 11 either with respect to VEGFR1 Domain 2 or VEGFR2 Domain 12:30:48 12 3, because as I just mentioned, if the length of the 12:30:59 13 domain varies, then by definition the amino acid sequence 12:31:02 14 must be different. 12:31:09 15 Q. For the moment, let's stick with the references 12:31:16 16 that you rely on in describing VEGFR2 Domain 3, which are 12:31:20 17 Exhibits 6 and 11 through 14. Can you do that? 12:31:25 18 A. Sure. 12:31:29 19 Q. To the extent the VEGFR2 Domain 3 sequences 12:31:35 20 overlap in these references, are there any differences in 12:31:38 21 those sequences? 12:31:43 22 MR. COBB: Objection. Form; vague. 12:31:46 23 THE WITNESS: As I just said, there must be 12:31:51 24 differences in sequences, because if the length of the 12:31:54 25 domain is different, then by definition the primary 12:31:57 Page 98	1 THE WITNESS: I -- I looked at them at some 12:34:02 2 point. I have not committed whatever differences there 12:34:05 3 may be to memory. As I said, that's not what my exercise 12:34:09 4 was. But sitting here today, I'm quite capable, I can 12:34:12 5 assure you, in comparing side by side the amino acid 12:34:15 6 sequences in question. 12:34:20 7 But even without doing that, I, and a POSA, 12:34:22 8 would know that the amino acid sequences are different 12:34:26 9 because even the domain length is different. 12:34:30 10 BY MS. CORK: 12:35:27 11 Q. And I'll ask you to consider the references 12:35:27 12 that you rely on between paragraphs 86 and 91 with 12:35:29 13 respect to their description of the VEGFR1 Domain 2. 12:35:33 14 That's Exhibits 6 to 11. Are you -- I mean Exhibits 6 to 12:35:38 15 10. Sorry. Are you with me? 12:35:43 16 A. Just a second. You said paragraphs 96 12:35:52 17 through -- 12:35:57 18 Q. 86 to 91. 12:35:58 19 A. Oh, 86 through 99? 12:36:00 20 Q. Withdrawn. 12:36:00 21 Between paragraphs 86 and 91, you analyze prior 12:36:01 22 art describing VEGFR1 Domain 2, correct? 12:36:05 23 A. That's correct. Yes. 12:36:13 24 Q. And those references we've marked as Exhibits 6 12:36:14 25 to 10, right? 12:36:18 Page 100
1 structure or the amino acid sequence is different. 12:32:03 2 BY MS. CORK: 12:32:07 3 Q. I'm not sure if you understood my question. 12:32:09 4 I'm referring to the overlapping regions of VEGFR2 12:32:11 5 Domain 3 that are discussed in Exhibits 6 and 11 through 12:32:17 6 14. 12:32:21 7 A. But as I just told you, I have not compared the 12:32:24 8 amino acid sequences in these different references. The 12:32:28 9 goal of my exercise was to compare the domain length; 12:32:33 10 because, as I explained, if the length of the domain is 12:32:39 11 different, the primary structure must be different, by 12:32:45 12 definition. 12:32:50 13 Q. Sitting here today, are you able to identify 12:33:01 14 any differences in the overlapping regions of VEGFR2 12:33:04 15 Domain 3 as set forth in Exhibits 6 and 11 through 14? 12:33:11 16 A. Sitting here today, I would have to conduct a 12:33:23 17 side-by-side comparison of the amino acid sequences in 12:33:30 18 these references next to each other. That's not the 12:33:33 19 exercise that I have conducted for the reasons that I 12:33:36 20 just repeatedly stated. 12:33:40 21 Q. So sitting here today, you are not able to 12:33:46 22 identify any differences in the overlapping regions of 12:33:49 23 VEGFR2 Domain 3 as set forth in Exhibits 6 and 11 through 12:33:53 24 14? 12:33:58 25 MR. COBB: Objection. Form. 12:34:02 Page 99	1 A. That's right. I think -- that's correct. Yes. 12:36:24 2 Q. Do any of those references refer to 12:36:27 3 aflibercept? 12:36:29 4 MR. COBB: Objection. Form. 12:36:30 5 THE WITNESS: I would need to look at those 12:36:32 6 references. I mean, I obviously haven't committed them 12:36:36 7 to memory. 12:36:39 8 BY MS. CORK: 12:36:39 9 Q. In your declaration, do you cite any teaching 12:36:40 10 from these references describing aflibercept? 12:36:43 11 A. I mean, I would just need to look through the 12:36:49 12 corresponding portions of my declaration; for example, 12:36:51 13 the portion -- the paragraphs that you directed me to, 12:36:56 14 and we'll be glad to tell you whether the word 12:37:00 15 "aflibercept" is there. 12:37:02 16 Q. Please do. 12:37:04 17 A. Okay. So, once again, this is paragraphs -- 12:37:05 18 what through what? 12:37:10 19 Q. I understand it to be 86 to 91, but if that's 12:37:16 20 not accurate, please correct me. 12:37:19 21 A. Sure. So let me just read these paragraphs to 12:37:22 22 myself. 12:37:25 23 Okay. So having reviewed paragraphs 86 through 12:40:39 24 91, the word "aflibercept" is not in those paragraphs. 12:40:43 25 Q. So to the extent you rely on teachings from 12:40:51 Page 101

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1 Exhibits 6 to 10 in support of your opinions, those 12:40:55 2 teachings don't relate to aflibercept, true? 12:40:58 3 MR. COBB: Objection. Mischaracterizes his 12:41:01 4 testimony. 12:41:03 5 THE WITNESS: I would not put it that way. 12:41:06 6 BY MS. CORK: 12:41:10 7 Q. Please point me to the place in your 12:41:12 8 declaration where you rely on a teaching from Exhibits 6 12:41:15 9 to 10 involving aflibercept. 12:41:18 10 MR. COBB: Objection. Form. 12:41:22 11 THE WITNESS: Could you just repeat the 12:41:29 12 previous question, please? 12:41:30 13 BY MS. CORK: 12:41:34 14 Q. Can you point me to a place in your declaration 12:41:34 15 where you rely on a teaching from Exhibit 6 to 10 12:41:39 16 involving aflibercept. 12:41:43 17 MR. COBB: Objection. Vague; form. 12:41:45 18 THE WITNESS: You misunderstood my inquiry. I 12:41:46 19 said, could you repeat the previous question, not the 12:41:49 20 last question, but the one before that. 12:41:51 21 BY MS. CORK: 12:42:40 22 Q. To the extent you rely on teachings -- 12:42:40 23 A. Slowly, please. 12:42:42 24 Q. To the extent you rely on teachings from 12:42:43 25 Exhibits 6 to 10 in support of your opinions, those 12:42:47 Page 102	1 to re-review Exhibits 6 through 10 to answer your 12:44:29 2 question. 12:44:34 3 BY MS. CORK: 12:44:36 4 Q. In the portions of your declaration where you 12:44:37 5 analyze VEGFR2 Domain 3, beginning at paragraph 92, do 12:44:43 6 any of those paragraphs rely on any teaching of 12:44:52 7 aflibercept? 12:44:58 8 MR. COBB: Objection. Vague. 12:45:00 9 THE WITNESS: Yeah, so to save time I can tell 12:45:05 10 you that I don't think they rely on that, but I think 12:45:07 11 that in the overall context, the -- the teachings are 12:45:10 12 relevant. 12:45:15 13 BY MS. CORK: 12:45:17 14 Q. Relevant to what? 12:45:40 15 A. To my discussion. I mean, obviously I address 12:45:42 16 the question of whether -- according to the literature, 12:45:46 17 whether there is more than one amino acid sequence 12:45:53 18 comprising VEGFR2 Domain 3. And addressing this 12:45:57 19 particular question, which is relevant to my overall 12:46:04 20 comparison of aflibercept with VEGFR1 R2, and related 12:46:12 21 Regeneron species, it is relevant to address the question 12:46:25 22 that I just mentioned. 12:46:35 23 Q. These references that you cite, which are 12:46:51 24 Exhibits 6 to 14, were created by different research 12:46:55 25 groups. Would you agree with that? 12:46:59 Page 104
1 teachings don't relate to aflibercept, true? 12:42:50 2 A. Don't relate, you said? 12:42:53 3 Q. Yes. 12:42:55 4 A. I wouldn't say that they don't relate. I mean, 12:42:55 5 I -- you know, I think that it's kind of -- I -- to me, 12:42:57 6 you know, they're relevant. 12:43:02 7 Q. Please point me to the place in your 12:43:08 8 declaration where you rely on a teaching from Exhibits 6 12:43:10 9 to 10 that involves aflibercept. 12:43:15 10 MR. COBB: Objection. Form. 12:43:17 11 THE WITNESS: I don't rely on them, but, to me, 12:43:20 12 they're relevant in the context in which I am -- which 12:43:24 13 I'm discussing in these paragraphs. But I don't rely on 12:43:30 14 them. 12:43:35 15 BY MS. CORK: 12:43:38 16 Q. What is it that you don't rely on? 12:43:38 17 A. What you just asked me about. 12:43:40 18 Q. Are you able to point me to any paragraph in 12:43:49 19 your declaration between paragraphs 86 and 91 where you 12:43:52 20 cite a teaching describing aflibercept? 12:43:59 21 MR. COBB: Objection. Vague. 12:44:05 22 THE WITNESS: As I already indicated, the word 12:44:09 23 "aflibercept" is not found in these paragraphs. If you 12:44:11 24 are now broadening your question specifically to 12:44:19 25 Exhibits -- I believe it was 6 through 10, I would need 12:44:23 Page 103	1 A. Different from each other or different from 12:47:02 2 Regeneron's? 12:47:05 3 Q. Different from each other. 12:47:07 4 A. Yes, I would agree with that. 12:47:10 5 Q. These references that are Exhibits 6 to 14 show 12:47:13 6 that different research groups might define VEGFR1 Domain 12:47:19 7 2 and VEGFR2 Domain 3 differently from each other, right? 12:47:25 8 A. Not quite. Not might define, as you said, but 12:47:33 9 do define differently. 12:47:37 10 Q. And, in fact, you calculate that looking at 12:47:42 11 these references, one could form 16 different amino acid 12:47:45 12 sequences? 12:47:51 13 A. That -- that's correct. Yes. Relying on just 12:47:56 14 sort of these representative publications. So it is 12:47:59 15 actually maybe more than that. But given these 12:48:04 16 representative publications, four in the case of VEGFR1 12:48:06 17 Domain 2, and the same number in the case of VEGFR2 12:48:13 18 Domain 3, we have 16 possibilities; which clearly shows 12:48:23 19 that, then, there is more than one amino acid sequence 12:48:32 20 comprising the corresponding domains. 12:48:39 21 Q. And just to be clear, in this section of your 12:48:50 22 declaration, which I believe has the header -- withdrawn. 12:48:53 23 The paragraphs that we've been discussing are 12:49:03 24 under the heading, "A POSA would understand that a given 12:49:05 25 protein domain structure does not necessarily correspond 12:49:11 Page 105

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1 to a single amino acid sequence." True? 12:49:15 2 A. Yes. 12:49:18 3 Q. Just to be clear, this portion of your 12:49:26 4 declaration does not rely on any teachings from 12:49:29 5 Exhibits 6 to 10 involving aflibercept, correct? 12:49:41 6 MR. COBB: Objection. Form. 12:49:50 7 THE WITNESS: Again, I don't know whether 12:49:52 8 aflibercept is mentioned in any of these publications. I 12:49:55 9 just don't remember. 12:49:59 10 So, listen, I mean, I think that I describe 12:50:01 11 very clearly what I'm doing here. Okay? And, you know, 12:50:06 12 if you want to know whether the word "aflibercept" is 12:50:10 13 mentioned in any of these publications, you know, I would 12:50:12 14 be glad to go through those publications, although I see 12:50:17 15 there is no point in it. 12:50:20 16 But, you know, that's all I can tell you. 12:50:22 17 BY MS. CORK: 12:50:25 18 Q. Well, my question is a little bit different. 12:50:25 19 What I'm asking is whether the word "aflibercept" is 12:50:28 20 mentioned in your declaration in this section? 12:50:31 21 MR. COBB: Objection. 12:50:33 22 BY MS. CORK: 12:50:34 23 Q. Insofar as any of these publications that you 12:50:34 24 rely on teach it. 12:50:37 25 MR. COBB: Objection. Form; vague. 12:50:39 Page 106	1 word "aflibercept" is -- does not appear in the paragraph 12:53:44 2 numbers of my declaration that we discussed previously. 12:53:50 3 I'm now talking about the underlying references that I 12:53:53 4 discussed in those paragraphs. 12:53:58 5 So, I mean, I don't see any need to change 12:54:00 6 anything. 12:54:05 7 Q. Are you relying on any of these references, 12:54:05 8 Exhibits 6 to 14, for their teachings of aflibercept's 12:54:07 9 structure? 12:54:11 10 MR. COBB: Objection. Asked and answered. 12:54:13 11 THE WITNESS: Okay. As I said, I -- you know, 12:54:15 12 I cannot say whether I'm relying on it or not, because I 12:54:17 13 would need to take a look and see whether, in fact, 12:54:21 14 aflibercept sequence is discussed. I'm relying on what 12:54:24 15 is in those references. That's what I'm relying on. 12:54:27 16 BY MS. CORK: 12:54:32 17 Q. By relying on it, I mean, is it discussed in 12:55:43 18 your declaration? Is that clear? 12:55:45 19 MR. COBB: Objection. Form. 12:55:52 20 THE WITNESS: I mean, my declaration speaks for 12:55:54 21 itself. And it says what it says. It doesn't say what 12:55:55 22 it doesn't say. And I already said repeatedly that those 12:56:00 23 paragraphs that you asked me about do not specifically 12:56:03 24 list the word "aflibercept." 12:56:07 25 // Page 108
1 BY MS. CORK: 12:50:40 2 Q. Do you understand that? 12:50:40 3 A. I'm struggling to understand the question. I 12:50:45 4 already said that the word "aflibercept" is not mentioned 12:50:49 5 in any of these paragraphs. So I would have thought that 12:50:53 6 we already established that. 12:50:55 7 But then you're sort of asking a complex 12:50:56 8 question, which is your prerogative, but I don't quite 12:50:59 9 understand the connection between the first part and the 12:51:01 10 second part of your question. 12:51:04 11 Q. Are you relying on any of these references, 12:52:50 12 which, in total, are Exhibits 6 to 14, for their 12:52:51 13 teachings of aflibercept's sequence? 12:52:57 14 MR. COBB: Objection. Form. 12:53:02 15 THE WITNESS: I do not remember, as I already 12:53:08 16 said, whether any of those references disclose 12:53:10 17 aflibercept sequences or -- or the aflibercept -- the 12:53:14 18 aflibercept sequence. So I can look through those 12:53:20 19 references if you instruct me to, and do so. But I 12:53:24 20 haven't done so. 12:53:29 21 BY MS. CORK: 12:53:31 22 Q. You previously testified that aflibercept, the 12:53:32 23 word, does not appear in this section. Do you wish to 12:53:35 24 change that testimony? 12:53:38 25 A. No, I don't wish to change that testimony. The 12:53:41 Page 107	1 BY MS. CORK: 12:56:11 2 Q. And they don't describe its structure. 12:56:11 3 MR. COBB: Objection. Vague; form. 12:56:15 4 THE WITNESS: The word "aflibercept" is not 12:56:16 5 mentioned there, and therefore none of the features of 12:56:17 6 aflibercept is mentioned in these paragraphs. But I'm 12:56:22 7 relying on the -- in these paragraphs, obviously, I'm 12:56:26 8 relying on certain references that you introduced in -- I 12:56:30 9 believe, they were numbers -- well, whatever those 12:56:37 10 exhibit numbers were, and I'm relying on those exhibits. 12:56:40 11 MS. CORK: It is almost 1:00. Is now a good 12:56:58 12 time for a lunch break? 12:57:01 13 MR. COBB: Sure. That's fine. 12:57:03 14 THE WITNESS: Pardon me? 12:57:04 15 MR. COBB: Lunch. We'll take lunch. 12:57:05 16 THE WITNESS: Okay. 12:57:06 17 THE VIDEOTAPE OPERATOR: Off the record at 12:57:07 18 12:57 p.m. 12:57:08 19 (Luncheon recess was taken.) 12:57:09 20 THE VIDEOTAPE OPERATOR: Back on the record 13:39:41 21 beginning Media Unit 4 at 1:40 p.m. 13:39:42 22 BY MS. CORK: 13:39:47 23 Q. Mr. Klibanov, could you please go to paragraph 13:39:48 24 101 of your declaration, Exhibit 1. 13:39:51 25 A. Sure. Let me just read it to myself. Okay. 13:40:07 Page 109

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1 Q. It's your opinion that proteins can tolerate 13:40:45 2 minor substitutions at certain positions without any 13:40:48 3 changes to the protein structure and function, true? 13:40:51 4 MR. COBB: Objection. Form. 13:40:55 5 THE WITNESS: That's a conclusion that one 13:40:57 6 makes on the basis of the prior art, the prior -- part 13:40:59 7 being prior to the '681 Patent. 13:41:03 8 BY MS. CORK: 13:41:10 9 Q. Specifically, it's your opinion that changing 13:41:12 10 aflibercept's amino acid sequence would not change its 13:41:15 11 three-dimensional structure? 13:41:19 12 MR. COBB: Objection. Mischaracterizes the 13:41:20 13 testimony; form. 13:41:22 14 THE WITNESS: I would say that as of today, it 13:41:29 15 is certainly my opinion, and it would have been my 13:41:34 16 opinion as of January 13, 2011, yes. 13:41:39 17 BY MS. CORK: 13:41:46 18 Q. Would you please go to Exhibit 4, which is 13:41:50 19 Exhibit 2065 to your declaration, and let me know when 13:41:54 20 you have it. 13:41:59 21 A. Okay. I'm looking at Exhibit 4, which is the 13:42:05 22 biochemistry textbook by Jeremy Berg and others. 13:42:08 23 Q. Would you please go to the page that is Bates 13:42:13 24 stamped page 10 in the bottom left. 13:42:16 25 A. Okay. 13:42:29 Page 110	1 Q. The one that starts with "Moreover." 13:45:03 2 A. With what? 13:45:06 3 Q. "Moreover." 13:45:06 4 A. Just a second. Oh, yes. Yes. I see that. 13:45:09 5 Q. Exhibit 2065 to your declaration states: 13:45:13 6 "Moreover, proteins with novel properties can be 13:45:15 7 generated by varying the sequence of known proteins." 13:45:19 8 Do you see that? 13:45:23 9 A. I do see that, yes. 13:45:23 10 Q. Do you agree with that statement? 13:45:27 11 A. In general, again, in the context of teaching 13:45:32 12 biochemistry to undergraduate students, I agree with that 13:45:35 13 statement, yes. 13:45:38 14 Q. Do you see sentence that follows the one that I 13:45:39 15 just read? 13:45:42 16 A. The one that starts with "The second"? 13:45:42 17 Q. Yes. 13:45:48 18 A. I do see it, yes. 13:45:48 19 Q. Exhibit 2065 to your declaration states that 13:45:50 20 "amino acid sequences determine the three-dimensional 13:45:53 21 structures of proteins." 13:45:56 22 Do you see that? 13:45:58 23 A. I do see that, yes. 13:45:58 24 Q. Do you agree with that statement? 13:46:00 25 A. I do, yeah, in the context, again, of teaching 13:46:02 Page 112
1 Q. In the right half of the page, you see a 13:42:32 2 section that's with the header, 3.2.1, "Proteins have 13:42:35 3 unique amino acid sequences that are specified by genes"? 13:42:41 4 A. Yes, I see that. 13:42:47 5 Q. In the third full paragraph, under this header, 13:42:50 6 section, Exhibit 2065 states in the middle of the 13:42:54 7 paragraph: "Alterations in --" 13:43:11 8 A. Just a second. Let me just find it. Could you 13:43:14 9 identify -- oh, okay. "Alterations." I can see that. 13:43:16 10 Just a second. Let me just read this paragraph to myself 13:43:19 11 just to orient myself. Okay. 13:43:22 12 BY MS. CORK: 13:44:15 13 Q. In this paragraph, Exhibit 2065 to your 13:44:18 14 declaration states, "The proteins with novel properties 13:44:23 15 can be generated by varying the sequence of known 13:44:26 16 proteins." 13:44:29 17 Do you see that? 13:44:30 18 A. No, I don't see that. I thought that you 13:44:30 19 wanted to read the sentence that starts with 13:44:32 20 "Alterations." I mean, I -- I don't know where you're 13:44:35 21 reading. Oh, you're reading the last two -- the 13:44:41 22 penultimate sentence of that paragraph? 13:44:45 23 Q. Do you see the third sentence of this 13:44:50 24 paragraph? 13:44:52 25 A. The one that starts with "Second"? 13:45:00 Page 111	1 biochemistry to undergraduate students, and specifically 13:46:05 2 meaning that the amino acid sequence is an important 13:46:09 3 parameter in determining the three-dimensional structure 13:46:15 4 of proteins. It's not the sole important parameter, but 13:46:21 5 it is an important parameter, as I already testified, I 13:46:27 6 believe, before lunch. 13:46:31 7 Q. A few sentences down, do you see the sentence 13:46:36 8 beginning with the word "Alterations"? 13:46:39 9 A. Ma'am, I'm very sorry. You are obviously under 13:46:42 10 the weather, and I feel for you, I really do, but you 13:46:46 11 speak so softly that I can barely hear you. I know it 13:46:50 12 must be hard for you to speak loudly. But you'll have 13:46:54 13 to -- we'll just have work on it together. 13:46:56 14 Q. A few sentences down, do you see the sentence 13:46:58 15 beginning with the word, "Alterations"? 13:47:00 16 A. Yes, I do see it. 13:47:05 17 Q. Exhibit 2065 to your declaration states: 13:47:07 18 "Alterations in amino acid sequence can produce abnormal 13:47:08 19 function and disease. Severe and sometimes fatal 13:47:13 20 diseases, such as sickle cell anemia and cystic fibrosis, 13:47:18 21 can result from a change in a single amino acid within a 13:47:20 22 protein." 13:47:25 23 Do you see that? 13:47:27 24 A. I see those two sentences, yes. 13:47:27 25 Q. Do you agree with those statements? 13:47:29 Page 113

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1 A. I -- 13:47:31 2 MR. COBB: Objection. The document speaks for 13:47:32 3 itself; form. 13:47:33 4 THE WITNESS: I do agree with those statements 13:47:34 5 in the context of teaching biochemistry to undergraduate 13:47:35 6 students. In both of those sentences I specifically want 13:47:40 7 to invite your attention to the word "can." So 13:47:44 8 alterations in amino acid sequence can produce abnormal 13:47:48 9 function and disease, followed by severe and sometimes 13:47:53 10 fatal diseases; such as sickle cell anemia and cystic 13:47:58 11 fibrosis can result from a change in a single amino acid 13:48:03 12 within a protein. 13:48:08 13 It doesn't necessarily happen. It doesn't even 13:48:09 14 say that it often happens, which it doesn't. Okay? But, 13:48:12 15 yes, there is such a possibility. 13:48:16 16 BY MS. CORK: 13:48:19 17 Q. Would a person of ordinary skill in the art for 13:48:19 18 the '681 Patent be aware that even a single amino acid 13:48:21 19 change within a protein could produce abnormal protein 13:48:27 20 function? 13:48:30 21 MR. COBB: Objection. Form. 13:48:32 22 THE WITNESS: With the word "can" being the key 13:48:35 23 word there, and this person, by definition, would also be 13:48:36 24 familiar with all the other prior art literature, 13:48:42 25 relevant prior art publicly-available literature, and 13:48:46 Page 114	1 structure, you cite to a paper by Mihailescu. 13:51:53 2 Do you see that? 13:51:58 3 A. I cite to the paper by Mihailescu, and I also 13:51:58 4 cite to the very same textbook that we discussed 13:52:03 5 previously, which is the Berg biochemistry textbook, 13:52:07 6 which is Klibanov Exhibit 4. 13:52:11 7 Q. And you cite to Klibanov Exhibit 4 for its 13:52:13 8 discussion of lactoferrin; is that correct? 13:52:16 9 A. No. I discuss it in the context of talking 13:52:34 10 about hemoglobin. It's in -- right before paragraph 74, 13:52:50 11 it says Exhibit 2077, which according to the footnote is 13:52:56 12 an excerpt from the Berg biochemistry textbook, which is 13:53:00 13 Klibanov Exhibit 4. 13:53:04 14 Q. I'd just like to note for the record that you 13:53:16 15 were citing to Exhibit 2077, whereas Klibanov Exhibit 4 13:53:18 16 is Exhibit 2065 to your declaration. 13:53:23 17 A. So, then, it may be a typo. I -- I don't know. 13:53:28 18 I'm just reading what it says here. "Here" being on 13:53:31 19 page 34 of my '681 declaration. 13:53:38 20 Q. I just want the record to be clear that you are 13:53:42 21 pointing to an exhibit, Exhibit 2077, which is not the 13:53:44 22 same exhibit that we marked as Klibanov Exhibit 4. 13:53:48 23 A. Just a second. Well, Klibanov Exhibit 4, which 13:54:02 24 is Exhibit 2065, is not the entire biochemistry textbook. 13:54:05 25 It is a certain chapter in the Berg biochemistry 13:54:09 Page 116
1 therefore will know that, yes, it can happen, although in 13:48:50 2 reality it's actually quite rare. But in any event, even 13:48:53 3 literally, the word "can" in both sentences is highly 13:48:58 4 appropriate. 13:49:05 5 BY MS. CORK: 13:49:07 6 Q. So a person of skill in the art for the '681 13:49:10 7 Patent would recognize that changing a single amino acid 13:49:13 8 in aflibercept could also change its structure? 13:49:18 9 MR. COBB: Objection. Form. 13:49:22 10 THE WITNESS: Certainly not -- well, I mean, if 13:49:26 11 we talk about the primary structure, by definition it 13:49:28 12 will change its primary structure. If you are talking 13:49:32 13 about other levels, subsequent, higher levels of 13:49:34 14 structures, I mean, it's a -- it's a possibility. It 13:49:39 15 doesn't necessarily happen. And that's what I understand 13:49:42 16 is critical in the case. Does it necessarily happen? 13:49:46 17 And the answer is, absolutely not. 13:49:50 18 BY MS. CORK: 13:49:53 19 Q. I'll direct you to paragraph 73 of your 13:50:20 20 declaration. Please let me know when you get there. 13:50:22 21 A. Sure. I got there, and let me just read it to 13:50:30 22 myself. Yes, ma'am. 13:50:38 23 Q. As support for your position that a protein's 13:51:41 24 amino acid sequence does not necessarily drive or 13:51:45 25 unambiguously define the protein's three-dimensional 13:51:49 Page 115	1 textbook. So it may be that Exhibit 2077 is a different 13:54:12 2 chapter in the Berg biochemistry textbook. But it's 13:54:17 3 still a reference to the same textbook. 13:54:22 4 And the significance of that is that surely one 13:54:27 5 of skill in the art that you kept asking me about surely 13:54:31 6 would have at least read this biochemistry textbook. 13:54:35 7 Q. So, again, to make sure that the record is 13:54:39 8 clear, Klibanov Exhibit 4 is the fifth edition of the 13:54:41 9 biochemistry textbook as shown on the first page? Would 13:54:46 10 you agree with that? 13:54:50 11 A. No, it's not -- it's a fifth edition, but it's 13:54:51 12 a -- a -- a certain chapter from this textbook. I mean, 13:54:55 13 Klibanov Exhibit 4, which is Exhibit 2065, undeniably, is 13:54:59 14 not the entirety of the biochemistry textbook. 13:55:05 15 And, yes, what is -- Exhibit 2077 is the next 13:55:11 16 edition, the sixth edition of the biochemistry textbook, 13:55:17 17 which was published in 2007, which, of course, is also a 13:55:22 18 prior art vis-a-vis the priority date of the '681 Patent. 13:55:26 19 Q. I'm just trying to be very clear here that 13:55:35 20 Klibanov Exhibit 4, which is Exhibit 2065 to your 13:55:38 21 declaration, is not from the same source as Exhibit 2077, 13:55:41 22 because that -- 2077 comes from the later edition of that 13:55:50 23 textbook. Would you agree? 13:55:54 24 A. Yeah, I mean, you -- your voice sadly kind of 13:55:56 25 died off in the middle of the question. So, I mean, I 13:55:59 Page 117

1 may have missed some words there. 13:56:04	1 secondary structure that they have in common. I, you 13:59:40
2 But, you know, I just said that it's a 13:56:05	2 know, have not compared them. I'm just here illustrating 13:59:46
3 different edition of biochemistry -- of the biochemistry 13:56:09	3 the basic principle of protein chemistry and biochemistry 13:59:49
4 textbook by Berg and others, but the fact of the matter 13:56:13	4 that a person of ordinary skill in the art certainly 13:59:54
5 is that both of them are prior art with respect to the 13:56:17	5 wouldn't turn a blind eye to. 13:59:57
6 '681 Patent. So I think the record is quite clear on 13:56:21	6 Q. Sitting here today, you're not able to identify 14:00:06
7 that. 13:56:24	7 any aspects of molecular structure that hemoglobin and 14:00:09
8 MS. CORK: I'd like to mark as Exhibit 15 an 13:56:47	8 aflibercept have in common; is that correct? 14:00:14
9 article titled, "A Signature of the T to R transition in 13:56:50	9 A. That's not correct. I'm sure there are some 14:00:19
10 human hemoglobin," designated Exhibit 2069, with a copy 13:56:54	10 overlap in the -- I mean, they obviously consist of the 14:00:26
11 to counsel. 13:57:13	11 same, very same 20 amino acid residues. There is no 14:00:29
12 (Exhibit 15 was marked for identification.) 13:57:14	12 question about that. So that's a great similarity right 14:00:35
13 THE REPORTER: Exhibit 15. 13:57:15	13 there. 14:00:37
14 THE WITNESS: Thank you. 13:57:16	14 And furthermore, it very well may be, I just 14:00:38
15 BY MS. CORK: 13:57:16	15 haven't looked into it, because it wasn't relevant to my 14:00:42
16 Q. Dr. Klibanov, do you recognize Exhibit 15 as 13:57:17	16 discussion, that they have the same amino acid residues 14:00:46
17 the Mihailescu publication cited in paragraph 73 of your 13:57:19	17 in -- some of the same amino acid residues in some of the 14:00:49
18 declaration? 13:57:25	18 same positions. You know, and the only point I'm making 14:00:56
19 A. And paragraph 74 of my declaration, yes. 13:57:26	19 here is that the POSA wouldn't kind of, you know, turn a 14:00:59
20 Q. You cite Mihailescu, Exhibit 16 -- 13:57:32	20 blind eye to the fact that there are some basic 14:01:04
21 MR. COBB: Exhibit 15? 13:57:51	21 principles of protein chemistry and biochemistry that are 14:01:06
22 BY MS. CORK: 13:57:52	22 applicable both to hemoglobin and to aflibercept and to 14:01:11
23 Q. So the record is clear, we're looking at 13:57:52	23 other proteins. 14:01:16
24 Exhibit 15, which is the Mihailescu article, Exhibit 2069 13:57:55	24 Q. How is hemoglobin's ability to bind oxygen 14:01:18
25 to your declaration? 13:58:01	25 relevant to any aspect of aflibercept's structure? 14:01:22
Page 118	Page 120
1 A. That's what I'm looking at, yes. 13:58:03	1 A. Aflibercept binds certain ligands and 14:01:31
2 Q. In paragraph 73 of your declaration, you cite 13:58:06	2 hemoglobin binds certain ligands. So the ability to bind 14:01:36
3 to Mihailescu for the proposition that: "Human 13:58:13	3 ligands is a common feature of these two distinct 14:01:40
4 hemoglobin from red blood cells is known to be able to 13:58:17	4 proteins, and of many others. 14:01:45
5 adopt at least two different three-dimensional shapes 13:58:21	5 Q. When aflibercept binds VEGF, does that binding 14:01:48
6 depending on the 'energetic state of the molecule.'" 13:58:24	6 change aflibercept's structure? 14:01:56
7 Do you agree? 13:58:29	7 MR. COBB: Objection. Vague; form. 14:01:58
8 A. Yes, you skipped the fact that it is human red 13:58:30	8 THE WITNESS: It has to. 14:02:01
9 blood cells, but, yes. 13:58:33	9 BY MS. CORK: 14:02:05
10 Q. Hemoglobin binds oxygen? 13:58:39	10 Q. How do you know? 14:02:05
11 A. It does, among other things. 13:58:42	11 A. Well, because the structure is determined by a 14:02:06
12 Q. In your declaration, you discuss hemoglobin for 13:58:45	12 sum of all known covalent interactions that lead to it. 14:02:09
13 the principle that binding oxygen changes hemoglobin 13:58:48	13 And when -- so when any ligand binds to a protein, the 14:02:18
14 structure? 13:58:53	14 structure of the protein will change. This change may be 14:02:31
15 A. Changes the tertiary structure of hemoglobin. 13:58:55	15 a large change, may be a small change, but the structure 14:02:36
16 Obviously, it doesn't change the primary structure. The 13:59:03	16 has to change. 14:02:40
17 primary structure remains exactly the same, which, of 13:59:06	17 Q. Do you discuss in your declaration the binding 14:02:44
18 course, is the essence of the argument that I advance in 13:59:10	18 of aflibercept to VEGF and how that affects aflibercept's 14:02:48
19 paragraph 73. 13:59:13	19 structure? 14:02:57
20 Q. Does aflibercept bind oxygen? 13:59:15	20 A. My declaration speaks for itself. I certainly 14:02:58
21 A. It's possible. I don't know. 13:59:21	21 do discuss that aflibercept binds -- that aflibercept, 14:03:01
22 Q. Do hemoglobin and aflibercept have the same 13:59:28	22 you know, can bind sort of ligands, including VEGF, so I 14:03:11
23 structure in any respects? 13:59:30	23 certainly talk about it. I don't think I specifically 14:03:19
24 A. I mean, there may be some fragments of the 13:59:34	24 discuss structural changes, specific structural changes, 14:03:21
25 primary structure, there may be some fragments of the 13:59:36	25 but as I said, the structure will have to change. 14:03:26
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1 Q. When aflibercept binds VEGF, is it still 14:03:30 2 considered aflibercept? 14:03:35 3 MR. COBB: Objection. Form. 14:03:37 4 THE WITNESS: Well, I don't know what the word 14:03:47 5 "it" means there, but when aflibercept binds -- when 14:03:49 6 aflibercept binds to VEGF, it becomes a complex -- I'm 14:03:54 7 sorry, a non-covalent complex of aflibercept and VEGF. 14:04:00 8 BY MS. CORK: 14:04:08 9 Q. So in that complex of aflibercept and VEGF, the 14:04:09 10 protein aflibercept still exists. 14:04:15 11 A. It exists in a somewhat altered 14:04:19 12 three-dimensional configuration. So the 14:04:22 13 three-dimensional structure is somewhat altered. But, 14:04:26 14 yes, the -- the primary structure, the amino acid 14:04:30 15 sequence still exists. 14:04:35 16 Q. And because the primary structure still exists, 14:04:41 17 aflibercept still exists even though it's in a complex? 14:04:46 18 MR. COBB: Objection. Form. 14:04:50 19 THE WITNESS: It depends how you define 14:04:52 20 "aflibercept." The -- the primary structure of 14:04:53 21 aflibercept exists. The three-dimensional structure has 14:04:57 22 been altered. I don't know how significantly. 14:05:04 23 So, you know, it depends on what exactly you 14:05:09 24 mean by your question. 14:05:12 25 // Page 122	1 perhaps I misunderstood your question. 14:06:47 2 So I can say once again, the primary structure 14:06:49 3 of the amino acid sequence of aflibercept will still 14:06:55 4 exist. The three-dimensional structure of aflibercept 14:06:57 5 will be somewhat altered. So when you say "aflibercept," 14:07:03 6 I don't know whether you're referring to the primary 14:07:08 7 structure or you're referring to the tertiary structure. 14:07:10 8 I don't want to play word games, madam, but, I 14:07:15 9 just want to make sure I understand your question. 14:07:19 10 Q. What is aflibercept? 14:07:25 11 A. Aflibercept is a protein. 14:07:29 12 Q. Does that protein still exist when it is bound 14:07:34 13 to VEGF? 14:07:43 14 A. You are asking me the same question, but in 14:07:46 15 disguise. All right? As I already told you, the primary 14:07:49 16 structure of that same protein will exist. The tertiary 14:07:52 17 structure, for example, of that protein will no longer 14:07:56 18 exist. It will be replaced by a slightly altered 14:08:00 19 structure form due to the formation of a complex with 14:08:04 20 VEGF. 14:08:10 21 Q. How would you know if any particular protein 14:08:34 22 was aflibercept? 14:08:37 23 A. I would need to know what particular aspect of, 14:08:42 24 quote/unquote, "aflibercept" is being discussed. If 14:08:45 25 what's being discussed is the primary structure, then I 14:08:52 Page 124
1 BY MS. CORK: 14:05:13 2 Q. Is it your opinion that when aflibercept binds 14:05:22 3 VEGF, the three-dimensional structure of aflibercept no 14:05:26 4 longer exists? 14:05:32 5 MR. COBB: Objection. Form. 14:05:33 6 THE WITNESS: The exact structure that existed 14:05:36 7 prior to the formation of the complex will no longer 14:05:40 8 exist. It will be replaced by a somewhat modified 14:05:44 9 three-dimensional structure, which may greatly differ or 14:05:49 10 only slightly differ from the prior structure that 14:05:55 11 existed before the complex formation. 14:05:59 12 BY MS. CORK: 14:06:05 13 Q. In your opinion, does aflibercept still exist 14:06:09 14 when aflibercept binds to VEGF? 14:06:14 15 A. What do you mean when you say "aflibercept"? 14:06:18 16 What do you mean by that? 14:06:20 17 Q. I'm asking you, Doctor. 14:06:21 18 A. But I'm asking you, because I want to make sure 14:06:24 19 I understand what you mean by the question. You told me 14:06:26 20 in the beginning, if I don't understand your question, I 14:06:29 21 should tell you, I don't understand it. I don't 14:06:31 22 understand what you mean by "aflibercept." 14:06:33 23 You asked me the very same question a moment 14:06:36 24 ago. I already answered it. You found it necessary to 14:06:39 25 ask this question again, which suggests to me that 14:06:42 Page 123	1 would just compare the amino acid sequence. 14:08:55 2 If what's being discussed is, for instance, the 14:09:00 3 secondary or tertiary structure, I would need to compare 14:09:04 4 those. 14:09:08 5 Q. When aflibercept binds VEGF, that doesn't 14:09:24 6 change its primary amino acid sequence in any way that 14:09:28 7 you're aware of, does it? 14:09:31 8 A. As I said on at least half a dozen occasions 14:09:33 9 previously. 14:09:38 10 Q. Does Exhibit 15, the Mihailescu reference, 14:09:48 11 discuss angiogenic eye disorders? 14:09:54 12 A. I'm sorry, discuss what? 14:09:56 13 Q. Angiogenic eye disorders? 14:09:58 14 A. You know very well that it does not. It 14:10:01 15 specifically refers to human hemoglobin. 14:10:06 16 Q. So Exhibit 15 does not discuss diagnosing or 14:10:09 17 treating angiogenic eye disorders. 14:10:13 18 A. That's correct. Exhibit 15 is a paper dealing 14:10:18 19 with hemoglobin -- with hemoglobin, which teaches or 14:10:23 20 discloses one of the fundamental principles of protein 14:10:29 21 chemistry and biochemistry, namely that you can have more 14:10:35 22 than one three-dimensional structure of a protein, while 14:10:41 23 the primary structure with the amino acid sequence 14:10:49 24 remains the same. 14:10:53 25 Q. Does Exhibit 15 mention aflibercept or a VEGF 14:10:55 Page 125

1 Trap-Eye? 14:11:00	1 lactoferrin to illustrate the basic principle -- one of 14:15:24
2 A. No. It specifically talks about human 14:11:03	2 the basic principles of protein chemistry and 14:15:29
3 hemoglobin; although I don't remember every word that it 14:11:08	3 biochemistry that you can have a given amino acid 14:15:32
4 uses, this article, I would be very surprised if it 14:11:13	4 sequence, exactly the same, I mean, as a sequence, and 14:15:38
5 mentioned, for example, aflibercept. 14:11:16	5 yet it will give rise to more than one tertiary structure 14:15:43
6 As I said, the point of this paper and the 14:11:19	6 of a protein. 14:15:48
7 reason why I cited this paper in my declaration is to 14:11:21	7 Q. Could you please go to paragraph 65 of your 14:15:52
8 illustrate one of the fundamental principles of protein 14:11:27	8 declaration, and let me know when -- 14:15:57
9 chemistry; namely that you can have more than one 14:11:32	9 A. Paragraph what? 14:15:58
10 three-dimensional structure of a protein while the 14:11:42	10 Q. 65 of your declaration, and please let me know 14:15:59
11 protein retains exactly the same amino acid sequence or 14:11:45	11 when you've had a chance to look at it. 14:16:02
12 exactly the same primary structure. 14:11:49	12 A. It's a long paragraph. So let me just review 14:16:09
13 Q. Is Exhibit 15 relevant to the development of 14:11:54	13 it to myself. Yes, ma'am. 14:16:11
14 anti-angiogenic therapeutics? 14:11:57	14 Q. Paragraph 65 of your declaration begins, 14:18:02
15 MR. COBB: Objection. Scope. 14:12:06	15 "Indeed, as of the priority date" -- 14:18:04
16 THE WITNESS: I think it is relevant to the 14:12:06	16 A. Just a second. Yes, yes, please continue. 14:18:07
17 extent that the development of anti-angiogenic 14:12:08	17 Q. Paragraph 65 of your declaration begins, 14:18:11
18 therapeutics relies on basic principles of protein 14:12:11	18 "Indeed, as of the priority date, the term 'molecular 14:18:13
19 chemistry and biochemistry. 14:12:15	19 structure' was often used in the protein literature to 14:18:19
20 BY MS. CORK: 14:12:17	20 refer to the three-dimensional structure of the protein 14:18:22
21 Q. Could you please look at paragraph 75 of your 14:12:41	21 molecule rather than its amino acid sequence." 14:18:25
22 declaration. 14:12:44	22 Do you see that? 14:18:34
23 A. Sure. Let me read it to myself. Yes, ma'am. 14:12:45	23 A. I do see that. You neglected to mention 14:18:35
24 Q. You say that lactoferrin can adopt two 14:13:18	24 quotation marks around the phrase "molecular structure." 14:18:38
25 different three-dimensional structures without any 14:13:23	25 But I do see that. 14:18:43
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1 changes to the underlying amino acid sequence. 14:13:26	1 Q. After this sentence, there is a series of 14:18:45
2 Do you see that? 14:13:30	2 citations to scientific literature references, true? 14:18:50
3 A. I do see that. So, for the record, you chose 14:13:31	3 A. Yes. Several examples of scientific citations 14:18:58
4 to read a fraction of a second sentence in that 14:13:33	4 that support the point made in the first sentence of 14:19:02
5 paragraph. 14:13:38	5 paragraph 65 of my '681 Patent declaration. 14:19:09
6 Q. Lactoferrin binds iron? 14:13:47	6 MS. CORK: I'd like to mark as Exhibit 16 an 14:19:31
7 A. It can bind iron ions, yes. 14:13:50	7 article titled, "The molecular structure of spider 14:19:34
8 Q. And are you relying on lactoferrin in your 14:13:55	8 dragline silk: Folding and orientation of the protein 14:19:38
9 declaration for the principle that binding iron can 14:13:58	9 backbone," designated Exhibit 2070. A copy to counsel. 14:19:43
10 change the three-dimensional structure of lactoferrin? 14:14:01	10 (Exhibit 16 was marked for identification.) 14:19:46
11 A. No. I'm relying on the principle that you can 14:14:06	11 THE REPORTER: Exhibit 16. 14:20:01
12 have more than one tertiary structure of a protein, which 14:14:09	12 THE WITNESS: Thank you. Just a second, 14:20:02
13 would correspond to exactly the same primary structure, 14:14:18	13 please. Okay. 14:20:04
14 meaning to exactly the same amino acid sequence. 14:14:22	14 MS. CORK: I'd like to mark as Exhibit 17 an 14:20:12
15 Q. Do lactoferrin and aflibercept have the same 14:14:32	15 article titled, "Relationship of protein molecular 14:20:16
16 molecular structure in any respect? 14:14:35	16 structure to metabolisable proteins in different types of 14:20:19
17 A. I don't know. I have not compared their 14:14:44	17 dried distillers grains with solubles: a novel approach," 14:20:25
18 molecular structures, not to mention that molecular 14:14:45	18 designated Exhibit 2072, with a copy to counsel. 14:20:29
19 structure, as you know full well from my declaration, you 14:14:48	19 (Exhibit 17 was marked for identification.) 14:20:33
20 know, that it may refer to sort of -- to different levels 14:14:56	20 THE REPORTER: Exhibit 17. 14:20:51
21 of structure. It may refer to the primary structure, 14:14:59	21 THE WITNESS: Thank you. 14:20:53
22 secondary structure, tertiary structure, domain 14:15:05	22 MS. CORK: I'd like to mark as Exhibit 18 an 14:20:55
23 structure, quaternary structure, but not necessarily to 14:15:13	23 article titled, "Molecular Dynamics Study of Onset of 14:20:58
24 just one of those. 14:15:17	24 Water Gelation around the Collagen Triple Helix," 14:21:02
25 But as I said, I'm relying -- excuse me -- on 14:15:19	25 designated Exhibit 2071, with a copy to counsel. 14:21:07
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1 (Exhibit 18 was marked for identification.) 14:21:12	1 each other into a linear chain. 14:25:26
2 THE REPORTER: Exhibit 18. 14:21:26	2 Q. And if we could please go to the fifth page of 14:25:30
3 THE WITNESS: Thank you. 14:21:26	3 Exhibit 16, which has Figure 5 on it. 14:25:33
4 MS. CORK: I'd like to mark as Exhibit 19 an 14:21:41	4 Do you see that? 14:25:45
5 article titled, "The Folding of Spectrin Domains I: 14:21:43	5 A. Yes, ma'am. 14:25:49
6 Wild-type Domains Have the Same Stability, but very 14:21:47	6 Q. In the legend for Figure 5, Exhibit 16 states: 14:25:53
7 Different Kinetic Properties," designated Exhibit 2073, 14:21:50	7 "A proposed model for spider dragline silk... the 14:25:57
8 with a copy to counsel. 14:21:56	8 molecular structure consists of beta sheet --" 14:26:07
9 (Exhibit 19 was marked for identification.) 14:21:57	9 A. I'm sorry, ma'am. Are you -- are you reading 14:26:10
10 THE REPORTER: Exhibit 19. 14:21:57	10 the first sentence? 14:26:12
11 THE WITNESS: Thank you. 14:22:21	11 Q. I'm reading the second sentence. 14:26:13
12 BY MS. CORK: 14:22:22	12 A. Okay. It would be helpful for you to tell me 14:26:14
13 Q. Dr. Klibanov, do you recognize Exhibits 16 14:22:22	13 which sentence you are going to read. Okay. Please. 14:26:17
14 through 19? 14:22:27	14 Q. In the second sentence of Figure 5's legend, 14:26:21
15 A. Well, if by "do you recognize" you mean whether 14:22:28	15 Exhibit 16 states that: "The molecular structure 14:26:24
16 these are some of the exhibits that I cite on pages -- on 14:22:31	16 consists of beta sheet regions containing alanine (red 14:26:27
17 page -- pages 29 and 30 of my '681 Patent declaration, 14:22:38	17 lines) and glycine (blue lines) interleaved with 14:26:32
18 then the answer to your question is, yes. 14:22:48	18 predominantly 3 sub one helical parts (blue curls), which 14:26:36
19 Q. Exhibits 16 through 19 are analyzed in 14:22:52	19 do not contain alanine." 14:26:39
20 paragraph 65 of your declaration, is what you are saying? 14:22:58	20 Do you see that? 14:26:44
21 A. I wasn't saying that. But they are briefly 14:23:05	21 A. I do. 14:26:44
22 analyzed in that paragraph, paragraph 65. Correct. 14:23:11	22 Q. Could I ask you to look back at paragraph 65 of 14:26:48
23 Q. Could you please look at Exhibit 16. 14:23:21	23 your declaration. 14:26:52
24 A. Yes. 14:23:33	24 A. Any particular portion of it? 14:26:55
25 Q. Exhibit 16 relates to the molecular structure 14:23:34	25 Q. Yes, the portion where you cite to Exhibit 2070 14:26:57
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1 of spider dragline silk? 14:23:36	1 to your declaration, which is Exhibit 16 here. 14:27:00
2 A. That's a portion of the title of this article. 14:23:40	2 A. Just a second. Okay. 14:27:03
3 Q. In the left column of the first page of 14:23:52	3 Q. In your declaration, you quote the portion of 14:27:23
4 Exhibit 2070 to your declaration, Exhibit 16 here, do you 14:23:55	4 the legend to Figure 5 that I just read in part. 14:27:26
5 see the second full paragraph of the introduction? 14:24:02	5 Do you see that? 14:27:32
6 A. Are you referring to the sentence that -- I 14:24:11	6 A. Yes. 14:27:33
7 mean, I see the paragraph. Are you referring 14:24:13	7 Q. Do you see ellipses indicating where you 14:27:35
8 specifically to the first sentence? 14:24:16	8 omitted certain parts of Exhibit 16? 14:27:38
9 Q. Let's look at the third sentence beginning 14:24:22	9 A. Do I see what? 14:27:43
10 with, "Spider dragline silk." 14:24:25	10 Q. Ellipses, three dots? 14:27:45
11 Do you see that? 14:24:28	11 A. Oh, okay. Yeah. Yes, I do see it. Yes. 14:27:47
12 A. Yes. 14:24:34	12 Q. You omitted references to amino acids when you 14:27:54
13 Q. The sentence begins, "Spider dragline silk is 14:24:38	13 quoted from Exhibit 16 in your declaration, true? 14:27:59
14 thought to be composed mainly of two proteins, Spidroin I 14:24:42	14 A. Just a second. Let me -- yeah. I mean, I 14:28:07
15 and II," and then the reference goes on to say that, 14:24:46	15 obviously specifically indicated that that's what I'm 14:28:18
16 "These proteins can be described, in a simplified 14:24:50	16 doing, and I specifically said where this particular 14:28:22
17 picture, as black copolymers with poly-Ala blocks 14:24:53	17 quote is found. So, I mean, anybody who is interested in 14:28:26
18 (consisting of approximately eight monomers) and of 14:24:57	18 seeing it clearly has every opportunity to immediately 14:28:31
19 glycine-rich domains, with (GLY-GLY-X) as most abundant 14:25:01	19 see it. 14:28:34
20 motive in Spidroin I." 14:25:04	20 Q. Why do you omit the references to amino acids 14:28:36
21 Do you see that? 14:25:07	21 in describing the molecular structure of spider silk 14:28:41
22 A. I do. 14:25:08	22 protein? 14:28:45
23 Q. Poly-Ala here means polyamine, meaning multiple 14:25:08	23 A. Because the point of the entire paragraph, 14:28:52
24 alanine residues? 14:25:16	24 number 65 of my '685 Patent declaration in this case, was 14:28:55
25 A. Multiple alanine revenues covalently bonded to 14:25:20	25 to indicate that contrary to Dr. Chaum's assertions, the 14:29:05
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1 term "molecular structure" in the prior art literature, 14:29:13 2 prior art with respect to the '681 Patent, was routinely 14:29:19 3 and repeatedly used; not with respect to the primary 14:29:24 4 structure, as he had indicated as sort of a necessity, 14:29:29 5 but, in fact, this term, quote/unquote, "molecular 14:29:40 6 structure," was used to specifically refer to higher 14:29:43 7 levels of structure, such as secondary structure, in this 14:29:48 8 particular case, in the case of Klibanov Exhibit 16; or 14:29:53 9 tertiary structure, which is what I illustrate in other 14:30:03 10 prior art references listed in paragraph 65. 14:30:09 11 Q. In fact, the part of Exhibit 16 that you quote 14:30:16 12 does refer to amino acids. You just chose to omit those 14:30:20 13 amino acids from your quotation in your declaration, 14:30:25 14 true? 14:30:30 15 MR. COBB: Objection. Form. 14:30:31 16 THE WITNESS: No. It doesn't refer to amino 14:30:34 17 acids. It refers to beta sheet regions. That's what it 14:30:37 18 refers to. And then it says in the part that's omitted 14:30:42 19 what those regions consist of. 14:30:49 20 But the reference -- the molecular structure is 14:30:53 21 a reference to the beta sheet regions. 14:30:55 22 BY MS. CORK: 14:31:06 23 Q. And those beta sheet regions, as described in 14:31:06 24 Exhibit 16, consist of alanine and glycine, which are 14:31:08 25 amino acids, true? 14:31:13 Page 134	1 THE WITNESS: Independent of what? 14:32:55 2 BY MS. CORK: 14:32:57 3 Q. Independent of context. 14:32:58 4 A. Yeah, it's one of those many things in science 14:33:04 5 that is context-dependent. In one context it could mean 14:33:06 6 a tertiary structure. In another context it could mean a 14:33:13 7 domain structure. The important point being that it does 14:33:19 8 not necessarily refer to the primary structure, as 14:33:23 9 Dr. Chaum opined. 14:33:26 10 Q. Do spider silk protein and aflibercept have the 14:33:40 11 same molecular structure under any definition of that 14:33:43 12 term? 14:33:47 13 A. They may have some of the same elements of the 14:33:51 14 secondary structure, like, for example, they may have 14:33:56 15 beta sheets, both -- well, the spider cell protein 14:33:59 16 certainly does. Aflibercept may as well. 14:34:07 17 They may have alpha helices. In fact, again, 14:34:10 18 the spider protein certainly does. And aflibercept, I 14:34:14 19 think, does as well. 14:34:18 20 So they have some of the same elements of 14:34:20 21 the -- of the higher levels of structure, of protein 14:34:23 22 structure. 14:34:30 23 Q. Do you know whether aflibercept has alpha 14:34:51 24 helices or beta sheets? 14:34:55 25 A. I don't specifically recall. I would be 14:35:01 Page 136
1 A. Well, to be exact, they consist of amino acid 14:31:14 2 residues, not amino acids, to be accurate. 14:31:18 3 But the point here is that the term "molecular 14:31:26 4 structure" refers to beta sheet regions, whatever they 14:31:30 5 consist of. So it's a reference to the secondary 14:31:35 6 structure, not to the primary structure, which is what 14:31:38 7 Dr. Chaum opined the term "molecular structure" would 14:31:45 8 have to be. 14:31:51 9 Q. Do spider silk protein and aflibercept have the 14:31:58 10 same molecular structure in any respect? 14:32:03 11 A. What do you mean by "molecular structure"? I'm 14:32:08 12 just clarifying your question as you instructed me to do 14:32:10 13 in the beginning of this deposition. 14:32:14 14 Q. You offer multiple opinions regarding molecular 14:32:15 15 structure in your declaration, sir; isn't that true? 14:32:27 16 A. It certainly is. 14:32:30 17 Q. Do you have an understanding of what "molecular 14:32:31 18 structure" means? 14:32:32 19 A. My understanding is that the term "molecular 14:32:36 20 structure" can mean different things depending on the 14:32:39 21 context in which it appears. 14:32:43 22 Q. So the term "molecular structure" has no 14:32:48 23 independent meaning? 14:32:51 24 MR. COBB: Objection. Misstates his testimony; 14:32:53 25 form. 14:32:55 Page 135	1 shocked if aflibercept had no alpha helices and/or beta 14:35:06 2 sheets. I mean, again, it's not relevant to what I'm 14:35:12 3 discussing in paragraph 65, but that's my testimony. 14:35:17 4 Q. Does Exhibit 16 discuss angiogenic eye 14:35:24 5 disorders? 14:35:28 6 A. I don't think it does, but if it's important 14:35:33 7 for you to get an accurate answer to this question, I 14:35:35 8 would need to re-review Exhibit 16 with that particular 14:35:38 9 question in mind. 14:35:43 10 Q. To your knowledge, does Exhibit 16 discuss 14:35:46 11 aflibercept or VEGF Trap-Eye or any anti-angiogenic 14:35:51 12 therapeutic whatsoever? 14:35:55 13 A. Again, I don't think it does, but if it's 14:35:58 14 important for you to get a firm answer to this question, 14:36:03 15 I would need to re-review Exhibit 16 with this particular 14:36:07 16 question in mind. And just to reiterate that that's not 14:36:12 17 why Exhibit 16 is cited in my declaration. It is cited 14:36:17 18 to illustrate and repeatedly illustrate some basic 14:36:25 19 principles of protein chemistry and biochemistry that 14:36:29 20 fully apply to aflibercept, as well as other proteins. 14:36:34 21 Q. Is Exhibit 16 relevant to the development of 14:36:40 22 anti-angiogenic therapeutics? 14:36:44 23 A. I think it is to the extent that protein 14:36:49 24 chemistry and biochemistry is relevant to the development 14:36:53 25 of such therapeutics. 14:36:58 Page 137

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1 Q. The structure of spider silk protein is 14:37:02	1 A. I would say that to the extent that Exhibit 17 14:42:12
2 relevant to the development of anti-angiogenic 14:37:04	2 illustrates a principle of protein chemistry and 14:42:16
3 therapeutics? 14:37:06	3 biochemistry, namely that molecular -- the term 14:42:21
4 A. The basic principles of protein chemistry and 14:37:09	4 "molecular structure," two words, can refer to structures 14:42:26
5 biochemistry, as illustrated by example 16 as well as 14:37:13	5 other than the primary structure, or the amino acid 14:42:35
6 many others, or that I cite as representative examples, 14:37:19	6 sequence, the answer would have to be yes; because the 14:42:41
7 are relevant to the development of protein-based 14:37:25	7 development of protein-based therapeutics is based on 14:42:48
8 therapeutics. 14:37:28	8 fundamental principles of protein chemistry and 14:42:51
9 Q. Can you please turn to Exhibit 17. 14:37:53	9 biochemistry. 14:42:56
10 A. Yes, ma'am. I'm looking at it. 14:37:55	10 Bless you. 14:43:05
11 Q. Would you agree that Exhibit 17 relates to the 14:37:57	11 Q. Thank you. 14:43:06
12 structure of proteins from different types of dried 14:38:01	12 A. And just for the record, the "Bless you" was 14:43:06
13 distillers grains? 14:38:06	13 stated by me in response to a sneeze by Ms. Cork. 14:43:09
14 A. The title of Exhibit 17 is, "Relationship of 14:38:10	14 Q. May I ask you to turn to Exhibit 18, please. 14:43:28
15 protein molecular structure to metabolisable proteins in 14:38:13	15 A. Okay. I'm looking at it. 14:43:36
16 different types of dried distillers grains with solubles: 14:38:13	16 Q. Exhibit 18 relates to a collagen triple helix 14:43:44
17 a novel approach." 14:38:13	17 peptide? 14:43:50
18 Q. What types of proteins are described in 14:38:36	18 A. The title of Exhibit 18 is, "Molecular Dynamic 14:43:53
19 Exhibit 17? 14:38:39	19 Study of Onset of Water Gelation Around the Collagen 14:43:57
20 A. Proteins present in distillers grains. 14:38:42	20 Triple Helix." 14:44:05
21 Q. Distillers grains like wheat and maize, which 14:38:49	21 Q. Does aflibercept have a collagen-like triple 14:44:11
22 is corn? 14:38:53	22 helix? 14:44:15
23 A. It could be. 14:38:56	23 A. I don't think so, but it -- but aflibercept 14:44:20
24 Q. Grains are plants? 14:38:59	24 follows the same basic principles of protein chemistry 14:44:28
25 A. Grains are plants, correct. 14:39:03	25 and biochemistry as collagen's triple helix. 14:44:33
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1 Q. Do any of the proteins in Exhibit 17 from 14:39:07	1 Q. What do you mean by "aflibercept follows the 14:44:40
2 distillers grains have the same molecular structure as 14:39:12	2 same basic principles of protein chemistry and 14:44:48
3 aflibercept in any respect? 14:39:15	3 biochemistry as collagen's triple helix"? 14:44:48
4 A. Since you included the phrase "in any respect" 14:39:23	4 A. What I mean by that is that fundamental 14:44:57
5 in your question, I would say that, yes, they also have 14:39:37	5 principles of protein chemistry and biochemistry apply to 14:45:01
6 beta sheets and alpha helices. And as I testified a 14:39:42	6 aflibercept and collagens triple helix and hemoglobin and 14:45:06
7 little earlier, I'm pretty sure that aflibercept has some 14:39:51	7 ferritin, and all the other proteins, including those 14:45:14
8 of these secondary structure elements of proteins as 14:39:58	8 that I -- those prior art references that I discussed in 14:45:20
9 well. 14:40:03	9 paragraph 65 of my '681 Patent declaration. 14:45:25
10 Q. Does Exhibit 16 -- withdrawn. 14:40:53	10 Q. Does aflibercept have the same molecular 14:45:34
11 Does Exhibit 17 discuss treating or diagnosing 14:40:56	11 structure as a collagen-like triple helix peptide in any 14:45:37
12 angiogenic eye disorders? 14:41:00	12 respect? 14:45:43
13 A. I doubt it, but, again, if you need to get an 14:41:02	13 MR. COBB: Objection. Vague. 14:45:47
14 unequivocal answer, I would need to re-review this paper 14:41:05	14 THE WITNESS: Yes, it very well may have. It 14:46:01
15 with this question in mind. That is not why this paper 14:41:12	15 may also have beta sheets and alpha helices, as 14:46:03
16 is included, though. It's included to demonstrate the 14:41:15	16 aflibercept most likely does. But if you need a 14:46:11
17 fact that the term "molecular structure," which is found 14:41:23	17 definitive answer, I'll be glad to re-review Klibanov 14:46:14
18 right in the title of Exhibit 17, can refer to things 14:41:27	18 Exhibit 18 with this particular question in mind. 14:46:20
19 other than the primary structure, which was a position 14:41:33	19 BY MS. CORK: 14:46:25
20 taken by Dr. Chaum, as I understand it. 14:41:40	20 Q. Could you look at paragraph 65 of your 14:46:25
21 Q. Does Exhibit 17 discuss aflibercept or VEGF 14:41:49	21 declaration again. 14:46:27
22 Trap-Eye? 14:41:54	22 A. Sure. 14:46:34
23 A. Same answer. 14:41:57	23 Q. And, specifically, the part where you cite to 14:46:35
24 Q. Is Exhibit 17 relevant to the development of 14:42:01	24 Exhibit 1071, which is Exhibit 18 to this deposition. 14:46:36
25 any angiogenic therapeutics? 14:42:07	25 A. Just a second, please. Yes, ma'am. 14:46:41
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1 Q. And I think I said 1071. I meant 2071. 14:46:52 2 A. Fine. 14:46:58 3 Q. In paragraph 65 of your declaration, you refer 14:47:03 4 to Exhibit 2071 as providing a figure illustrating the 14:47:07 5 molecular structure of the collagen-like, with the 14:47:14 6 structure in brackets, triple helix peptide. 14:47:19 7 Do you see that? 14:47:23 8 A. I do. 14:47:23 9 Q. And the structure in brackets includes three 14:47:24 10 amino acids, true? 14:47:32 11 A. No. 14:47:35 12 Q. Is it your understanding that "Gly" refers to 14:47:39 13 the amino acid glycine? 14:47:42 14 A. It refers to an amino acid residue, which is 14:47:46 15 called glycine. 14:47:52 16 Q. Is it your understanding that the notation 14:47:55 17 "Pro" refers to the amino acid residue proline? 14:47:59 18 A. That's correct. 14:48:05 19 Q. Is it your understanding that the notation 14:48:07 20 "Hyp" relates to a post-translational modification of the 14:48:09 21 amino acid proline called 4-hydroxy proline? 14:48:18 22 A. I would not put it that way. It doesn't refer 14:48:23 23 to post translational modification. It refers to an 14:48:25 24 amino acid residue that is formed as a result of such a 14:48:30 25 post-translational modification. 14:48:34 Page 142	1 A. That's correct. That's what I just said. 14:51:02 2 Q. Exhibit 18 describes its molecular structure in 14:51:12 3 terms of its amino acid primary sequence, true? 14:51:14 4 MR. COBB: Objection. Mischaracterizes the 14:51:20 5 document; form. 14:51:21 6 THE WITNESS: No. The molecular structure here 14:51:24 7 refers to the fact that it's a triple helix. So it 14:51:26 8 actually refers to the spatial structure of this peptide. 14:51:30 9 So the term "molecular structure" here relates to the 14:51:41 10 term "triple helix." So it's a helical structure, which, 14:51:45 11 by definition, is an element of a secondary structure. 14:51:51 12 BY MS. CORK: 14:51:55 13 Q. Is it true that the helical structure is 14:51:57 14 dictated by the 18 amino acids that you just identified? 14:52:00 15 A. It certainly depends on that sequence, but it 14:52:16 16 also depends on other things. You said "determines," I 14:52:19 17 believe. So it's one of the determinants, but not the 14:52:22 18 only determinant. 14:52:27 19 Q. Does Exhibit 18 discuss diagnosing or treating 14:52:37 20 angiogenic eye disorders? 14:52:51 21 A. I doubt it, but if you need a definitive 14:52:54 22 answer, I would have to take a look at the entirety of 14:52:56 23 this paper with this particular question in mind. 14:53:00 24 But that's not why I cited this paper as an 14:53:04 25 example. I cited it to illustrate basic principles of 14:53:08 Page 144
1 Q. Okay. As reflected in Exhibit -- withdrawn. 14:48:43 2 As reflected in your declaration, "Hyp" refers 14:48:48 3 to an amino acid residue that is post-translationally 14:48:55 4 modified. 14:49:00 5 A. An amino acid residue that has undergone a 14:49:08 6 post-translational modification. 14:49:12 7 Q. Looking back at paragraph 65 of your 14:49:40 8 declaration -- 14:49:44 9 A. Yeah. 14:49:48 10 Q. -- you state that the molecular structure of 14:49:48 11 the collagen-like triple helix peptide, and you -- 14:49:50 12 withdrawn. 14:49:57 13 The structure in brackets, when you're 14:50:00 14 referring to the molecular structure of the collagen-like 14:50:06 15 triple helix peptide in Exhibit 2071, includes two amino 14:50:10 16 acid residues and a third amino acid residue that has 14:50:15 17 undergone a post-translational modification, true? 14:50:19 18 A. No. 14:50:23 19 Q. Why do you say that? 14:50:29 20 A. Because it's not true. What you just said is 14:50:31 21 not true. It includes 18 amino acid residues, which are 14:50:33 22 comprised of three different amino acid residues. 14:50:40 23 Q. The collagen-like triple helix peptide in 14:50:51 24 Exhibit 2071 includes 18 amino acid residues comprised of 14:50:55 25 three different amino acid residues, true? 14:51:00 Page 143	1 protein chemistry and biochemistry that apply to things 14:53:16 2 like aflibercept and to other proteins and polypeptides. 14:53:23 3 Q. Does Exhibit 18 discuss aflibercept or VEGF 14:53:33 4 Trap-Eye? 14:53:38 5 A. Same answer. 14:53:42 6 Q. Does Exhibit 18 -- withdrawn. 14:53:43 7 Is Exhibit 18 relevant to the development of 14:53:47 8 anti-angiogenic therapeutics? 14:53:50 9 A. I think it is relevant to the extent that it 14:53:55 10 supports and underscores the fact that the term 14:54:00 11 "molecular structure" can refer to secondary, tertiary, 14:54:05 12 domain, or quaternary structure, in contrast to 14:54:14 13 Dr. Chaum's opinion that it necessarily applies to the 14:54:19 14 primary structure. 14:54:25 15 Q. I'll ask you to turn to Exhibit 19, please. 14:54:39 16 A. Okay. 14:54:56 17 Q. And Exhibit 19, which is Exhibit 2073 to your 14:54:56 18 declaration, is discussed in paragraph 66. 14:55:00 19 Do you see that? 14:55:03 20 A. I do see that, yes. 14:55:04 21 Q. You discuss Exhibit 19 for the principle of a 14:55:20 22 comparison of folding pathways in proteins with the same 14:55:26 23 structure, but a different sequence; is that right? 14:55:31 24 A. Just a second. Let me find it in paragraph 65. 14:55:34 25 Exhibit 2073 is actually cited in paragraph 66, as I -- 14:56:20 Page 145

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1 as I'm seeing now, not in paragraph 65. 14:56:27	1 to -- to read. 14:59:48
2 Q. Yes. 14:56:37	2 BY MS. CORK: 14:59:49
3 A. Okay. 14:56:38	3 Q. Do you have an understanding of what it means 14:59:50
4 Q. You see it in paragraph 66? 14:56:39	4 that it's uncommon that there would be very few highly 14:59:52
5 A. Okay. So with that -- with that sort of 14:56:40	5 conserved amino acid residues in spectrin domains? 14:59:56
6 statement in mind, could you please slowly repeat your 14:56:48	6 A. Uncommon means not very common. 15:00:03
7 question? 14:56:51	7 Q. Isn't it true that commonly a family of protein 15:00:09
8 Q. Exhibit 19 relates to spectrin domains, true? 14:56:55	8 domains would have conserved amino acid sequences? 15:00:12
9 A. It relates to what? 14:57:01	9 MR. COBB: Objection. Form. 15:00:17
10 Q. Spectrin domains. 14:57:02	10 THE WITNESS: Well, this one also has conserved 15:00:22
11 A. Well, the title of Exhibit 19 is, "The Folding 14:57:07	11 amino acid residues, as obviously the plain text 15:00:27
12 of Spectrin Domains I: Wild-type Domains Have the Same 14:57:15	12 indicates; is just that there are very few of them. But 15:00:33
13 Stability, but very Different Kinetic Properties." 14:57:24	13 the phenomenon that is referred to here, namely the 15:00:38
14 Q. In the "Introduction," there is a left column 14:57:35	14 presence of highly-conserved residues, is -- is a common 15:00:44
15 and a right column, and I'm going to read from the first 14:57:38	15 phenomenon in proteins. It's just a question of 15:00:54
16 full paragraph in the right-hand column. 14:57:41	16 statistics, like, you know, how frequent or how common 15:00:58
17 Do you see that? 14:57:43	17 that is. 15:01:01
18 A. I -- I see the first -- yeah. There is only 14:57:45	18 BY MS. CORK: 15:01:03
19 one paragraph in the left column. 14:57:48	19 Q. Commonly a family of protein domains would have 15:01:05
20 Q. Exhibit 19 states: "Spectrin domains are --" 14:57:52	20 conserved amino acid sequences in those domains. 15:01:09
21 A. Just a second. Where? Which particular 14:57:57	21 MR. COBB: Objection. Vague. 15:01:14
22 sentence are you reading? 14:57:59	22 THE WITNESS: Would have more than very few 15:01:15
23 Q. From the first paragraph in the right-hand 14:58:01	23 highly-conserved residues, and here there are very few 15:01:18
24 column of the "Introduction." 14:58:02	24 highly-conserved residues, but it doesn't change the fact 15:01:24
25 A. Oh, oh, I'm sorry. I apologize. I actually 14:58:05	25 that this protein, like other proteins, does have 15:01:28
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1 was looking at the left-hand column. My fault. Sorry. 14:58:08	1 highly-conserved residues. It's just a question of how 15:01:34
2 Please. 14:58:11	2 many. 15:01:38
3 Q. Exhibit 19 states: "Spectrin domains are found 14:58:12	3 BY MS. CORK: 15:01:39
4 as multiple tandem repeats in cytoskeletal proteins 14:58:16	4 Q. And to be clear, we're talking about protein 15:01:46
5 including spectrin, alpha-actinin, and dystrophin. The 14:58:22	5 domains, not full proteins, correct? 15:01:49
6 106 amino acid residue repeat unit folds into a coiled 14:58:26	6 MR. COBB: Objection. Form. 15:01:53
7 coil with three antiparallel helices," and it refers to 14:58:32	7 THE WITNESS: Just a second. Let me re-read 15:02:04
8 Figure 1. 14:58:38	8 this paragraph to myself. 15:02:06
9 Exhibit 19 goes on to state, "Uncommonly, there 14:58:39	9 Yes, we are talking about protein domains, 15:02:18
10 are very few highly conserved residues; only a tryptophan 14:58:42	10 correct. 15:02:22
11 residue in helix A and a leucine two residues from the 14:58:49	11 BY MS. CORK: 15:02:22
12 carboxyl terminus of helix C are conserved in more than 14:58:51	12 Q. Specifically spectrin domains. 15:02:23
13 80% of sequences in the Pfam database." 14:58:51	13 A. Yeah, not only spectrin, but also alpha-actinin 15:02:26
14 Do you see that? 14:59:02	14 and dystrophin. 15:02:30
15 A. I do see that. Yes. You omitted several 14:59:02	15 Q. Does aflibercept contain a spectrin domain? 15:02:45
16 references, but I do see what you were reading. 14:59:05	16 A. It contains domains. I'm sure that these 15:02:53
17 Q. Would you agree that Exhibit 19 is saying that 14:59:12	17 domains are distinct from the domains that are found -- 15:02:59
18 there are very few highly conserved amino acid residues 14:59:16	18 from the spectrin domains, but it does contain domains as 15:03:04
19 in spectrin domains? 14:59:22	19 elements of its tertiary structure. 15:03:09
20 MR. COBB: Objection. The document speaks for 14:59:24	20 Q. So you're not aware that aflibercept contains a 15:03:14
21 itself; form. 14:59:25	21 spectrin domain? 15:03:16
22 THE WITNESS: It does say that there are very 14:59:33	22 A. I'm actually not aware one way or the other. I 15:03:21
23 few highly conserved residues, and it says that it's 14:59:36	23 have not compared aflibercept with spectrin. The purpose 15:03:27
24 uncommon. Yes. That's what it says in this particular 14:59:40	24 of providing this paper is just to illustrate -- just as 15:03:31
25 paragraph that -- a portion of which you have chosen 14:59:44	25 previously, to illustrate some basic principles of 15:03:34
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1 protein chemistry and biochemistry. 15:03:41	1 of it, and I've certainly seen it, and I've used it. 15:23:43
2 Q. Do spectrin domains and aflibercept have the 15:03:48	2 Q. In English, the article "a" refers to the 15:23:48
3 same molecular structure in any respect? 15:03:51	3 singular, not the plural, correct? 15:23:51
4 A. I mean, I -- they certainly have different 15:03:58	4 MR. COBB: Objection. Form. 15:23:54
5 primary structures. I have not compared their domain 15:04:02	5 THE WITNESS: Not necessarily. Again, it 15:24:00
6 structure. I think generally speaking they will not be 15:04:07	6 depends on the context. It may refer to a family of 15:24:02
7 the same, but the important thing is that both of them 15:04:10	7 drugs. Some of the patents that I have seen specifically 15:24:07
8 have domains, which is merely independent regions of the 15:04:15	8 say that "a" should equally apply to singular and plural. 15:24:11
9 protein molecules, which was the point of introducing 15:04:22	9 So like many other things, it depends on the context. 15:24:17
10 this reference in my '681 declaration. 15:04:26	10 BY MS. CORK: 15:24:20
11 Q. Does Exhibit 19 discuss angiogenic eye 15:04:31	11 Q. In scientific literature, does the article "a" 15:24:23
12 disorders? 15:04:35	12 refer to the singular rather than the plural? 15:24:26
13 A. I doubt it, but, again, if it's important to 15:04:38	13 MR. COBB: Objection. Form. 15:24:29
14 you, I'll be glad to re-review this paper with this 15:04:41	14 THE WITNESS: Well, I just specifically made 15:24:31
15 particular question in mind. 15:04:46	15 the reference to patents, which I view as a part of a 15:24:33
16 Q. Does Exhibit 19 discuss aflibercept or VEGF 15:04:48	16 scientific literature. Some of them expressly say that 15:24:37
17 Trap-Eye? 15:04:52	17 "a" refers to both singular and plural. 15:24:41
18 A. Same answer. 15:04:55	18 And in some instances "a," as I said, may refer 15:24:47
19 Q. Does -- withdrawn. 15:04:58	19 to a family of drugs if we are talking about drugs in a 15:24:52
20 Is Exhibit 19 relevant to the development of 15:04:59	20 scientific literature. 15:24:56
21 anti-angiogenic therapeutics? 15:05:03	21 BY MS. CORK: 15:24:58
22 A. In my opinion, it is relevant to the extent 15:05:07	22 Q. Let's leave aside patents for the time being, 15:24:59
23 that it illustrates some of the principles of protein 15:05:09	23 and talk about scientific publications. Do you know what 15:25:01
24 chemistry and biochemistry, and those principles are 15:05:15	24 I'm talking about? 15:25:06
25 relevant to the development of protein-based 15:05:19	25 A. I think so. Yes. 15:25:07
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1 therapeutics. 15:05:23	1 Q. You've published more than 300 scientific 15:25:10
2 MS. CORK: Would now be a good time for a 15:05:29	2 publications. 15:25:13
3 break? 15:05:32	3 A. Yes. 15:25:15
4 MR. COBB: Yes. I was going to suggest it. 15:05:33	4 Q. In scientific publications, would you say "a 15:25:18
5 THE VIDEOTAPE OPERATOR: Off the record at 3:06 15:05:34	5 drug" if you were talking about more than one drug? 15:25:21
6 p.m. 15:05:36	6 MR. COBB: Objection. Incomplete hypothetical. 15:25:28
7 (Recess was taken.) 15:05:36	7 THE WITNESS: Well, as I just said, it could 15:25:31
8 THE VIDEOTAPE OPERATOR: Back on the record 15:20:56	8 refer to a family of drugs; for example, you know, 15:25:33
9 beginning -- hang on. 15:20:57	9 certainly it wouldn't be unusual to see something like 15:25:36
10 (Technical interruption.) 15:20:59	10 statins, plural, is a drug to treat cardiovascular 15:25:41
11 THE VIDEOTAPE OPERATOR: Back on the record 15:22:45	11 diseases. I've seen sort of statements of this sort in 15:25:49
12 beginning Media Unit 5 at 3:23 p.m. 15:22:46	12 the literature, I think. 15:25:53
13 BY MS. CORK: 15:22:50	13 BY MS. CORK: 15:25:55
14 Q. Dr. Klibanov, you've testified that you're 15:22:55	14 Q. You would say statins, the family of drugs, is 15:25:55
15 fluent in English, true? 15:22:57	15 a drug? 15:25:58
16 A. I don't think that I specifically said it. I 15:23:01	16 A. Yeah. I -- I wouldn't be surprised. I mean, 15:26:00
17 mean, I would like to think that my command of the 15:23:04	17 people who write scientific articles are typically not 15:26:05
18 English language is satisfactory, since I taught in 15:23:09	18 English language and literature majors, and neither am I, 15:26:09
19 English at MIT for more than 40 years, but I -- I am 15:23:13	19 you know, so sometimes there are imprecise expressions, 15:26:12
20 aware of the fact that I have an accent. 15:23:18	20 which are totally understandable, provided that the 15:26:21
21 Q. Are you familiar with the article "a" as in "a 15:23:23	21 common sense is used in analyzing such statements. 15:26:26
22 drug"? 15:23:27	22 Q. So leaving aside the technical context of a 15:26:33
23 A. I'm sorry. I don't understand. 15:23:31	23 patent, in basic English language, the article "a" refers 15:26:36
24 Q. Are you familiar with the article "a"? 15:23:34	24 to the singular rather than the plural, right? 15:26:43
25 A. Yes. When I'm saying I'm familiar, I've heard 15:23:37	25 MR. COBB: Objection. Form. 15:26:47
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39 (Pages 150 - 153)

1 THE WITNESS: I'm not an expert in the basic 15:26:49 2 English language, so I would defer to you in this regard. 15:26:51 3 I am an expert in scientific publications, and 15:26:57 4 specifically scientific publications dealing with, among 15:27:03 5 other things, protein chemistry and biochemistry. 15:27:07 6 And in the context of such publications, "a" 15:27:11 7 may refer to both singular and plural, depending on the 15:27:16 8 context. 15:27:21 9 BY MS. CORK: 15:27:27 10 Q. Do you speak the English language? 15:27:28 11 MR. COBB: Objection. Form. 15:27:32 12 THE WITNESS: Repeat the question, please. 15:27:33 13 BY MS. CORK: 15:27:35 14 Q. Do you speak the English language? 15:27:35 15 MR. COBB: Objection. Argumentative. 15:27:38 16 THE WITNESS: I thought that -- that was the 15:27:41 17 language in which the prior portion of these depositions 15:27:42 18 have been conducted, unless I'm mistaken. So I guess the 15:27:46 19 answer would have to be yes. But I'm not an expert in 15:27:51 20 the English language or English literature or linguistic 15:27:57 21 analysis or anything like that. 15:28:04 22 BY MS. CORK: 15:28:05 23 Q. Would you use the term "a drug" if you were 15:28:09 24 talking about more than one drug? 15:28:12 25 MR. COBB: Objection. Asked and answered; 15:28:15 Page 154	1 MR. COBB: Objection. Form. 15:29:50 2 THE WITNESS: I desire to speak clearly, but I 15:29:53 3 also recognize that if you dot all the I's and cross all 15:29:56 4 the T's, so to speak, the lecture or the seminar will 15:30:02 5 never end. So we all have shortcuts in the way that we 15:30:09 6 speak, and I can assure you that you've taken quite a few 15:30:16 7 of those during your questioning today. 15:30:20 8 MS. CORK: I'd like to mark as Exhibit 20 a 15:30:36 9 document titled, "VEGF Trap-Eye for the treatment of 15:30:38 10 neovascular age-related macular degeneration," annotated 15:30:39 11 as Exhibit 1006, with copies to counsel. 15:30:44 12 (Exhibit 20 was marked for identification.) 15:30:48 13 THE REPORTER: Thank you. Exhibit 20. 15:31:00 14 THE WITNESS: Thank you. 15:31:03 15 BY MS. CORK: 15:31:04 16 Q. Dr. Klivanov, do you recognize Exhibit 20? 15:31:04 17 A. I do. 15:31:07 18 Q. In your declaration do you refer to Exhibit 20, 15:31:14 19 which is Exhibit 1006, as Dixon? 15:31:18 20 A. Yes, because that's how Dr. Chaum referred to 15:31:26 21 that publication, and as I already said repeatedly, my 15:31:29 22 declaration was in response to Dr. Chaum's declaration. 15:31:34 23 Q. So if I refer to Exhibit 20 as just "Dixon," 15:31:40 24 you understand that I'm referring to Exhibit 20. 15:31:43 25 A. Yes. 15:31:47 Page 156
1 form. 15:28:16 2 THE WITNESS: It depends on the context. There 15:28:18 3 may be some context where it is appropriate. For 15:28:21 4 example, if I were to say an analgesic, it is a drug that 15:28:27 5 relieves pain. But there are several such drugs. So it 15:28:34 6 could refer to a group of compounds. So it's possible. 15:28:39 7 BY MS. CORK: 15:28:44 8 Q. How would you indicate if you were talking 15:28:45 9 about one and only one drug? 15:28:46 10 MR. COBB: Objection. Incomplete hypothetical; 15:28:51 11 form. 15:28:53 12 THE WITNESS: Again, I -- I don't know. I 15:28:54 13 think that, you know, the context would be such that it 15:28:56 14 would indicate that, and I would rely on the common sense 15:28:59 15 of -- of the reader, and the goodwill of the reader, and 15:29:06 16 also the reader's desire to understand rather than 15:29:10 17 obfuscate. 15:29:15 18 BY MS. CORK: 15:29:16 19 Q. You said the reader's desire to understand 15:29:26 20 rather than obfuscate. 15:29:29 21 A. Yes. If I were to put it in writing, then it 15:29:32 22 will be the reader who will read it. And if I were to 15:29:34 23 speak, it will have to be a listener. 15:29:37 24 Q. As the speaker, do you desire to speak clearly 15:29:42 25 or to obfuscate? 15:29:48 Page 155	1 Q. You've reviewed Dixon, true? 15:31:53 2 A. True. 15:31:55 3 Q. You've been deposed on Dixon before; isn't that 15:31:56 4 right? 15:32:01 5 A. I have been questioned on Dixon in my prior 15:32:01 6 depositions. I'm just trying to be very clear since you 15:32:04 7 brought up the question of clarity in my answers. So I 15:32:08 8 will now be extra vigilant in this regard, madam. 15:32:12 9 Q. And, of course, you opine on Dixon in your 15:32:20 10 declaration, true? 15:32:23 11 A. I don't know what you mean by "of course," but 15:32:24 12 I do opine on Dixon in my declaration. 15:32:27 13 Q. Is it fair to say that you're very familiar 15:32:35 14 with the Dixon reference? 15:32:37 15 A. I don't think that will be fair to say. I'm 15:32:42 16 familiar with it. I -- I don't understand the difference 15:32:44 17 between "familiar" and "very familiar." There are some 15:32:47 18 portions of Dixon that I'm more familiar than others. 15:32:53 19 And those are the ones that I cite from in my expert 15:32:58 20 report; for example, from the left column of page 1575 of 15:33:04 21 Dixon. 15:33:11 22 Q. Have you read Dixon in its entirety? 15:33:12 23 A. Yes. Not recently. 15:33:14 24 Q. Let's look at the abstract of Dixon on its 15:33:18 25 first page. 15:33:21 Page 157

1 Do you see that? 15:33:22 2 A. It doesn't use the word "abstract," but this is 15:33:33 3 what I view as an abstract, which consists of several 15:33:35 4 subsections. 15:33:40 5 Q. To be fair -- withdrawn. 15:33:44 6 Are you referring to the first paragraph in 15:33:48 7 Dixon that begins with, "Background:"? 15:33:52 8 A. Yes. Because I presume that that's what you 15:33:57 9 were referring to. 15:34:01 10 Q. Do you see in the middle of Dixon's abstract a 15:34:04 11 sentence that begins, "One promising new drug"? 15:34:10 12 A. Yes. 15:34:13 13 Q. Dixon states that: "One promising new drug is 15:34:16 14 aflibercept (VEGF Trap-Eye), a fusion protein that blocks 15:34:21 15 all isoforms of the VEGF-A and placental growth factors-1 15:34:29 16 and -2." 15:34:37 17 Do you see that? 15:34:38 18 A. I do see that sentence, yes, taken out of the 15:34:39 19 middle of the abstract, yes. 15:34:41 20 Q. And I read it correctly, right? 15:34:44 21 A. Yes. 15:34:46 22 Q. Two sentences from the bottom, there is another 15:34:54 23 sentence that begins, "VEGF Trap-Eye." 15:34:57 24 Do you see that? 15:35:00 25 A. Yes. 15:35:03 Page 158	1 But would I fault Dixon for saying it? No. 15:36:43 2 Because I read Dixon with the mind willing to understand, 15:36:47 3 and I would read Dixon in its entirety and would 15:36:52 4 interpret everything that Dixon said taken in the context 15:36:55 5 of the entirety of the -- of the Dixon paper. 15:36:59 6 BY MS. CORK: 15:37:04 7 Q. Also, in the middle of Dixon's abstract, there 15:37:08 8 is a sentence that begins: "In addition to two." 15:37:11 9 Do you see that sentence? 15:37:14 10 A. I do see that sentence, correct. 15:37:21 11 Q. Dixon states: "In addition to two anti-VEGF 15:37:23 12 drugs currently in widespread use, ranibizumab and 15:37:25 13 bevacizumab, a number of medications that interrupt 15:37:29 14 angiogenesis are currently under investigation." 15:37:33 15 Do you see that? 15:37:38 16 A. I do. 15:37:39 17 Q. Did I read that correctly? 15:37:39 18 A. Yes. 15:37:40 19 Q. Would you agree that Dixon knows how to refer 15:37:43 20 to multiple different drugs? 15:37:45 21 MR. COBB: Objection. Vague; the document 15:37:50 22 speaks for itself; form. 15:37:53 23 THE WITNESS: I mean, I don't know what Dixon 15:37:55 24 knows and what Dixon doesn't know. This -- the sentence 15:37:57 25 speaks for itself. And in some cases Dixon is being 15:38:03 Page 160
1 Q. Dixon states: "VEGF Trap-Eye is a novel 15:35:04 2 anti-VEGF therapy with Phase II, I" -- withdrawn. 15:35:08 3 Dixon states: "VEGF Trap-Eye is a novel 15:35:14 4 anti-VEGF therapy with Phase I and II trial data 15:35:18 5 indicating safety, tolerability, and efficacy for the 15:35:23 6 treatment of neovascular AMD." 15:35:26 7 Do you see that? 15:35:30 8 A. I do see that, yes. 15:35:31 9 Q. Did I read that correctly? 15:35:32 10 A. You did. 15:35:36 11 Q. In the two sentences of Dixon that I've read so 15:35:50 12 far, Dixon refers to aflibercept, VEGF Trap-Eye, as a 15:35:53 13 fusion protein, and VEGF Trap-Eye as a novel anti-VEGF 15:36:00 14 therapy. 15:36:08 15 Do you see that? 15:36:08 16 MR. COBB: Objection. Misstates the document; 15:36:09 17 form. 15:36:10 18 THE WITNESS: I mean, it says what it says, 15:36:11 19 yes. And, by the way, the very fact that -- speaking of 15:36:13 20 precise or imprecise use of the English language, it says 15:36:17 21 in the second sentence that you read, "VEGF Trap-Eye is a 15:36:21 22 novel anti-VEGF therapy," which obviously here Dixon and 15:36:26 23 co-workers have taken some shortcuts. VEGF Trap-Eye is 15:36:33 24 not a therapy. It's a molecule. It is a protein 15:36:37 25 molecule. It's not a therapy. 15:36:40 Page 159	1 precise -- may be precise, in some cases Dixon is 15:38:10 2 demonstrably imprecise. And that's how one of skill in 15:38:15 3 the art would read it, as opposed to a lawyer or an 15:38:20 4 English language scholar. That's -- these are not the 15:38:23 5 people for whom Dixon wrote the paper. 15:38:27 6 BY MS. CORK: 15:38:30 7 Q. It's true that Dixon used the phrase, "two 15:38:37 8 anti-VEGF drugs" to refer to ranibizumab and bevacizumab, 15:38:41 9 right? 15:38:47 10 MR. COBB: Objection. The document speaks for 15:38:47 11 itself; form. 15:38:48 12 THE WITNESS: In this particular sentence, 15:38:50 13 Dixon says, "In addition to two anti-VEGF drugs currently 15:38:52 14 in widespread use, ranibizumab and bevacizumab, a number 15:38:58 15 of medications that interrupt angiogenesis are currently 15:39:07 16 under investigation." That's what this particular 15:39:14 17 sentence says. 15:39:17 18 BY MS. CORK: 15:39:20 19 Q. Do you see the last sentence of Dixon's 15:39:23 20 abstract that starts, "Two Phase III clinical trials"? 15:39:26 21 A. I do. 15:39:31 22 Q. Dixon states: "Two Phase III clinical trials 15:39:34 23 (VIEW-1 and VIEW-2) comparing VEGF Trap-Eye to 15:39:38 24 ranibizumab are currently continuing and will provide 15:39:44 25 vital insight into the clinical applicability of this 15:39:49 Page 161

1 drug." 15:39:52	1 states: "A Phase I, randomized, double-blind, 15:43:44
2 Do you see that? 15:39:54	2 placebo-controlled trial of intravenous aflibercept 15:43:47
3 A. I do see that, yes. 15:39:55	3 (oncology formulation) was completed in 25 patients with 15:43:53
4 Q. Did I read it correctly? 15:39:56	4 AMD." 15:43:58
5 A. Yes. 15:39:58	5 Do you see that? 15:44:00
6 Q. Do you have an understanding of how many drugs 15:40:00	6 A. Yes. 15:44:00
7 were being tested in the VIEW-1 and VIEW-2 clinical 15:40:03	7 Q. The first sentence of the next paragraph 15:44:03
8 trials? 15:40:07	8 states: "The safety, tolerability, and biological 15:44:06
9 A. I think that this particular sentence refers to 15:40:15	9 activity of intravitreal VEGF Trap-Eye in the treatment 15:44:12
10 two -- to two drugs with these two active pharmaceutical 15:40:23	10 of neurovascular AMD was evaluated in the two-part 15:44:17
11 ingredients. 15:40:31	11 clinical evaluation of anti-angiogenesis in the Retina-1 15:44:21
12 Q. And what are those two drugs? 15:40:33	12 (CLEAR-IT-1) study." 15:44:24
13 A. VEGF Trap-Eye and ranibizumab. And why don't I 15:40:37	13 Do you see that? 15:44:28
14 help our court reporter by spelling it, 15:40:45	14 A. I do. 15:44:28
15 r-a-n-i-b-i-z-u-m-a-b. Again, that's just sort of my 15:40:47	15 Q. Do you have an understanding of how a person of 15:44:41
16 reading of this sentence right now. That's what it says 15:40:58	16 skill in the art for the '681 Patent would interpret the 15:44:44
17 on -- on the face of it. 15:41:02	17 phrase in parentheses (oncology formulation)? 15:44:50
18 Q. Let's go to the second page -- sorry, the third 15:41:04	18 A. Okay. Broadly speaking, my understanding is 15:44:58
19 page of Dixon. Do you see the section titled, 2.2 15:41:32	19 that one would -- one of skill in the art would 15:45:01
20 "Introduction to Compound"? 15:41:37	20 understand it in the context of the entire article, 15:45:04
21 A. Yes. 15:41:40	21 rather than cherry-picking statements here and there. 15:45:07
22 Q. The first sentence under the header, 15:41:43	22 And in particular, in the subsection 2.3, 15:45:12
23 "Introduction to Compound" reads: "VEGF Trap-Eye is a 15:41:45	23 entitled, "Chemistry," which you conspicuously skipped, 15:45:17
24 novel anti-VEGF drug currently in commercial development 15:41:51	24 it specifically says that "VEGF Trap-Eye and aflibercept 15:45:22
25 for the treatment of neovascular AMD by Regeneron 15:41:53	25 (the oncology product) have the same molecular structure, 15:45:27
Page 162	Page 164
1 Pharmaceuticals, Inc. (Tarrytown, NY, USA) in the US and 15:41:57	1 but there are substantial differences between the 15:45:32
2 in collaboration with Bayer HealthCare (Leverkusen, 15:42:04	2 preparation of the purified drug product and their 15:45:36
3 Germany) in global markets." 15:42:06	3 formulation." 15:45:40
4 Do you see that? 15:42:13	4 So to me, an oncology formulation is a 15:45:41
5 A. I do. 15:42:13	5 formulation that's used in oncology. 15:45:44
6 Q. Did I read that correctly? 15:42:14	6 Q. And, specifically, Dixon is talking about a 15:45:49
7 A. Yes. 15:42:15	7 formulation of aflibercept that is used in oncology, 15:45:52
8 Q. Do you understand that the compound referred to 15:42:17	8 correct? 15:45:55
9 here is VEGF Trap-Eye? 15:42:20	9 A. I mean, the sentence says what it says. 15:46:00
10 MR. COBB: Objection. Form. 15:42:25	10 Q. Do you have an understanding -- withdrawn. 15:46:04
11 THE WITNESS: Just reading this sentence by 15:42:29	11 Would a person of ordinary skill in the art for 15:46:07
12 itself, that -- that is the case. Yes. 15:42:31	12 the '681 Patent understand Dixon to be describing a 15:46:09
13 Just reading it by itself. 15:42:36	13 formulation of aflibercept used in oncology? 15:46:14
14 BY MS. CORK: 15:42:47	14 MR. COBB: Objection. Vague. 15:46:19
15 Q. The next sentence, Dixon states: 15:42:48	15 THE WITNESS: It's not necessarily clear. 15:46:21
16 "Structurally, VEGF Trap-Eye is a fusion protein of key 15:42:49	16 There are a number of statements in Dixon that are sort 15:46:23
17 binding domains of human VEGFR-1 and -2 combined with the 15:42:50	17 of ambiguous, starting with, of course, the very one that 15:46:27
18 human IgG Fc fragment," and then it cites to Figure 1. 15:42:55	18 has been discussed in much detail, which is molecular 15:46:32
19 Do you see that? 15:43:00	19 structure. So one of skill in the art would have to read 15:46:35
20 A. Yes, and there is a reference to Figure 1, 15:43:00	20 whatever Dixon says in the context of the entire paper, 15:46:42
21 correct. 15:43:05	21 and that's what I would have to do now to interpret this 15:46:47
22 Q. Do you see the header, 2.6, "Clinical efficacy" 15:43:33	22 sentence or that sentence. 15:46:52
23 on the same page? 15:43:36	23 BY MS. CORK: 15:46:57
24 A. Yes. 15:43:40	24 Q. And, again, you've opined on Dixon in your 15:47:07
25 Q. Under that header of "Clinical efficacy," Dixon 15:43:41	25 declaration, as well as previous declarations, and you've 15:47:10
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42 (Pages 162 - 165)

1 been deposed on it multiple times before, true? 15:47:14 2 A. Not true. First of all, I don't know what you 15:47:20 3 mean by "multiple," but more importantly I opined on 15:47:23 4 certain portions of Dixon that are expressly cited in my 15:47:27 5 declaration and in my prior declarations. That is what I 15:47:32 6 opined on, because these portions relate to my area of 15:47:37 7 expertise, which is protein chemistry and biochemistry 15:47:42 8 and pharmaceutical formulations. 15:47:47 9 I am not an expert on clinical trials or 15:47:50 10 clinical efficacy. I have not been asked to opine on 15:47:53 11 that. And therefore, it is incorrect and potentially 15:47:57 12 misleading to say that I have opined on Dixon, which 15:48:03 13 would suggest that I have opined on the entirety of 15:48:07 14 Dixon, which I did not do. 15:48:10 15 Q. How do you square that with your statement, 15:48:18 16 sir, that the phrase "oncology formulation" needs to be 15:48:20 17 read in the context of the entire Dixon reference? 15:48:24 18 A. I don't understand the question. I heard it, 15:48:35 19 but I just don't understand what you mean by that. 15:48:36 20 Q. You've accused me of cherry-picking statements 15:48:38 21 from Dixon, true? 15:48:41 22 A. I didn't accuse you. I stated the obvious, 15:48:42 23 because you're taking a sentence from this page and then 15:48:45 24 another sentence from that page and another one. I mean, 15:48:48 25 if that's not cherry-picking, then I don't know what 15:48:51 Page 166	1 Q. Are you able to offer any opinions regarding an 15:50:29 2 oncology formulation of aflibercept? 15:50:32 3 MR. COBB: Objection. Vague. 15:50:36 4 THE WITNESS: I already told you that I presume 15:50:38 5 that it refers to a formulation used in oncology. And 15:50:40 6 beyond that, you know, as I said, this is not the section 15:50:46 7 of Dixon that's within my area of expertise, and that's 15:50:51 8 not the one that I -- the section that I have offered any 15:50:55 9 opinions on. 15:50:59 10 BY MS. CORK: 15:51:01 11 Q. Are you aware of other formulations of 15:51:31 12 aflibercept besides oncology formulations? 15:51:33 13 MR. COBB: Objection. Scope. 15:51:42 14 THE WITNESS: I mean, there may be other 15:51:49 15 formulations. In fact, I'm not even sure that there is a 15:51:50 16 single oncology formulation. So, again, I would need to 15:51:53 17 consider it in the proper context. 15:51:57 18 BY MS. CORK: 15:51:59 19 Q. Sitting here today, are you able to identify 15:52:01 20 any formulation of aflibercept, other than an oncology 15:52:03 21 formulation? 15:52:07 22 MR. COBB: Objection. Scope. 15:52:09 23 THE WITNESS: I would need to -- to think about 15:52:26 24 it. It's not something that I opine on in the four 15:52:28 25 corners of my expert report. 15:52:32 Page 168
1 cherry-picking is. 15:48:54 2 Q. You also selected portions of Dixon -- 15:48:55 3 A. Yes. 15:48:58 4 Q. -- to cite in your declaration, and you 15:48:58 5 excluded others, true? 15:49:00 6 A. True, because as I said many times during this 15:49:02 7 deposition today, my goal was to refer to Dr. Chaum's 15:49:05 8 opinions expressed in his declaration. 15:49:11 9 So I used portions of the documents that are 15:49:15 10 relevant to this particular task. 15:49:21 11 What your task today is, I don't know. 15:49:24 12 But I do know what my task was. So I used what 15:49:27 13 was necessary to respond to Dr. Chaum's opinions. 15:49:31 14 Q. Are you an expert in formulation chemistry? 15:49:40 15 MR. COBB: Objection. Vague. 15:49:47 16 THE WITNESS: In general, I consider myself an 15:49:48 17 expert in pharmaceutical formulation chemistry, yes. 15:49:51 18 BY MS. CORK: 15:49:54 19 Q. I've been reading a sentence that refers to an 15:49:59 20 oncology formulation of aflibercept. Do you agree? 15:50:01 21 A. Which is a part of the section entitled, 15:50:06 22 "Clinical efficacy," and specifically Phase I. And 15:50:09 23 clinical efficacy is not something that I'm an expert in, 15:50:15 24 which is why I offer no opinions with respect to clinical 15:50:20 25 efficacy, as you know. 15:50:25 Page 167	1 BY MS. CORK: 15:52:34 2 Q. Are you aware of any intravitreal formulations 15:52:36 3 of aflibercept? 15:52:42 4 MR. COBB: Objection. Scope. 15:52:46 5 THE WITNESS: There are some statements to that 15:53:10 6 effect; for instance, in the chemistry section of Dixon, 15:53:11 7 which is Section 2.3, you know, there are some statements 15:53:18 8 to that effect. So I'm familiar with that, for example, 15:53:25 9 to the extent that Dixon talks about those. 15:53:29 10 BY MS. CORK: 15:53:35 11 Q. What statements are you referring to in the 15:53:35 12 chemistry section of Dixon? 15:53:37 13 A. For instance, it says, "VEGF Trap-Eye undergoes 15:53:41 14 further purification steps during manufacturing to 15:53:47 15 minimize the risk of irritation to the eye." And further 15:53:52 16 purification, that I understand to refer to the oncology 15:53:58 17 product. 15:54:02 18 And then it also says, "VEGF Trap-Eye is also 15:54:07 19 formulated with different buffers at different 15:54:11 20 concentrations for buffers in common suitable for the 15:54:14 21 comfortable, non-irritating direct injection into the 15:54:19 22 eye," which I understand is what an intravitreal 15:54:23 23 injection is. 15:54:28 24 Q. Does the term "VEGF Trap-Eye" refer to an 15:54:32 25 intravitreal formulation of aflibercept? 15:54:35 Page 169

1 MR. COBB: Objection. Form. 15:54:40	1 can mean both things, as is evident even by the short 15:58:40
2 THE WITNESS: I understand the term "VEGF 15:54:56	2 section 2.3, "Chemistry." And, also, as evidenced by the 15:58:49
3 Trap-Eye" to refer to the formulation that is to be 15:54:58	3 fact that VEGF Trap-Eye in the portion -- in the portion 15:58:57
4 injected into the eye. 15:55:04	4 of the abstract that you read, was referred to as a 15:59:03
5 BY MS. CORK: 15:55:11	5 therapy. 15:59:07
6 Q. Is that different from an intravitreal 15:55:12	6 Q. Do you know what Dixon is talking about when it 15:59:18
7 formulation of aflibercept? 15:55:16	7 talks about VEGF Trap-Eye? 15:59:20
8 A. I mean, that's what I understand. I mean, 15:55:17	8 A. For the third time, it depends on the context 15:59:25
9 there may be more to it. Again, I'm not an 15:55:19	9 in which Dixon uses it. Dixon is not a paragon of 15:59:29
10 ophthalmologist. I understand that that's what 15:55:22	10 clarity, as we discussed already in the context of the 15:59:36
11 intravitreal is, although it may have some other -- some 15:55:27	11 molecular structure. And there are some confusing 15:59:40
12 other aspects. 15:55:35	12 statements there. So Dixon talks about a number of 15:59:49
13 Q. And I want to make sure your testimony is 15:55:38	13 different things. 15:59:54
14 clear, because it looks from the real-time that you 15:55:40	14 Q. Is it your testimony that Dixon means one thing 15:59:59
15 previously testified that you understand the term "VEGF 15:55:43	15 by VEGF Trap-Eye in some cases, and a different thing by 16:00:03
16 Trap-Eye" to refer to the formulation that is to be 15:55:48	16 VEGF Trap-Eye in other cases? 16:00:08
17 injected into the eye. 15:55:51	17 A. It appears to be the case. So, again, I cannot 16:00:12
18 MR. COBB: Objection. Misstates his testimony. 15:55:56	18 speak for Dixon. I've never spoken with Dixon. But 16:00:16
19 THE WITNESS: Again, VEGF Trap-Eye may refer to 15:56:01	19 certainly just reading the plain text of the Dixon 16:00:20
20 the molecule, to the protein molecule, or may refer to a 15:56:05	20 article, I mean, that -- that appears to be the case. 16:00:26
21 formulation, depending on the context. 15:56:11	21 Q. And to be clear, certain parts of Dixon you 16:00:39
22 BY MS. CORK: 15:56:15	22 consider to be outside your expertise, true? 16:00:41
23 Q. To make sure I understand you, you can 15:56:17	23 A. Yes. And I don't know how much clarity you 16:00:47
24 formulate a protein such that you have the protein, and 15:56:21	24 want to obtain. I mean, it's something that I've 16:00:50
25 then the formulation that it is in, correct? 15:56:25	25 probably said five times already. So I don't know how 16:00:53
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1 A. I -- I don't understand. 15:56:35	1 much clarity the record can bare. 16:00:56
2 Q. These are two separate things, the protein and 15:56:37	2 But I specifically said that I'm an expert in 16:00:59
3 its formulation? 15:56:40	3 protein chemistry and biochemistry. I'm not an expert in 16:01:02
4 A. Yes. There are two separate things. One, 15:56:42	4 clinical efficacy or clinical trials. 16:01:07
5 generally speaking, is referred to as a drug substance; 15:56:47	5 And I just don't know how to make that 16:01:11
6 and the other one is generally referring to -- as a drug 15:56:51	6 statement even more clear so that you won't try to 16:01:13
7 product. So a drug substance is the active 15:56:56	7 clarify the record once again. 16:01:20
8 pharmaceutical ingredient in the drug product. 15:57:00	8 Q. Would you please list all of the different 16:01:23
9 Q. Does VEGF Trap-Eye refer to a formulation of 15:57:08	9 things that you believe Dixon teaches VEGF Trap-Eye is. 16:01:26
10 aflibercept that is injected into the eye? 15:57:14	10 MR. COBB: Objection. Vague; form. 16:01:34
11 A. Would you repeat the question slowly, please? 15:57:28	11 THE WITNESS: I would need to re-review Dixon 16:01:37
12 Q. Does VEGF Trap-Eye refer to a formulation of 15:57:30	12 with this particular question in mind. 16:01:40
13 aflibercept that is injected into the eye? 15:57:36	13 BY MS. CORK: 16:01:43
14 A. I mean, as I already told you, VEGF Trap-Eye 15:57:43	14 Q. Sitting here today, you are not able to list 16:01:44
15 may not even refer to formulation at all. It may refer 15:57:45	15 all of the different things that you believe Dixon 16:01:48
16 to a molecule. And, indeed, that seems to be the case 15:57:50	16 teaches VEGF Trap-Eye is? 16:01:53
17 when we look at the first sentence of this section 2.3, 15:57:58	17 A. That's not correct. Sitting here today, I'm 16:01:59
18 "Chemistry." Because the formulation -- or a formulation 15:58:01	18 very able to review the entirety of Dixon once again, and 16:02:02
19 doesn't have a molecular structure, whatever the term 15:58:11	19 I can assure you that it will continue to be today, 16:02:08
20 "molecular structure" means here. 15:58:15	20 meaning that we're not going to go into tomorrow. 16:02:11
21 Q. It's your opinion that VEGF Trap-Eye refers to 15:58:19	21 So sitting here today, I can re-review Dixon in 16:02:14
22 the drug substance which is the protein, and not its 15:58:22	22 its entirety with your particular question in mind, and 16:02:19
23 formulation? 15:58:26	23 then I will be able to answer your question. 16:02:22
24 A. No. As I already indicated, depending on the 15:58:28	24 Q. Is it your view that Dixon teaches that VEGF 16:02:32
25 context, it can mean -- again, in the Dixon article, it 15:58:33	25 Trap-Eye can be a drug substance? 16:02:35
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1	MR. COBB: Objection. Form.	16:02:46	1	BY MS. CORK:	16:06:52
2	THE WITNESS: It appears that in some portions	16:02:54	2	Q. Go to page 5 -- no, sorry, page 4 of Dixon.	16:07:20
3	of Dixon, when it talks about VEGF Trap-Eye, it talks	16:02:56	3	A. Yes.	16:07:33
4	about the drug substance. Yes.	16:03:02	4	Q. On page 4 of Dixon, do you see the headers,	16:07:33
5	BY MS. CORK:	16:03:04	5	"Phase II" and "Phase III"?	16:07:35
6	Q. Is this drug substance have the same molecular	16:03:05	6	A. Yes.	16:07:39
7	structure as aflibercept?	16:03:16	7	Q. Do you understand the sections that are	16:07:42
8	MR. COBB: Objection. Form.	16:03:23	8	associated with these headers to refer to clinical	16:07:43
9	BY MS. CORK:	16:03:24	9	studies of VEGF Trap-Eye?	16:07:46
10	Q. Withdrawn.	16:03:25	10	A. I know that they correspond to clinical trials,	16:07:57
11	Does this drug substance have the same	16:03:25	11	specifically Phase II and Phase III clinical trials. And	16:08:00
12	molecular structure as aflibercept?	16:03:28	12	in 2.6.3, it specifically says, "A two-part Phase III	16:08:06
13	A. Today we know that it has the same primary	16:03:38	13	trial of VEGF Trap-Eye was initiated in August of 2007."	16:08:15
14	structure, which I presume what you mean by molecular	16:03:41	14	But as I said, both of these sections are part	16:08:22
15	structure. As of -- as of January 13, 2011, we did not	16:03:45	15	of the clinical efficacy section of Dixon, and that's not	16:08:25
16	know that. That's the first part of the answer.	16:03:53	16	my area of expertise. I have not been asked to form	16:08:33
17	And the second part of the answer, I mean,	16:03:56	17	opinions, nor have I opined on these aspects of Dixon.	16:08:37
18	again, you are introducing the term, "molecular	16:03:59	18	Q. So you're not able to comment on how many drugs	16:08:46
19	structure," which you know has been very controversial in	16:04:03	19	were evaluated in the Phase I, Phase II, or Phase III	16:08:53
20	this case; and for somebody who wants to have a clear	16:04:09	20	clinical trials of VEGF Trap-Eye described in Dixon?	16:08:58
21	record, I mean, that's the way to achieve just the	16:04:12	21	MR. COBB: Objection. Form.	16:09:02
22	opposite.	16:04:14	22	THE WITNESS: Okay. I have nothing to add	16:09:05
23	Q. Is it also your view that Dixon refers to VEGF	16:04:44	23	beyond what, you know, I stated in my expert -- in my	16:09:08
24	Trap-Eye as a drug product?	16:04:47	24	declaration with respect to Dixon.	16:09:13
25	MR. COBB: Objection. Form.	16:04:51	25	My focus has not been on the clinical efficacy	16:09:19
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1	THE WITNESS: It appears that in some	16:05:08	1	sections of Dixon. I haven't even read those sections	16:09:22
2	instances, Dixon refers to VEGF Trap-Eye as a drug	16:05:09	2	for quite some time.	16:09:26
3	product, at least that's my understanding.	16:05:16	3	BY MS. CORK:	16:09:27
4	BY MS. CORK:	16:05:19	4	Q. Do you have any opinions regarding the number	16:09:33
5	Q. And what portions of Dixon do you believe	16:05:20	5	of drugs that are tested in the Phase I, Phase II, or	16:09:35
6	support your view that VEGF Trap-Eye is a drug product?	16:05:22	6	Phase III studies of VEGF Trap-Eye described in Dixon?	16:09:39
7	A. For example, when it refers to -- in the	16:05:34	7	A. I would need to refresh my memory with respect	16:09:50
8	abstract, when it refers to it as a therapy, and it	16:05:39	8	to the clinical trials sections of Dixon, because, as I	16:09:51
9	specifically says -- it is the first sentence in the	16:05:47	9	said, I haven't read those in quite some time, and that's	16:09:58
10	Results/Conclusions that VEGF Trap-Eye is a novel VEGF	16:05:49	10	what I would need to do and read them, of course, in the	16:10:03
11	therapy.	16:05:56	11	context of the entirety of Dixon.	16:10:06
12	A drug substance cannot be a therapy. So I	16:06:00	12	Q. Let's go to page 5 of Dixon.	16:10:31
13	think that most likely is a reference to the drug	16:06:05	13	A. Okay.	16:10:33
14	product.	16:06:10	14	Q. Do you see the header, "Expert opinion"?	16:10:33
15	Q. An active ingredient can't have a therapeutic	16:06:12	15	A. I do.	16:10:36
16	effect?	16:06:15	16	Q. Do you see the top right column of page 5 of	16:10:42
17	MR. COBB: Objection. Form.	16:06:16	17	Dixon, the first full paragraph?	16:10:45
18	THE WITNESS: An active ingredient can and does	16:06:19	18	A. Yes.	16:10:48
19	have a therapeutic effect, but you don't use an active	16:06:22	19	Q. Dixon states: "VEGF Trap-Eye represents the	16:10:51
20	ingredient by itself to exert a therapeutic effect or to	16:06:29	20	most promising anti-VEGF investigational drug that is	16:10:55
21	exert therapeutic treatment. It has to be formulated in	16:06:34	21	currently in a Phase III trial."	16:10:59
22	a certain way, and that is what the therapy would be	16:06:38	22	Do you see that?	16:11:02
23	understood to be by a person of ordinary skill in the	16:06:47	23	A. I do.	16:11:03
24	art.	16:06:49	24	Q. Dixon states: "VEGF Trap-Eye, a decoy VEGF	16:11:05
25	//		25	receptor protein, binds all isoforms of free VEGF with	16:11:11
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1 high affinity, in addition to placental growth factor." 16:11:18	1 said in my previous answer. 16:15:18
2 Do you see that? 16:11:20	2 BY MS. CORK: 16:15:55
3 A. I do. 16:11:21	3 Q. Let's go back to page 4, which has the 16:15:55
4 Q. Do you dispute that Dixon refers to VEGF 16:11:21	4 Figure 1, of Dixon. 16:16:00
5 Trap-Eye as a decoy VEGF receptor protein? 16:11:25	5 Do you see that? 16:16:01
6 MR. COBB: Objection. The document speaks for 16:11:33	6 A. I do. 16:16:02
7 itself; form. 16:11:34	7 Q. Is it your opinion that Figure 1 of Dixon is 16:16:03
8 THE WITNESS: All I can tell you right now is 16:11:36	8 not limited to representing a structure with a single 16:16:05
9 that you correctly read these two sentences. This is not 16:11:37	9 amino acid sequence of VEGF Trap-Eye? 16:16:13
10 the portion of Dixon that I've been asked to form 16:11:41	10 A. I will ask you to repeat this question slowly 16:16:17
11 opinions on, and that's not the section of Dixon that I 16:11:43	11 and louder, please. 16:16:20
12 have opined on. But you read the two sentences 16:11:46	12 Q. How many fusion proteins do you see in Figure 1 16:16:28
13 correctly. 16:11:49	13 of Dixon? 16:16:31
14 BY MS. CORK: 16:11:50	14 A. Dixon, as stated in caption to Figure 1, 16:16:44
15 Q. You are not offering any opinions about the 16:11:54	15 provides a schematic diagram, so a schematic diagram of 16:16:48
16 portion of Dixon that is described as the expert opinion? 16:11:56	16 VEGF Trap-Eye, which is a fusion protein. And as I 16:16:55
17 MR. COBB: Objection. Mischaracterizes his 16:12:01	17 discuss in much detail in my declaration, this particular 16:17:00
18 testimony. 16:12:05	18 schematic diagram encompasses a number of different amino 16:17:06
19 THE WITNESS: The opinions that I formed on 16:12:06	19 acid sequences, or can encounter -- can, I'm sorry, 16:17:15
20 Dixon are those that are in my '681 declaration. That's 16:12:07	20 encompass a number of different amino acid sequences. 16:17:22
21 the extent of my opinions that I offer with respect to 16:12:16	21 Q. Does Figure 1 of Dixon describe VEGF Trap-Eye 16:17:27
22 this particular reference. 16:12:23	22 as a genus of structures? 16:17:31
23 BY MS. CORK: 16:12:25	23 MR. COBB: Objection. Form. 16:17:36
24 Q. Would you describe yourself as an expert in 16:12:53	24 THE WITNESS: Okay. I don't want to use legal 16:17:49
25 protein chemistry? 16:12:55	25 terms. Okay? As I just said, this schematic diagram in 16:17:51
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1 A. I would, and I have today. 16:13:02	1 scheme 1 of Dixon encompasses a number -- or can 16:17:58
2 Q. When you see the sentence in Dixon that "VEGF 16:13:05	2 encompass a number of different amino acid sequences. 16:18:02
3 Trap-Eye is a decoy VEGF receptor protein," do you 16:13:08	3 Due to the intrinsic imprecision of what's involved or 16:18:06
4 understand that to refer to a single protein? 16:13:13	4 what is here, VEGFR1 receptor -- I'm sorry -- R1 Domain 16:18:15
5 A. We already had that discussion about an "a," 16:13:17	5 2, VEGFR2 Domain 3, and the Fc portion of the molecule 16:18:29
6 the article "a" previously, and, as I said, it -- its 16:13:22	6 schematically represented in Figure 1. 16:18:45
7 meaning depends on the context; and to evaluate this 16:13:28	7 BY MS. CORK: 16:18:58
8 context, I would need to re-review Dixon in its entirety. 16:13:32	8 Q. But as you just read, the legend of Figure 1 16:18:58
9 Q. So you can't understand what a sentence means 16:13:41	9 refers to a schematic diagram of VEGF Trap-Eye, a fusion 16:19:01
10 in Dixon unless you re-read the entire article? 16:13:44	10 protein, correct? 16:19:08
11 A. I need to read some of the particular -- some 16:13:47	11 MR. COBB: Objection. The document speaks for 16:19:09
12 of the sentences, including this sentence, in the context 16:13:51	12 itself; form. 16:19:10
13 of the article, because, as I already indicated and 16:13:55	13 THE WITNESS: I mean, the sentence says what it 16:19:11
14 illustrated, Dixon uses the terms inconsistently. 16:14:02	14 says. 16:19:13
15 And therefore, given that, I would need to -- 16:14:10	15 BY MS. CORK: 16:19:13
16 in particular that late in the deposition, I would need 16:14:13	16 Q. And it's true that there is only one fusion 16:19:14
17 to re-evaluate, or evaluate the meaning of this sentence 16:14:18	17 protein structure reflected in Figure 1 of Dixon, right? 16:19:17
18 in the context of the entirety of Dixon. 16:14:24	18 MR. COBB: Objection. Form. 16:19:22
19 Q. So simply reading the sentence VEGF Trap-Eye 16:14:56	19 THE WITNESS: Well, as I just indicated to you, 16:19:30
20 that is described as a decoy VEGF receptor protein, you 16:15:00	20 the schematic diagram that's provided there, today we 16:19:32
21 can't interpret that sentence one way or the other in 16:15:05	21 know what it is, but as of the time of the Dixon 16:19:39
22 isolation. 16:15:13	22 publication, which was 2009, it could have encompassed a 16:19:41
23 MR. COBB: Objection. Asked and answered; 16:15:14	23 number of different primary structures. 16:19:48
24 form. 16:15:15	24 BY MS. CORK: 16:19:56
25 THE WITNESS: I have nothing to add to what I 16:15:15	25 Q. How many of those primary structures does Dixon 16:20:01
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1 describe? 16:20:05	1 A. Among others. 16:23:53
2 A. Dixon doesn't use the term "primary structure." 16:20:08	2 Q. Do any of those references, to the extent you 16:23:54
3 It doesn't provide any primary structures. It doesn't 16:20:12	3 rely on them, describe combinations of VEGF receptor 16:23:57
4 talk about that at all. 16:20:15	4 domains? 16:24:04
5 The closest that Dixon has come to it is using 16:20:17	5 MR. COBB: Objection. Vague; form. 16:24:07
6 the term "molecular structure," which, of course, has 16:20:20	6 THE WITNESS: They discuss the basic principles 16:24:14
7 been much discussed in the context of the '681 Patent. 16:20:23	7 of protein chemistry and biochemistry, and the 16:24:16
8 Q. Does Dixon identify any structural differences 16:20:35	8 combination of the domains that you referred to certainly 16:24:18
9 of any kind between aflibercept and VEGF Trap-Eye? 16:20:39	9 falls under that umbrella. 16:24:27
10 A. Dixon just doesn't deal with that issue at all. 16:20:47	10 BY MS. CORK: 16:24:29
11 The only thing that Dixon says, as, you know, we 16:20:50	11 Q. Do any of those references describe 16:24:34
12 discussed previously, and as I indicate and discuss in my 16:20:54	12 combinations of VEGF receptor domains in the form of 16:24:37
13 declaration, is, in Section 2.3, "Chemistry," where Dixon 16:21:01	13 fusion proteins, to the extent you rely on them? 16:24:42
14 says that VEGF Trap-Eye and aflibercept (the oncology 16:21:06	14 MR. COBB: Objection. Vague. 16:24:46
15 product) have the same molecular structure. 16:21:11	15 THE WITNESS: Not specifically, but they 16:24:50
16 But there are substantial differences between 16:21:17	16 describe general principles of protein chemistry and 16:24:51
17 the preparation of the purified drug product and their 16:21:20	17 biochemistry, as I've already discussed in much detail 16:24:56
18 formulations. So that's the closest -- the term 16:21:24	18 today, that govern a number of things, including such 16:24:58
19 "molecular structure" is the closest that Dixon comes to 16:21:27	19 combinations; and namely that the boundaries, if you -- 16:25:02
20 discussing any structural aspects, along with Figure 1. 16:21:32	20 if you will, of the domains are not precisely defined, 16:25:07
21 Q. And Dixon says that aflibercept and VEGF 16:21:40	21 which is really what the issue at hand is. 16:25:11
22 Trap-Eye have the same molecular structure? 16:21:45	22 BY MS. CORK: 16:25:15
23 MR. COBB: Objection. Form; the document 16:21:48	23 Q. Are you aware of any specific combination of 16:25:32
24 speaks for itself. 16:21:50	24 VEGF receptor domains in the form of a fusion protein, 16:25:35
25 THE WITNESS: Dixon specifically says VEGF 16:21:55	25 other than the structure reflected in Figure 1 of Dixon? 16:25:41
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1 Trap-Eye and aflibercept have the same molecular 16:21:57	1 A. I'm also aware of what I view as an equivalent 16:26:01
2 structure. That's what Dixon says, as I obviously 16:22:01	2 presentation or equivalent depiction in the Holash 16:26:06
3 discuss in much detail in my declaration. 16:22:06	3 article, H-o-l-a-s-h, article, and I discuss both of 16:26:13
4 BY MS. CORK: 16:22:10	4 those side by side in my declaration. 16:26:18
5 Q. Looking at Dixon, and only Dixon, is there 16:22:14	5 And I could specifically invite you to 16:26:27
6 anything in Dixon that you are aware of that suggests 16:22:17	6 paragraph 81 on page 39 of my '681 Patent declaration. 16:26:42
7 that VEGF Trap-Eye has more than one amino acid sequence? 16:22:21	7 Q. Are you able -- withdrawn. 16:27:11
8 A. Yes. 16:22:28	8 Are you unable to answer the question of 16:27:13
9 Q. What do you mean? 16:22:31	9 whether VEGF Trap-Eye has more than one amino acid 16:27:16
10 A. Because when you look -- when -- if a person of 16:22:34	10 sequence looking only at the Dixon reference? 16:27:19
11 ordinary skill in the art looks at Dixon, and of course 16:22:37	11 MR. COBB: Objection. Form. 16:27:27
12 this person would not look at only Dixon, would not have 16:22:41	12 THE WITNESS: First of all, I didn't evaluate 16:27:28
13 the blinders on, okay, but the fact -- this person would 16:22:44	13 issues -- I mean, I cannot delete from my mind what I 16:27:31
14 immediately understand that as of the date of Dixon's 16:22:49	14 know, and I obviously have reviewed the literature in its 16:27:36
15 publication, which is 2009, there were more than one 16:22:55	15 entirety. So I cannot look just at the Dixon alone and 16:27:41
16 structures that would be encompassed by what is shown on 16:23:02	16 pretend that I don't know anything else, because I do. 16:27:47
17 the right-hand side in Figure 1. 16:23:10	17 But the fact of the matter is that Dixon does 16:27:50
18 Q. What other references are you referring to that 16:23:21	18 not define where the domain ends, where the domain 16:27:53
19 show those structures? 16:23:24	19 begins, and therefore necessarily, even looking just at 16:28:00
20 A. Those that I discussed in my declaration, 16:23:28	20 Dixon itself, one would know that more than one -- that 16:28:06
21 specifically in paragraphs, for instance, 65 and 66 that 16:23:31	21 more than one molecule is encompassed. 16:28:13
22 we talked about, and the multiple references that are 16:23:39	22 And, indeed, that is what I discuss, as we 16:28:18
23 referenced there. 16:23:42	23 talked about earlier, in a section that begins on page 41 16:28:21
24 Q. You're referring to section 10-A-2 of your 16:23:45	24 of my declaration. 16:28:28
25 declaration? 16:23:50	25 //
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1 BY MS. CORK: 16:28:35 2 Q. Could you go to paragraph 80 of your 16:28:53 3 declaration. 16:28:55 4 A. Okay. I'm reading it to myself. Yes, ma'am. 16:28:59 5 Q. Near the bottom of paragraph 80 you say that 16:29:53 6 "Dixon defines VEGF Trap-Eye's" -- 16:29:55 7 A. I'm sorry. Which sentence are you reading? 16:29:58 8 Q. Do you see the sentence that begins, "In some"? 16:30:02 9 A. Yes. 16:30:06 10 Q. You say that, "given that Dixon defines VEGF 16:30:08 11 Trap-Eye's structure only by its domain's composition, 16:30:13 12 and nothing more." 16:30:17 13 Do you see that? 16:30:18 14 A. I do. 16:30:19 15 Q. Isn't it true that Dixon defines VEGF Trap-Eye 16:30:20 16 with respect to the molecular structure of aflibercept? 16:30:24 17 MR. COBB: Objection. Form. 16:30:42 18 THE WITNESS: Well, what is -- what is 16:30:52 19 described in Figure 1 is outlined in Section 2.2, which 16:30:54 20 is "Introduction to compound." And what it says there 16:31:02 21 is, "Structurally, VEGF Trap-Eye is a fusion protein of 16:31:04 22 key binding domains of human VEGFR-1 and -2 combined with 16:31:11 23 human IgG Fc fragment (Figure 1)." That is what Dixon 16:31:21 24 says in the text is described in Figure 1. 16:31:28 25 // Page 186	1 combined with a human IgG Fc fragment (Figure 1)," full 16:33:27 2 stop. So it is very clear what Figure 1 does or depicts 16:33:37 3 according to Dixon's own description. There is no 16:33:44 4 ambiguity here. 16:33:49 5 Q. Do you understand that you have to answer the 16:33:53 6 questions that I ask you, and not the questions that you 16:33:56 7 would like to answer? 16:33:59 8 A. I do. And I also understand that I don't 16:34:02 9 necessarily have to give you the answer that you want. I 16:34:05 10 give you the best answer I can give you, because I am 16:34:09 11 under oath. And that is what I have been trying to do 16:34:14 12 throughout this deposition. 16:34:20 13 Q. My previous question did not mention Figure 1 16:34:23 14 at all, but maybe you misunderstood. So I'll ask it 16:34:26 15 again. Okay? Is that okay? 16:34:30 16 A. I don't know what "okay" means here. Are you 16:34:38 17 asking my permission to ask a question? I don't know 16:34:41 18 what you mean by "okay." 16:34:44 19 Q. Is it your opinion that the VEGF Trap-Eye 16:34:46 20 described in the section titled, "Introduction to 16:34:48 21 compound" is a different structure than the VEGF Trap-Eye 16:34:51 22 referred to in Section 2.3 of Dixon titled, "Chemistry"? 16:34:56 23 A. I don't think it's a different structure. But 16:35:04 24 it's not entirely clear where -- whether VEGF Trap-Eye in 16:35:07 25 the context of Section 2.3 refers to the drug substance, 16:35:14 Page 188
1 BY MS. CORK: 16:31:36 2 Q. You're cherry-picking, to use your word, from 16:31:42 3 Section 2.2, and not from Section 2.3, where Dixon states 16:31:44 4 that VEGF Trap-Eye and aflibercept have the same 16:31:50 5 molecular structure, right? 16:31:54 6 MR. COBB: Objection. Form. Is that a 16:31:57 7 question? 16:32:02 8 THE WITNESS: I disagree with your 16:32:03 9 characterization. There is no reference to Figure 1 in 16:32:04 10 Section 2.3, "Chemistry." It's not there. 16:32:07 11 But there is an express reference to Figure 1 16:32:11 12 in Section 2.2, "Introduction to compound." 16:32:16 13 So you're mistaken, madam. 16:32:24 14 BY MS. CORK: 16:32:26 15 Q. Is it your opinion that the VEGF Trap-Eye 16:32:27 16 described in the section titled, "Introduction to 16:32:29 17 compound" is a different structure than the VEGF Trap-Eye 16:32:31 18 referred to in Section 2.3, titled, "Chemistry"? 16:32:36 19 A. As I said, there is some ambiguity about what 16:32:51 20 the term "VEGF Trap-Eye" means in Dixon, because it 16:32:54 21 varies depending on where it is cited. 16:32:58 22 But the fact of the matter is that it's very 16:33:02 23 clear how Dixon refers to Figure 1, and specifically 16:33:04 24 Dixon says, "Structurally, VEGF Trap-Eye is a fusion 16:33:12 25 protein of key binding domains of human VEGFR-1 and -2 16:33:17 Page 187	1 as opposed to a drug product. It's not entirely clear. 16:35:22 2 It's a contra -- it's an intrinsically contradictory 16:35:25 3 statement. Because aflibercept, it specifically says, 16:35:32 4 the oncology product. So that's a product, not a 16:35:35 5 substance. 16:35:38 6 So it's not entirely clear, and that's what I 16:35:40 7 think I've already answered. But there is no such 16:35:42 8 ambiguity with respect to Section 2.2. 16:35:47 9 Q. Do you recall previously testifying that you 16:36:08 10 couldn't recall if you had been involved in the 16:36:10 11 development of an ophthalmologic formulation for 16:36:15 12 intravitreal administration? 16:36:17 13 A. I think I recall something to that effect, yes. 16:36:20 14 Q. That was nearly two years ago? 16:36:24 15 MR. COBB: Objection. Vague. 16:36:29 16 THE WITNESS: I -- 16:36:30 17 MR. COBB: Form. 16:36:31 18 THE WITNESS: I -- I don't understand. Are you 16:36:32 19 referring to today's deposition, or are you referring to 16:36:35 20 a deposition that took place about two years ago? 16:36:39 21 BY MS. CORK: 16:36:41 22 Q. I'm referring to your prior testimony. That 16:36:42 23 was nearly two years ago, right? 16:36:44 24 A. I don't remember what I -- excuse me -- what I 16:36:46 25 may have said about two years ago. 16:36:51 Page 189

1 Q. Can you clarify today whether you have ever 16:36:55	1 law." 16:47:34
2 developed an ophthalmologic formulation for intravitreal 16:36:58	2 Q. Have you ever heard of a molecule called 16:47:38
3 administration? 16:37:05	3 ZIV-aflibercept? 16:47:41
4 A. I mean, I just -- at the moment, sitting here 16:37:06	4 A. How do you spell it? Slowly. 16:47:44
5 today, I just don't recall. If I previously said that I 16:37:08	5 Q. Z-I-V, hyphen, aflibercept. 16:47:47
6 was involved in that, then I was. Right now, I have no 16:37:12	6 A. Again, I'm not sure one way or the other. 16:47:55
7 clear recollection. 16:37:16	7 MS. CORK: I'd like to mark as Exhibit 21 16:48:16
8 Q. Sitting here today, you have no recollection of 16:37:20	8 Exhibit 2012 in this proceeding, a copy to counsel. 16:48:18
9 whether you have ever developed an ophthalmologic 16:37:22	9 (Exhibit 21 was marked for identification.) 16:48:21
10 formulation for intravitreal administration. 16:37:26	10 THE REPORTER: Exhibit 21. 16:48:35
11 A. For what? 16:37:30	11 THE WITNESS: Thank you. 16:48:37
12 Q. Intravitreal administration. 16:37:30	12 BY MS. CORK: 16:48:38
13 A. I don't understand. Just -- repeat the 16:37:35	13 Q. Do you recognize Exhibit 21? 16:48:38
14 question again, please, slowly. 16:37:38	14 A. Yes. 16:48:42
15 Q. Have you ever developed a drug formulation for 16:37:40	15 Q. Do you refer to Exhibit 21 in your declaration 16:48:44
16 injection into the eye? 16:37:43	16 as the Adis, A-d-i-s, reference? 16:48:47
17 A. I already told you, sitting here right now, I 16:37:47	17 A. Correct. 16:48:52
18 do not specifically recall one way or the other. If I 16:37:49	18 Q. Sitting here today, are you aware of anything 16:48:55
19 testified two years ago that I had, then that's the 16:37:54	19 factually inaccurate in the Adis reference? 16:48:59
20 answer. I apparently remembered it then, but I do not 16:37:58	20 MR. COBB: Objection. Form. 16:49:15
21 recall it now during this seventh hour of a deposition. 16:38:04	21 THE WITNESS: I mean, there are several 16:49:16
22 MR. COBB: Counsel, we've been going about an 16:38:10	22 inaccuracies, but one of them is right on -- and, you 16:49:18
23 hour and 20 minutes, and it seems like you've moved on 16:38:11	23 know, I obviously -- in answering your question in more 16:49:22
24 from that previous exhibit. So maybe we'd break. 16:38:14	24 detail, I will just go to my declaration, where I 16:49:25
25 MS. CORK: I think I only have about five more 16:38:19	25 specifically discuss Adis, but I can tell you right now, 16:49:29
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1 minutes. 16:38:21	1 just looking at Adis, that even the title of Adis, where 16:49:32
2 MR. COBB: Okay. Sure. 16:38:22	2 it first says, aflibercept, and then it names a number of 16:49:39
3 THE WITNESS: I would still like to take a 16:38:23	3 different species, including VEGF Trap - Regeneron, VEGF 16:49:47
4 break if at all possible. There is no question pending, 16:38:24	4 Trap (R1R2), and VEGF Trap-Eye, so it -- it seems to 16:49:56
5 right? 16:38:30	5 equate aflibercept to those, and that's just inaccurate. 16:50:05
6 MS. CORK: Yes, that's fine. We can take a 16:38:32	6 Because aflibercept is a particular molecule, and those 16:50:10
7 break. 16:38:33	7 species I just mentioned are groups of molecules. 16:50:15
8 THE WITNESS: Thank you. 16:38:34	8 But, you know, if you want a more complete 16:50:23
9 THE VIDEOTAPE OPERATOR: Off the record at 4:39 16:38:35	9 answer, I'll be happy to go to my declaration and, you 16:50:26
10 p.m. 16:38:37	10 know, cite from there, or basically tell you more, based 16:50:34
11 (Recess was taken.) 16:38:37	11 on what I said there, where, as you know, I specifically 16:50:38
12 THE VIDEOTAPE OPERATOR: Back on the record 16:46:23	12 discuss Adis starting on page 15. 16:50:42
13 beginning Media Unit 6 at 4:47 p.m. 16:46:24	13 BY MS. CORK: 16:50:50
14 BY MS. CORK: 16:46:32	14 Q. Would it be fair to say that any factual 16:50:56
15 Q. Dr. Klibanov, have you ever developed a VEGF 16:46:34	15 inaccuracies that you found in Adis are listed in your 16:50:58
16 antagonist formulation? 16:46:36	16 declaration? 16:51:02
17 A. I have no specific recollection one way or the 16:46:49	17 A. Well, first of all, I already mentioned one of 16:51:08
18 other. 16:46:52	18 them to you now; also not any factual inaccuracies, but 16:51:11
19 Q. You're not a patent lawyer; is that right? 16:46:57	19 factual inaccuracies that pertain to my area of 16:51:16
20 A. That, I do know that I'm not. 16:47:00	20 expertise. 16:51:21
21 Q. Do you have any training in patent law? 16:47:04	21 Q. Are you aware of any factual inaccuracies in 16:51:23
22 A. No. In fact, I would specifically invite your 16:47:07	22 Adis that are not listed in your declaration? 16:51:27
23 attention to section 5, paragraph 22 of my '681 Patent 16:47:14	23 A. I mean, I -- I didn't make it my objective to 16:51:34
24 declaration, which says -- the first sentence of which 16:47:26	24 provide an exhaustive list of factual inaccuracies in 16:51:37
25 says, "I am not an attorney or an expert in U.S. patent 16:47:30	25 Adis, which, you know, I -- as I discuss in my 16:51:43
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1 declaration, is an anonymous document. We don't know who 16:51:47 2 wrote it. We don't know whether those views and opinions 16:51:53 3 were ever peer-reviewed. You know, it doesn't read like 16:51:59 4 a scientific paper. 16:52:07 5 But in any event, I did not make it -- I did 16:52:09 6 not make it my objective to provide an exhaustive list of 16:52:11 7 inaccuracies in Adis. I said what I said about Adis in 16:52:17 8 paragraphs 44 and 45, which are lengthy paragraphs, 16:52:26 9 because I believe that that's what was necessary to 16:52:38 10 respond to Dr. Chaum's opinions. 16:52:42 11 Q. Did you discuss the substance of your testimony 16:53:01 12 with your counsel in any of the breaks today? 16:53:04 13 A. No. 16:53:07 14 MS. CORK: No more questions. 16:53:14 15 MR. COBB: I have no redirect. 16:53:15 16 THE VIDEOTAPE OPERATOR: Off the record at 4:54 17 p.m. 18 (The deposition adjourned at 4:54 p.m.) 19 * * * 20 21 22 23 24 25 // Page 194	1 REPORTER'S CERTIFICATE 2 3 I, Rosalie A. Kramm, Certified Shorthand 4 Reporter for the State of California, do hereby 5 certify: 6 That the witness named in the foregoing 7 deposition was by me duly sworn; that the 8 deposition was then taken before me at the time 9 and place herein set forth; that the testimony 10 and proceedings were reported stenographically 11 by me and were transcribed through computerized 12 transcription by me; that the foregoing is a 13 true record of the testimony and proceedings 14 taken at that time; and that I am not 15 interested in the event of the action. 16 Witness my hand dated December 21, 2023. 17 18 19 20 21 22 23 24 25  Rosalie A. Kramm CSR 5469, RPR, CRR Page 196
1 I declare under penalty of perjury, under the 2 laws of the State of California, that the foregoing 3 testimony, as corrected, is the truth, the whole truth, 4 and nothing but the truth. 5 6 7 8 <u>ALEXANDER M. KLIBANOV, PH.D.</u> 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 Page 195	

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[agree - angiogenic]

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