

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

3 -----
4 MYLAN PHARMACEUTICALS INC.,
5 Petitioner

6 vs

7 NOVO NORDISK A/S,
8 Patent Owner
9 -----

10 Case IPR2023-00724

11 U.S. Patent No. 10,335,462

12
13 Oral deposition of
14 JULIO ROSENSTOCK, M.D.

15
16 WASHINGTON, DC

17 WEDNESDAY, MAY 15, 2024

18 9:08 a.m. EASTERN TIME
19

20 Job No.: 534432

21 Pages: 1 - 242

22 Reported by: Lisa V. Feissner, RDR, CRR, CLR

1
2
3 Oral deposition of JULIO ROSENSTOCK,
4 M.D., held at the offices of:

5
6 PERKINS COIE, LLP
7 700 THIRTEENTH STREET, NW
8 SUITE 800
9 WASHINGTON, DC 20005
10 202.654.6200
11

12 Pursuant to Notice, before Lisa V.
13 Feissner, RDR, CRR, CLR, Notary Public.
14
15
16
17
18
19
20
21
22

1 A P P E A R A N C E S:

2 ON BEHALF OF PETITIONER:

3 DAVID L. ANSTAETT, ESQUIRE

4 BRANDON M. WHITE, ESQUIRE (DC office)

5 AARON SCHINDLER, ESQUIRE (Zoom)

6 PERKINS COIE LLP

7 33 East Main Street, Suite 201

8 Madison, WI 53703-3095

9 608.663.5408

10 danstaett@perkinscoie.com

11 bmwhite@perkinscoie.com

12 aschindler@perkinscoie.com

13
14 ON BEHALF OF PATENT OWNER:

15 J. STEVEN BAUGHMAN, ESQUIRE

16 JOSHUA REICH, ESQUIRE (NY office)

17 GROOMBRIDGE WU BAUGHMAN & STONE LLP

18 801 17th Street, NW, Suite 1050

19 Washington, DC 20006

20 202.539.6620

21 steve.baughman@groombridgewu.com

22 joshua.reich@groombridgewu.com

C O N T E N T S

EXAMINATION OF JULIO ROSENSTOCK, M.D.	PAGE
By Mr. Anstaett	6
By Mr. Baughman	234
By Mr. Anstaett	238

E X H I B I T S

(Attached to transcript)

MPI EXHIBITS	PAGE
1130 Novo Nordisk Annual Report 2011	109
1131 Novo Nordisk A/S Form 6-K dated February 2, 2011	130

P R E V I O U S L Y

M A R K E D E X H I B I T S

(identified but not attached)

EXHIBITS	PAGE
MPI Exhibit 1001	9
MPI Exhibit 1012	188
MPI Exhibit 1014	75
Novo Nordisk Exhibit 2006	85
Novo Nordisk Exhibit 2010	8
Novo Nordisk Exhibit 2060	41
Novo Nordisk Exhibit 2061	39
Novo Nordisk Exhibit 2062	54
Novo Nordisk Exhibit 2063	47
Novo Nordisk Exhibit 2064	69
Novo Nordisk Exhibit 2065	103
Novo Nordisk Exhibit 2075	209

Transcript of Julio Rosenstock, M.D.
Conducted on May 15, 2024

6

P R O C E E D I N G S

JULIO ROSENSTOCK, M.D.,

having been first duly sworn, was examined and
testified as follows:

09:08:56

EXAMINATION

09:08:56

BY MR. ANSTAETT:

09:08:56

Q Good morning, Doctor. Could you please
state your name for the record.

09:08:57

09:08:59

A Julio Rosenstock.

09:08:59

Q Have you ever had your deposition taken?

09:09:02

A First time.

09:09:03

Q I will do my best today to ask clear
questions, but I'm sure at some point I'll fail to
do that. So if you don't understand a question,
please let me know, and I will try to rephrase it
and ask a better one, okay?

09:09:04

09:09:08

09:09:11

09:09:12

09:09:15

A Thanks.

09:09:17

Q It's very natural in a deposition to nod
your head or shake your head as an answer, but you
have to give verbal answers because we're creating a
transcript. So please remember to do that, okay?

09:09:17

09:09:22

09:09:24

09:09:27

A Understand.

09:09:29

PLANET DEPOS

888.433.3767 | WWW.PLANETDEPOS.COM

MPI EXHIBIT 1313 PAGE 6

1 Q All right. We'll try not to talk over
2 each other. That will make Lisa's job a lot easier
3 today.

4 Your counsel may object from time to
5 time, which he is perfectly entitled to do. But
6 unless he instructs you not to answer the question,
7 please go ahead and answer, all right?

8 A I'm sorry. If he instructs me?

9 Q If he instructs you not to answer the
10 question, then I'll leave it up to you whether to
11 follow that instruction. But if he doesn't instruct
12 you not to answer, you can go ahead and answer,
13 notwithstanding the objection, okay?

14 A I understand.

15 Q If you want to break at any time today,
16 just let me know, and we'll do that.

17 A Thanks.

18 Q What did you do to prepare for your
19 deposition today?

20 A I read all the documents. I went through
21 all the documents that were given to me. I read the
22 deposition from Dr. Bantle, Dr. Jusko, and I read

1 all the evidence that I could get and analyzed it.

09:10:23

2 Q Okay. And I want to be clear. I don't
3 want to hear about any conversations you had with
4 your lawyers. But did you meet with your lawyers to
5 prepare for your deposition?

09:10:26

09:10:28

09:10:30

09:10:32

6 A Yes, I did.

09:10:33

7 Q How long did you meet with them?

09:10:34

8 A Several times.

09:10:38

9 Q About how many hours all together, would
10 you estimate?

09:10:38

09:10:41

11 A A good number of hours.

09:10:41

12 Q Ten?

09:10:42

13 A Oh, more than that.

09:10:44

14 Q More than that? 20?

09:10:45

15 A It could be. I mean, depends -- I spent
16 hours reading the literature. I spent hours reading
17 the documents. I also spent a fair amount of time
18 over the phone and face to face with them.

09:10:47

09:10:51

09:10:55

09:10:59

19 MR. ANSTAETT: Okay. All right. Well,
20 let's go ahead and mark an exhibit for you -- or
21 give you an exhibit which has already been marked.

09:11:02

09:11:04

09:11:12

22 (Previously marked Exhibit 2010 presented

09:11:12

1	to the witness.)	09:11:12
2	BY MR. ANSTAETT:	09:11:21
3	Q So I'm handing you what's been marked as	09:11:21
4	Exhibit 2010.	09:11:23
5	A Thank you.	09:11:25
6	Q Do you recognize what's been marked as	09:11:31
7	Exhibit 2010 as the declaration that you submitted	09:11:34
8	in these proceedings?	09:11:36
9	A Yes, I do.	09:11:37
10	MR. ANSTAETT: And then let me give you	09:11:38
11	one more exhibit.	09:11:40
12	(Previously marked Exhibit 1001 presented	09:11:40
13	to the witness.)	09:11:40
14	BY MR. ANSTAETT:	09:12:05
15	Q I'm handing you what's been marked as	09:12:05
16	Exhibit 1001.	09:12:08
17	And do you recognize that what I've	09:12:15
18	handed you marked as Exhibit 1001 is the Novo	09:12:18
19	Nordisk's U.S. Patent No. 10,335,462?	09:12:23
20	A What's the number again?	09:12:29
21	Q 10,335,462.	09:12:31
22	A Yes.	09:12:35

1	Q	And you're familiar with that patent, I	09:12:36
2		take it?	09:12:38
3	A	Yes, sir.	09:12:38
4	Q	And if I refer to that today as the '462	09:12:38
5		patent, you'll understand what I'm talking about?	09:12:41
6	A	Yes, sir.	09:12:43
7	Q	In your declaration, Exhibit 2010, at	09:12:44
8		paragraph 39 -- you say at paragraph 39 --	09:12:54
9	A	39, I'm sorry.	09:13:13
10	Q	Oh, that's okay.	09:13:14
11		You say at paragraph 39 that, My	09:13:22
12		conclusions of nonobviousness herein do not depend	09:13:25
13		on considerations of objective indicia of	09:13:28
14		nonobviousness, which I understand are being	09:13:32
15		addressed elsewhere?	09:13:33
16		Do you see that?	09:13:34
17	A	Yes, sir.	09:13:35
18	Q	Okay. So in your declaration, you're not	09:13:35
19		offering any opinions on objective indicia of	09:13:37
20		nonobviousness, correct?	09:13:42
21	A	Correct.	09:13:42
22	Q	Okay. And did you review the	09:13:43

1	declarations of any of Novo Nordisk's other expert	09:13:45
2	witnesses in this matter?	09:13:48
3	A Can you repeat again?	09:13:51
4	Q Sure. Did you review the declarations of	09:13:52
5	any of Novo Nordisk's other expert witnesses in this	09:13:54
6	matter? So Dr. Goland or Dr. Bakris, Dr. Blaha?	09:13:58
7	A No, sir.	09:14:05
8	Q And then you say in paragraph 46 of your	09:14:06
9	declaration that you understand that the board has	09:14:10
10	instituted an IPR of claims 1 to 10 of the '462	09:14:15
11	patent.	09:14:20
12	Do you see that?	09:14:20
13	A Yes, sir.	09:14:22
14	Q Did you review the board's institution	09:14:22
15	decision?	09:14:25
16	A The actual board institution decision? I	09:14:26
17	reviewed this, but the -- this is what I know. But	09:14:32
18	the actual board documents, you refer?	09:14:37
19	Q The board issues an opinion explaining	09:14:41
20	their reasoning for instituting an Inter Partes	09:14:43
21	Review.	09:14:46
22	Did you review that document?	09:14:46

1	A	It was not given to me.	09:14:49
2	Q	Okay. In paragraph 65 of your	09:14:50
3		declaration, you say there that, Although I do not	09:14:59
4		offer an opinion as to the specific additional	09:15:08
5		limitations of claims 4 to 10 of the '462 patent, I	09:15:10
6		further understand that Ozempic practices the	09:15:15
7		additional limitations of claims 4 to 10.	09:15:18
8		Do you see that?	09:15:21
9	A	Yes, sir.	09:15:21
10	Q	How did you arrive at that understanding?	09:15:22
11	A	I focused basically on the -- on the	09:15:25
12		claims 1 to 3, basically. And I don't think that my	09:15:30
13		task was to focus on the 4 to 10. And I assumed	09:15:37
14		what I was given based on that.	09:15:40
15	Q	So if I understand it correctly, you were	09:15:43
16		told by the lawyers that Ozempic practices the	09:15:46
17		additional limitations of claims 4 to 10, and you	09:15:52
18		accepted that understanding?	09:15:54
19	A	This, and also that somebody else was	09:15:56
20		going to be taking care of the 4-10. There was	09:15:59
21		another expert witness that will be analyzing there.	09:16:04
22		And I think that in my deposition, I point out to	09:16:06

1	that issue, not just to the Ozempic, but also that	09:16:09
2	somebody else will be focusing on that. That was	09:16:12
3	not my task.	09:16:15
4	Q It was not your task. The additional	09:16:16
5	limitations of claims 4 to 10 were not your task?	09:16:18
6	A Correct.	09:16:23
7	Q Okay. Then I'm going to have you move	09:16:24
8	forward in your declaration to paragraphs 202 and	09:16:27
9	205.	09:16:34
10	A Mm-hmm.	09:16:48
11	Q And in those paragraphs, you have a	09:16:49
12	section on claim construction, correct?	09:16:51
13	A Yes, sir.	09:16:55
14	Q Okay. And in paragraph 203, you state	09:16:57
15	that you've been instructed to assume that a method	09:17:16
16	for treating type 2 diabetes means the claimed	09:17:20
17	administration is for the purpose of care or	09:17:24
18	management of a patient with type 2 diabetes where	09:17:29
19	the claimed administration is intended to care for	09:17:31
20	and manage a patient with type 2 diabetes, correct?	09:17:34
21	MR. BAUGHMAN: Object to the form.	09:17:37
22	A Correct.	09:17:40

1	Q	Okay. And you're aware that the parties	09:17:41
2		and the board agree that the method recited in the	09:17:44
3		claims of the '462 patent does not require any	09:17:48
4		particular level of efficacy, correct?	09:17:51
5	MR. BAUGHMAN:	Object to the form and	09:17:53
6		foundation.	09:17:54
7	A	Does not -- does not mention anything	09:17:55
8		about specific efficacy.	09:17:59
9	Q	Right. So the claims of the '462 patent	09:18:00
10		don't require any particular level of efficacy,	09:18:02
11		correct?	09:18:05
12	MR. BAUGHMAN:	Same objection.	09:18:05
13	A	It doesn't mention anything about any	09:18:07
14		numbers or any efficacy in specific.	09:18:10
15	Q	Okay. And the claims of the '462 patent	09:18:12
16		also say nothing about tolerability, correct?	09:18:16
17	MR. BAUGHMAN:	Object to the form and	09:18:20
18		foundation.	09:18:21
19	A	In the 462? Let me review that,	09:18:25
20		because --	09:18:29
21	Q	Sure.	09:18:30
22	A	-- it goes -- obviously, when you go like	09:18:30

1	this, it is a combination of efficacy, safety, and	09:18:34
2	tolerability.	09:18:38
3	Q And I will -- if it helps you, I'll tell	09:18:41
4	you that --	09:18:43
5	A Where does it say -- where do you	09:18:44
6	indicate that it doesn't say?	09:18:47
7	Q Sure. What I'm focused on are the	09:18:49
8	claims. And the claims are on the last page of the	09:18:52
9	patent in columns 35 and 36.	09:18:55
10	A Which page?	09:19:06
11	Q See how at the top -- at the very top of	09:19:07
12	the page there are numbers above each column?	09:19:10
13	A Yes.	09:19:12
14	Q So it's the very last page of the patent,	09:19:13
15	and it's columns 35 and 36. At the bottom, you'll	09:19:16
16	see, there's something that says, The invention	09:19:19
17	claimed is, and then there's the numbered list of	09:19:22
18	claims 1 to 10.	09:19:25
19	Do you see that?	09:19:27
20	A Yes, sir.	09:19:28
21	Q All right. And my question for you is,	09:19:28
22	the claims of the '462 patent say nothing about	09:19:30

1	tolerability, correct?	09:19:34
2	MR. BAUGHMAN: Object to the form and	09:19:35
3	foundation.	09:19:37
4	A Let me read it again --	09:19:37
5	Q Of course.	09:19:39
6	A -- because you asked me something very	09:19:39
7	specific.	09:19:41
8	Q Sure.	09:19:42
9	A It doesn't specifically mention it. But	09:20:15
10	to get to a 1.0 milligram, you have to tolerate the	09:20:18
11	dose. If you don't tolerate the dose, then they	09:20:22
12	cannot have the claim 1.	09:20:26
13	Q Okay. Is it your understanding that	09:20:27
14	claim 1 requires a particular level of tolerability?	09:20:30
15	A It doesn't specify -- in my	09:20:35
16	understanding, it doesn't specify that has to be	09:20:40
17	tolerated. But to get to 1 milligram, it needs to	09:20:42
18	be tolerated. Otherwise, you cannot get there.	09:20:47
19	Q And you say, to get to 1 milligram, it	09:20:49
20	needs to be tolerated, and you need to get there.	09:20:53
21	How do you get there? What do you mean	09:20:57
22	by that?	09:20:59

1 A I mean that the -- there is -- it's based 09:21:01
2 on a study with specific dosages, and then -- and 09:21:06
3 you looked at the different dosages and whether or 09:21:13
4 not the dosages from 0.1 to 1.6 were tolerated or 09:21:16
5 not, which I don't know. 09:21:20

6 Q So I just want to make sure I understand 09:21:24
7 it. 09:21:32

8 When you were reaching your opinions that 09:21:32
9 you express in your declaration, it was your 09:21:36
10 understanding that the claims of the '462 patent 09:21:40
11 require tolerability. 09:21:45

12 Is that correct? 09:21:47

13 MR. BAUGHMAN: Object to the form. 09:21:49

14 Sorry. You can answer. 09:21:51

15 A It doesn't specify, but in part of what 09:21:53
16 the claim is based, what the data that is shown, it 09:22:00
17 has to be tolerability. If it's not tolerable, any 09:22:04
18 of the dosages, which I don't know, then you cannot 09:22:08
19 get to whatever dose has been tested. 09:22:13

20 Q Okay. Do the claims -- you agree, I take 09:22:15
21 it, then, that the claims don't require any 09:22:17
22 particular level of tolerability. 09:22:19

1	Is that right?	09:22:21
2	A It doesn't specify there.	09:22:21
3	Q Okay. The claims of the '462 patent also	09:22:23
4	say nothing about weight loss.	09:22:28
5	Is that fair?	09:22:30
6	MR. BAUGHMAN: Object to the form.	09:22:31
7	A In the list that you mentioned?	09:22:33
8	Q The claims, yes, that we were looking at,	09:22:39
9	1 to 10.	09:22:41
10	A It's not listed there.	09:22:41
11	Q Weight loss is not an element of the	09:22:42
12	claims, correct?	09:22:45
13	MR. BAUGHMAN: Object to the form and	09:22:45
14	foundation.	09:22:47
15	A It's not listed in that claim.	09:22:47
16	Q Okay. And you would agree that the	09:22:52
17	claims of the '462 patent don't require that the	09:22:56
18	claimed method results in weight loss.	09:22:57
19	Is that fair?	09:23:00
20	A The '462, for the claim 1, there is no	09:23:03
21	requirement of efficacy or tolerability or safety.	09:23:10
22	That is not specified there.	09:23:15

1	Q	Okay. And that's also true that weight	09:23:16
2		loss is not an element of claim 1 either, correct?	09:23:21
3	A	It doesn't specify a specific weight loss	09:23:24
4		that you need to achieve or anything like that.	09:23:26
5	Q	And it doesn't require any weight loss	09:23:29
6		that you need to achieve, correct?	09:23:30
7		MR. BAUGHMAN: Object to the form and	09:23:32
8		foundation.	09:23:33
9	A	The data is presented there. The claim	09:23:38
10		does not specify a specific efficacy or safety.	09:23:42
11	Q	Okay. Including weight loss, right?	09:23:46
12	A	It doesn't mention weight loss.	09:23:48
13	Q	Okay. Now, you have this claim	09:23:51
14		construction section in your declaration. And aside	09:23:55
15		from the claim term, a method for treating type 2	09:24:00
16		diabetes, which we discussed, your opinions are	09:24:03
17		based on the assumption that the patent claim	09:24:06
18		terms -- the other claim terms would have their	09:24:11
19		ordinary meaning as understood by a person of	09:24:15
20		ordinary skill in the art at the time of the	09:24:17
21		invention, correct?	09:24:18
22		MR. BAUGHMAN: Object to the form.	09:24:19

1	Q	I think you say that in paragraph 204.	09:24:20
2	A	For what?	09:24:23
3	Q	The other claims. So in your	09:24:25
4		declaration, in paragraph 203, you say, I've been	09:24:31
5		instructed to assume that a method for treating	09:24:36
6		type 2 diabetes means, and then you --	09:24:39
7	A	Correct.	09:24:42
8	Q	-- give your explanation.	09:24:42
9		And then in paragraph -- in paragraph	09:24:44
10		205, you say, For all other terms, I have been asked	09:24:50
11		to assume that they have their plain and ordinary	09:24:54
12		meaning as they would have been understood by	09:24:56
13		persons of skill in the art in light of the	09:24:58
14		specification, correct?	09:25:01
15	A	That's what I stated.	09:25:02
16	Q	Okay. And in your declaration, the only	09:25:04
17		claim term you specifically discuss is a method for	09:25:09
18		treating type 2 diabetes in this claim construction	09:25:13
19		section.	09:25:15
20		Is that right?	09:25:16
21	A	What do you mean by "the only"?	09:25:18
22	Q	In paragraph 203, you said you were	09:25:20

1	instructed to assume that a method for treating	09:25:24
2	type 2 diabetes meant a certain thing, correct?	09:25:27
3	A In the claim 1, it says, a method to	09:25:31
4	treat type 2 diabetes comprising administration of	09:25:35
5	once-weekly semaglutide 1.0 milligram to a patient	09:25:40
6	thereof. So it's the whole thing.	09:25:45
7	Q Right. But just in paragraph 203, you	09:25:47
8	were instructed on what a method for treating type 2	09:25:52
9	diabetes means because the parties and the board had	09:25:57
10	discussed that.	09:26:00
11	Do you see that in paragraph 203 of your	09:26:00
12	declaration?	09:26:02
13	A Yes.	09:26:02
14	Q Okay. And then in paragraph 205, you	09:26:03
15	said all the other claim terms in claim 1 are to	09:26:06
16	have their plain and ordinary meaning, correct?	09:26:09
17	A Correct. But my understanding is that in	09:26:10
18	claim 1, it's not just method to treat type 2	09:26:14
19	diabetes.	09:26:18
20	Q Understood.	09:26:18
21	A It's method to treat type 2 diabetes	09:26:19
22	comprising administration of once-weekly semaglutide	09:26:21

1	1.0 milligrams to a person thereof, not just method	09:26:26
2	to treat diabetes, because that's too general.	09:26:30
3	Q Understood. Understood.	09:26:33
4	And one of the other claim terms, as you	09:26:34
5	mentioned, in claim 1, is 1.0 milligrams of	09:26:37
6	semaglutide, correct?	09:26:43
7	A That's correct.	09:26:44
8	Q And the ordinary meaning of 1.0 would	09:26:44
9	exclude zero and it would exclude 2.0, correct?	09:26:49
10	MR. BAUGHMAN: Object to the form and	09:26:52
11	foundation, scope.	09:26:53
12	A 1.0 is not part of the thing. I did not	09:26:56
13	see any 1.0 in any of the data that was shown to me.	09:27:01
14	Q You're talking about the testing that's	09:27:06
15	in the specification, correct?	09:27:08
16	MR. BAUGHMAN: Object to the form and	09:27:09
17	foundation.	09:27:10
18	A I'm talking about the 1.0, it was not	09:27:10
19	included in the basis for this. In the data that I	09:27:16
20	analyze, it was 0.1, 0.2, 0.4, 0.8, and 1.6.	09:27:20
21	Q Correct. And I think what you're	09:27:28
22	pointing out is, in the patent specification,	09:27:30

1	there's no data for a 1.0 milligram dose of	09:27:32
2	semaglutide, correct?	09:27:36
3	MR. BAUGHMAN: Object to the form,	09:27:36
4	foundation and scope.	09:27:37
5	A I did not see any 1.0.	09:27:38
6	Q But 1.0 milligrams is an element of the	09:27:41
7	claims that we looked at; claim 1 claims using a	09:27:44
8	dose of 1.0 milligrams of semaglutide to treat	09:27:49
9	type 2 diabetes, correct?	09:27:53
10	A That's what the claim specifically	09:27:54
11	states.	09:27:59
12	Q Okay. And 1.0 milligrams in the claim	09:27:59
13	would get its plain and ordinary meaning as	09:28:01
14	understood by a person of ordinary skill in the art,	09:28:04
15	correct?	09:28:06
16	A Can you repeat that question?	09:28:07
17	Q Sure. We were talking about how all the	09:28:09
18	other claim terms get their plain and ordinary	09:28:11
19	meaning as a skilled artisan would understand the	09:28:13
20	term.	09:28:16
21	Do you recall that?	09:28:17
22	A Mm-hmm.	09:28:17

1	Q	Okay. And so 1.0 milligrams would have	09:28:18
2		it plain and ordinary meaning to a person of skill	09:28:21
3		in the art, correct?	09:28:23
4	A	Yes, but it was not in the data.	09:28:23
5	Q	Understood. But the ordinary meaning of	09:28:25
6		1.0, apart from the data -- I agree with you there's	09:28:29
7		no data in the specification as to that dose. But	09:28:32
8		1.0, to a skilled artisan, would exclude zero, and	09:28:35
9		it would exclude 2.0, correct?	09:28:40
10		MR. BAUGHMAN: Object to the form,	09:28:42
11		foundation and scope.	09:28:43
12	A	1.0 will exclude? I mean, not	09:28:50
13		necessarily.	09:28:54
14	Q	Do you think a -- as used in the claims	09:28:54
15		of the '462 patent, do you think a 1.0 milligram	09:28:58
16		dose of semaglutide could include doses as high as	09:29:01
17		2.0?	09:29:05
18		MR. BAUGHMAN: Object to the form,	09:29:07
19		foundation and scope.	09:29:08
20		Sorry, I didn't mean to interrupt you,	09:29:09
21		David.	09:29:12
22		MR. ANSTAETT: That's okay.	09:29:12

1 A In my statement, it says there that based
2 on the data, the evidence showed that anything above
3 0.8 milligrams is there. So 0.8 and above was
4 effective and safe. So the 1.0 does not exclude
5 because it includes even 0.7 to 0.8.

6 Q And I think we're -- you're maybe getting
7 ahead a little bit of where I am. We'll talk about
8 those opinions, and I understand that. We'll
9 definitely get into that today.

10 But I'm look asking you to look at
11 claim 1 of the '462 patent, and it recites a dose of
12 1.0 milligrams, correct?

13 A Correct.

14 Q Okay. And just as a person of ordinary
15 skill in this art at the time of the invention,
16 looking at the number 1.0, is it fair to say that
17 that would exclude zero, a dose of zero milligrams,
18 and it would else exclude a dose of 2.0 milligrams?

19 MR. BAUGHMAN: Object to the form,
20 foundation and scope.

21 A I think that that's a very general
22 statement. I cannot say that it will exclude all

1 these dosages. There will be some dosages are
2 excluded, some other dosages are not excluded. So I
3 cannot affirm anything that -- what you said. So I
4 don't understand the question.

5 Q Would you agree that the ordinary meaning
6 of 1.0 would exclude 0.5 and 1.5 milligram doses of
7 semaglutide, or is that something you can't offer an
8 opinion on?

9 MR. BAUGHMAN: Object to the form,
10 foundation and scope.

11 You can answer.

12 A Again, without knowing the data, I cannot
13 exclude it. I have to see the data.

14 Q And I'm not -- and just to be clear, I
15 want to give you every chance to answer this
16 question. I'm not asking about the data. I'm not
17 asking about whether a particular dose is effective
18 or not effective or tolerable or not tolerable. I'm
19 just understanding [sic] what somebody of ordinary
20 skill in your art at the time of the invention would
21 understand what doses would be covered by 1.0
22 milligrams.

1 So would a person of ordinary skill in 09:31:19
2 your art, reading the '462 patent, claim 1, at the 09:31:21
3 time of the invention understand that a 1.0 09:31:25
4 milligram dose of semaglutide also included 0.5 and 09:31:27
5 1.5 milligram doses? 09:31:33

6 MR. BAUGHMAN: Object to the form, 09:31:35
7 foundation and scope. 09:31:36

8 A According to the data that I reviewed and 09:31:37
9 what it says, I cannot affirm that excludes because 09:31:40
10 it says 0.7 and above or 0.8 and above in there. So 09:31:44
11 1.0 is included. And I can -- without looking at 09:31:49
12 the whole data, I cannot make any statement in that 09:31:52
13 respect, because in my statement -- you can point it 09:31:55
14 out where I said that. Do you know where I put it 09:31:57
15 there, 0.7, 0.8? 09:32:02

16 Q I do know. I understand you talk about 09:32:05
17 that in your declaration, and we'll come on to that. 09:32:07

18 But I'm just asking, as you were reaching 09:32:09
19 your opinions in this case -- you understand that 09:32:12
20 the claims in a patent define the scope of the 09:32:16
21 invention, correct? 09:32:19

22 A Yes. 09:32:21

1	Q	Okay. And so what I'm trying to	09:32:22
2		understand is, when you looked at claim 1 of the	09:32:25
3		'462 patent, and you saw that it claims a 1.0	09:32:27
4		milligram dose of semaglutide, what doses did you	09:32:31
5		understand 1.0 milligrams to cover?	09:32:36
6	A	Cover the 1.0.	09:32:43
7	Q	Would it cover -- beyond the 1.0, would	09:32:45
8		it cover a dose of 0.9 milligrams?	09:32:49
9		MR. BAUGHMAN: Object to the form,	09:32:53
10		foundation and scope.	09:32:54
11	A	Again, the claim covers 1.0. What the	09:32:55
12		data shows is that 0.7 and 0.8 and above is	09:33:00
13		effective.	09:33:03
14		Now, it was a decision to go to 1.0.	09:33:04
15		Without knowing the data, I cannot make that --	09:33:11
16		affirm that. But it says that it's effective 0.7,	09:33:15
17		0.8 and above.	09:33:19
18		There are certainly -- in the range that	09:33:20
19		was tested there, there were significant	09:33:23
20		differences. I mean, all the dosages are different.	09:33:26
21		So the dosages are different there and behave	09:33:29
22		differently.	09:33:34

1	So without looking at the dosages, I	09:33:34
2	cannot make that statement because the dosages	09:33:38
3	behave differently within the range.	09:33:42
4	Q In the claim that recites 1.0 milligrams,	09:33:45
5	how many significant figures are there in 1.0?	09:33:51
6	A 1.0.	09:33:56
7	Q Are you familiar -- are you familiar with	09:33:58
8	the concept of significant figures?	09:34:01
9	A Can you explain to me?	09:34:04
10	Q Well, when you look at a number, numbers	09:34:05
11	can have a different level of precision, correct?	09:34:09
12	A Correct.	09:34:11
13	Q And the level of precision here is 1.0	09:34:12
14	milligrams, correct?	09:34:15
15	MR. BAUGHMAN: Object to the form,	09:34:16
16	foundation and scope.	09:34:17
17	A It says 1.0.	09:34:19
18	Q And how many significant figures does 1.0	09:34:20
19	have to a person of skill in the art?	09:34:23
20	A I can see only one decimal there.	09:34:25
21	Q Okay. So it has one significant figure?	09:34:27
22	A At that time.	09:34:30

1	Q	Okay. And because it has one significant	09:34:31
2		figure, the ordinary meaning to a person of skill in	09:34:38
3		the art of 1.0, it would not exclude, for example, a	09:34:42
4		dose of 0.99 milligrams or a dose of 1.01	09:34:46
5		milligrams.	09:34:52
6		Is that fair?	09:34:52
7	MR. BAUGHMAN:	Object to the form, scope,	09:34:52
8		and foundation.	09:34:57
9	A	I mean, it will not exclude. I mean,	09:34:58
10		this is for a 1.0. At 0.99, it could have been	09:35:02
11		effective. At 1.01, could have been effective and	09:35:09
12		so on. But there is a decision to go to 1.0.	09:35:13
13		Again, the data shows that 0.8 and above	09:35:16
14		is effective.	09:35:22
15	Q	And I'm just -- again, without -- I'm not	09:35:24
16		asking whether any particular dose is effective or	09:35:27
17		not effective. But you would agree because the	09:35:29
18		claims recite 1.0 milligrams of semaglutide, one	09:35:31
19		significant figure, 1.0 milligrams would include a	09:35:36
20		dose of, for example, 0.99 milligrams and a dose of	09:35:39
21		1.01 milligrams.	09:35:44
22		Is that fair?	09:35:46

1	MR. BAUGHMAN: Object to the form,	09:35:47
2	foundation and scope.	09:35:49
3	A Again, you have for 1.0 milligrams.	09:35:51
4	Whether it includes 0.99 or 1.01, I cannot make a	09:35:58
5	statement without knowing the data --	09:36:03
6	Q Okay. All right.	09:36:04
7	A -- because minor differences could make a	09:36:06
8	significant difference.	09:36:09
9	Q So again --	09:36:10
10	A Minor --	09:36:11
11	Q -- I just want to be clear. I'm not	09:36:12
12	talking about whether any particular dose is	09:36:14
13	effective.	09:36:16
14	What I'm hearing you say is, you don't	09:36:16
15	have an opinion as to whether or not -- when the	09:36:18
16	claims recite 1.0 milligram, whether or not that	09:36:21
17	would include a dose of 0.99 milligrams or a dose of	09:36:24
18	1.01 milligrams?	09:36:31
19	A I did not say that I don't have an	09:36:32
20	opinion. I'm saying that the 1.0 milligram is what	09:36:34
21	it is there, and I would like to see the data to	09:36:38
22	have an opinion.	09:36:40

1	Q	I'm going to have to ask you -- you said	09:36:41
2		you have an opinion. What is your opinion? As	09:36:43
3		recited in the claims, does 1.0 cover a dose of 0.99	09:36:46
4		and 1.01, yes or no?	09:36:52
5	MR. BAUGHMAN:	Object to the form, scope,	09:36:54
6		and foundation.	09:36:55
7		You can answer.	09:36:56
8	A	The 1.0 is 1.0. I don't see the data to	09:36:56
9		cover 0.99 or 1.001.	09:37:01
10		When there is -- when the data is	09:37:05
11		analyzed, minor differences in dosages make a	09:37:09
12		difference in responses.	09:37:13
13	Q	Sir, there's no data in the patent	09:37:14
14		specification on a 1.0 milligram dose, correct?	09:37:17
15	MR. BAUGHMAN:	Object to the form, scope,	09:37:20
16		and foundation.	09:37:21
17	A	Excuse me?	09:37:22
18	Q	There's no data in the patent	09:37:22
19		specification on a 1.0 milligram dose of	09:37:24
20		semaglutide, right?	09:37:27
21	MR. BAUGHMAN:	Same objection.	09:37:27
22	A	1.0 was not tested.	09:37:28

1	Q	So there's no data in the specification	09:37:31
2		concerning a 1.0 milligram dose, correct?	09:37:32
3	MR. BAUGHMAN:	Same objection.	09:37:34
4	A	The dosages that were tested was 0.1,	09:37:36
5		0.2, 0.4, 0.8, and 1.6.	09:37:42
6	Q	Correct. And so therefore, the 1.0	09:37:45
7		milligram dose was not tested, correct?	09:37:50
8	A	It was not tested.	09:37:53
9	Q	And therefore, there is no data on a 1.0	09:37:54
10		milligram dose in the patent specification, correct?	09:37:58
11	MR. BAUGHMAN:	Object to the form, scope,	09:37:59
12		and foundation.	09:38:01
13		You can answer.	09:38:02
14	A	I'm not privy to the data. The sponsor	09:38:02
15		presumably have the data, have the dose response,	09:38:08
16		and they make a decision, when they look at the dose	09:38:10
17		response, what they are going to get there. And	09:38:13
18		that's where the 1.0 was chosen.	09:38:16
19	Q	Understood.	09:38:18
20	A	But I don't have the data.	09:38:19
21	Q	You don't have the data, nor does the	09:38:20
22		person reading the patent specification have the	09:38:23

1 data, right, because the data is not in the patent 09:38:24

2 specification, correct? 09:38:27

3 MR. BAUGHMAN: Object to the form, scope, 09:38:28

4 and foundation. 09:38:29

5 A The data is on the patent specification 09:38:29

6 for the dosages that were tested. 09:38:32

7 Q I understand that, sir, but I'm talking 09:38:33

8 about the 1 milligram dose. I'm trying to agree 09:38:35

9 with you that -- I think what you're saying is, 09:38:39

10 there is no data in the patent specification on a 09:38:41

11 1.0 milligram dose of semaglutide. 09:38:46

12 That's true, isn't it? 09:38:47

13 MR. BAUGHMAN: Object to the form, scope, 09:38:48

14 and foundation. 09:38:50

15 A The data was present to confirm a dose 09:38:51

16 response. And based on this data, the sponsor, Novo 09:38:56

17 Nordisk, analyzed that data and decided to have 1.0. 09:39:01

18 Q I understand that, sir. 09:39:04

19 But you understand there's a difference 09:39:06

20 between -- I think you understand there's a 09:39:07

21 difference between what data Novo Nordisk had and 09:39:10

22 the data that is -- appears in the patent 09:39:13

1 specification, the '462 patent specification?

09:39:16

2 Do you understand what I mean when I
3 refer to the '462 patent specification?

09:39:19

4 MR. BAUGHMAN: Object to the form, scope,
5 and foundation.

09:39:20

09:39:22

09:39:23

6 A I have the patent in front of me.

09:39:23

7 Q Okay. And the patent in front of you has
8 no data with respect to a 1.0 milligram dose of
9 semaglutide.

09:39:26

09:39:30

09:39:34

10 Do you agree with that or disagree?

09:39:35

11 MR. BAUGHMAN: Object to the form, scope,
12 and foundation.

09:39:36

09:39:37

13 A The data that is shown is for the 0.1,
14 0.2, 0.4, 0.8, and 1.6. With that presumably, Novo
15 had the dose response and decided to get the 1.0.

09:39:38

09:39:42

09:39:52

16 Q But as I think you said, you listed the
17 doses for which there are data in the patent
18 specification, correct?

09:39:56

09:39:59

09:40:02

19 MR. BAUGHMAN: Object to the form, scope,
20 and foundation.

09:40:04

09:40:05

21 A The data is there related to the dosages
22 that were tested.

09:40:06

09:40:09

1	Q	Okay. Let's just do it this way.	09:40:09
2		Show me in the '462 patent specification	09:40:12
3		where there is data on a 1.0 milligram dose of	09:40:14
4		semaglutide.	09:40:18
5	MR. BAUGHMAN:	Object to the form, scope,	09:40:18
6		and foundation.	09:40:19
7	A	That data was with Novo Nordisk, and Novo	09:40:19
8		Nordisk made the decision in the claim to have the	09:40:24
9		1.0.	09:40:27
10	Q	Okay. And you assume that Novo Nordisk	09:40:27
11		had that data on a 1.0 milligram dose even though	09:40:30
12		it's not in the patent specification, correct?	09:40:33
13	MR. BAUGHMAN:	Object to the form, scope,	09:40:36
14		and foundation.	09:40:37
15	A	I cannot assume because I don't know what	09:40:37
16		Novo had. But based on the data, Novo made the	09:40:41
17		decision to go to 1.0.	09:40:46
18	Q	And just to be clear, you can't point to	09:40:47
19		any data on a 1.0 milligram dose in the '462 patent	09:40:51
20		specification? If you can, I'd like you to show me	09:40:56
21		in Exhibit 1001 where that data is.	09:41:00
22	MR. BAUGHMAN:	Object to the form, scope,	09:41:02

1	and foundation.	09:41:03
2	A When the dose was done, 0.1, 0.2, 0.4,	09:41:04
3	0.8, and 1.6, there's a whole array of options there	09:41:10
4	where they have different dosages that could be	09:41:16
5	tested in a dose response there. Multiple there.	09:41:18
6	And based on the data that they have, Novo decided	09:41:22
7	to choose the 1.0.	09:41:27
8	Q I'll give you one last chance. If you	09:41:30
9	would like to point me to any data in the '462	09:41:32
10	patent specification, which you have sitting in	09:41:37
11	front of you as Exhibit 1001, showing -- or data on	09:41:38
12	a 1.0 milligram dose of semaglutide, efficacy,	09:41:45
13	tolerability, safety, please point it out now.	09:41:49
14	MR. BAUGHMAN: Object to the form,	09:41:52
15	foundation and scope.	09:41:53
16	A Again, the data clearly shows --	09:41:54
17	Q Which data? You're pointing to the	09:41:57
18	patent and saying "data." Can you point to me in	09:42:01
19	the specification --	09:42:03
20	MR. BAUGHMAN: Counsel, you have to let	09:42:03
21	him finish answering the question before you	09:42:05
22	interrupt him.	09:42:07

1	A	I was trying to say, Counsel, that the	09:42:07
2		data is on 0.1, 0.2, 0.4, 0.8, one dose, 0.8	09:42:09
3		titrated, and 1.6 titrated. That is the data that	09:42:19
4		was shown. The 1.0 milligrams was not tested.	09:42:23
5	Q	Okay. Turn to paragraph 88 of your	09:42:26
6		declaration, please.	09:42:31
7	A	Yeah.	09:43:05
8	Q	In paragraph 88, you discuss the GLP-1	09:43:11
9		receptor agonist taspoglutide that was under	09:43:29
10		development by Roche.	09:43:32
11		Do you see that?	09:43:33
12	A	Yes, sir.	09:43:33
13	Q	And you say that development of	09:43:34
14		taspoglutide was abandoned because of systemic	09:43:35
15		allergic reactions, injection site reactions, and	09:43:39
16		also unacceptable levels of nausea and vomiting.	09:43:41
17		Do you see that?	09:43:44
18		MR. BAUGHMAN: Object to the form.	09:43:44
19	A	Yes, sir.	09:43:45
20	Q	And you content that a skilled artisan	09:43:45
21		would have been aware of this abandonment in	09:43:49
22		September of 2010 based on an article that you cite	09:43:52

1	as Exhibit 2061.	09:43:54
2	Do you see that?	09:43:56
3	A Exhibit 2061?	09:43:58
4	Q Yeah. And I'm referring to paragraph 88	09:44:01
5	of your declaration. You contend in that paragraph	09:44:03
6	that skilled artisans would have been aware of the	09:44:05
7	abandonment of taspoglutide by Roche in September	09:44:10
8	2010 based on an article that you cite,	09:44:15
9	Exhibit 2061, correct?	09:44:19
10	A Correct.	09:44:19
11	(Previously marked Exhibit 2061 presented	09:44:19
12	to the witness.)	09:44:38
13	BY MR. ANSTAETT:	09:44:38
14	Q I'm going to give you what is marked as	09:44:39
15	Exhibit 2061.	09:44:41
16	And do you recognize Exhibit 2061 as the	09:44:49
17	article that you cite in paragraph 88 of your	09:44:52
18	declaration?	09:44:54
19	A Yes, sir.	09:44:56
20	Q Now, in the second paragraph of	09:44:59
21	Exhibit 2061, it's on the first page, the authors	09:45:03
22	state that the Swiss pharmaceutical company,	09:45:07

1	referring to Roche, says it is not abandoning	09:45:09
2	taspoglutide, correct?	09:45:15
3	A At that time, that's what the author	09:45:16
4	assumed that.	09:45:18
5	Q Okay. And when you say "at that time,"	09:45:18
6	that's September 2010, correct?	09:45:22
7	A It reads, The Swiss pharmaceutical	09:45:25
8	company says it is not abandoning taspoglutide. In	09:45:29
9	an announcement the company says it is considering	09:45:34
10	reformulation of the medication. However, any kind	09:45:38
11	of reformulation will most likely result in a	09:45:41
12	significant delay in the approval process end date.	09:45:44
13	Q And that's as of September 2010, correct?	09:45:49
14	That's when this article was published?	09:45:51
15	A Yeah, that's what it is. It's a news --	09:45:54
16	it's an article in the Medical News, yeah.	09:45:58
17	Q And so the article says that Roche is not	09:46:01
18	abandoning taspoglutide, correct?	09:46:03
19	A At that time, the reporter says that.	09:46:06
20	Q Well, the reporter says that Roche said	09:46:08
21	that, right?	09:46:10
22	A Correct.	09:46:11

1 Q And this is an article you're relying on 09:46:12
2 in your expert report, correct? You're the one who 09:46:14
3 cited this article, correct? 09:46:17

4 A I relied this, and I also rely on the 09:46:19
5 fact that I was also conducting studies with 09:46:22
6 taspoglutide. 09:46:25

7 Q Okay. And as you pointed out, the 09:46:25
8 article that you cited said that Roche was 09:46:28
9 considering a reformulation of the medication, 09:46:31
10 correct? 09:46:34

11 A It says that in this thing. Never got 09:46:35
12 it. 09:46:38

13 Q Right. And a reformulation means keeping 09:46:38
14 the taspoglutide but changing other elements of the 09:46:41
15 drug product formulation, correct? 09:46:45

16 A I don't know. 09:46:48

17 MR. ANSTAETT: All right. Let's look at 09:46:54
18 another exhibit. 09:46:56

19 (Previously marked Exhibit 2060 presented 09:46:56
20 to the witness.) 09:47:12

21 BY MR. ANSTAETT: 09:47:12

22 Q I'm handing you what was marked as 09:47:13

1	Exhibit 2060.	09:47:14
2	A Yeah. I recognize the first author.	09:47:17
3	Q You're one of the authors of this	09:47:20
4	article, right?	09:47:23
5	A Yeah.	09:47:23
6	Q Okay. And this is another article that	09:47:24
7	you cite about the abandonment of taspoglutide in	09:47:26
8	your expert report.	09:47:31
9	Is that right?	09:47:32
10	MR. BAUGHMAN: Object to the form.	09:47:32
11	A Yes, sir.	09:47:35
12	Q And this article was published in 2013,	09:47:40
13	after the priority date of the '462 patent, correct?	09:47:43
14	A The date of publication is 2013.	09:47:50
15	Q Okay. So Exhibit 2060 is not prior art	09:47:52
16	to the '462 patent, correct?	09:47:57
17	MR. BAUGHMAN: Object to the form.	09:47:58
18	A Say it again?	09:47:59
19	Q Exhibit 2060 is not prior art --	09:48:00
20	A Are you referring to this?	09:48:03
21	Q Yes.	09:48:05
22	A It is -- this is -- this was published in	09:48:06

1 2013. The '462 is July 1st, 2012. But publications
2 are -- take months to be published. Manuscripts
3 take months to be written. Manuscripts take months
4 to be analyzed by the reviewers and the editors.

5 So it doesn't necessarily mean that when
6 it's published in 2013, it is there. But there was
7 already public domain known that the taspoglutide
8 was suspended.

9 Q You -- was it your impression, when you
10 reached your opinions in this case, that
11 Exhibit 2060 was prior art to the '462 patent?

12 A This?

13 Q Yes.

14 A The taspoglutide?

15 Q No, no. The article, your article. We
16 marked it as Exhibit 2060. So when I refer to
17 Exhibit 2060, I'm referring to the Rosenstock
18 article that you cite, The Fate of Taspoglutide, a
19 Weekly GLP-1 Receptor Agonist, Versus Twice-Daily
20 Exenatide for Type 2 Diabetes.

21 When you reached your opinions in this
22 case, were you under the impression that

1	Exhibit 2060 was prior art to the '462 patent?	09:49:19
2	MR. BAUGHMAN: Object to the form and	09:49:22
3	foundation.	09:49:23
4	A Yes, it was prior to. If you look	09:49:30
5	carefully here, the article was received 13 of April	09:49:31
6	of 2012. April of 2012 is before July 2012, which	09:49:36
7	is the date.	09:49:44
8	So this is prior art.	09:49:44
9	I mean -- and myself as a first author, I	09:49:46
10	have direct recognition acknowledged that	09:49:51
11	tas-poglutide was suspended.	09:49:54
12	So yes, this was prior art.	09:49:55
13	Q Okay. At page 6 of Exhibit 2060, you'll	09:49:57
14	see at the --	09:50:18
15	A This one?	09:50:19
16	Q Exactly. When I refer to page numbers,	09:50:20
17	it will be those numbers down there.	09:50:24
18	So I'm looking at the sentence that	09:50:26
19	bridges the first and second columns on page 6.	09:50:30
20	A Can you please direct me to that?	09:50:34
21	Q Sure. There's a -- in column -- we're	09:50:36
22	looking at different pages. I think you're on a	09:50:38

1	different page. You're on page 5. Can you just	09:50:41
2	turn one more page to page 6.	09:50:44
3	A Okay.	09:50:46
4	Q And then there's a -- the last paragraph	09:50:51
5	in the first column starts with the words, Systemic	09:50:53
6	allergic reactions.	09:50:57
7	Do you see that?	09:51:00
8	A Can you point it out to me, please?	09:51:00
9	MR. BAUGHMAN: Do you mind if I point it	09:51:04
10	out?	09:51:06
11	MR. ANSTAETT: No. Absolutely. Yeah,	09:51:06
12	you can point it out.	09:51:06
13	MR. BAUGHMAN: I think he's talking about	09:51:06
14	the paragraph.	09:51:06
15	THE WITNESS: Okay.	09:51:07
16	A Can I read it?	09:51:07
17	Q Yeah, why don't you read that whole	09:51:09
18	paragraph.	09:51:10
19	A Yeah.	09:51:35
20	Q You wrote in that paragraph of	09:51:36
21	Exhibit 2060, Although allergic reactions are	09:51:39
22	possible with protein-based therapies, the rate of	09:51:42

1 this adverse event with taspoglutide was higher than 09:51:45
2 anticipated and has rarely been reported with other 09:51:48
3 GLP-1 receptor agonists. 09:51:51

4 Correct? 09:51:54

5 A That's what I wrote. 09:51:54

6 Q And that was true as of March 2013 when 09:51:55
7 Exhibit 2060 was published. 09:52:00

8 Is that right? 09:52:02

9 A In terms of systemic allergic reactions, 09:52:05
10 and systemic allergic reactions is also equivalent 09:52:09
11 to anaphylactic reactions. So this is specific for 09:52:14
12 taspoglutide, that it happened with that high 09:52:17
13 frequency. 09:52:19

14 Q And those kind of systemic allergic 09:52:20
15 reactions were rarely seen with other GLP-1 receptor 09:52:22
16 agonists, correct? 09:52:25

17 A Rarely seen. 09:52:26

18 Q Okay. I'm going to turn you back to your 09:52:28
19 expert report and have you looked at paragraph 87. 09:52:33

20 In paragraph 87 of your expert report -- 09:52:51

21 A Yeah. 09:52:59

22 Q -- you write that the GLP-1 receptor 09:53:00

1	agonist albiglutide was withdrawn from the market	09:53:07
2	after approval, correct?	09:53:12
3	A Yes, sir.	09:53:12
4	Q And when was albiglutide withdrawn from	09:53:13
5	the market?	09:53:17
6	A I think I said it, but I cannot remember.	09:53:18
7	But that was a commercial decision by GSK.	09:53:22
8	Q They withdrew for commercial reasons?	09:53:27
9	A Yes, sir.	09:53:31
10	Q And let me --	09:53:34
11	A But I cannot remember -- it must be	09:53:38
12	somewhere. Let me look at this. One second.	09:53:42
13	Q And feel free to look as much as you	09:53:46
14	want. I can also give you an exhibit if that might	09:53:48
15	help.	09:53:51
16	A It says there that -- no, let's see. I	09:53:58
17	mean, if you can point it out to me where I stated	09:54:08
18	when it was done, I would appreciate it.	09:54:14
19	Q I'm not sure if you stated in your report	09:54:15
20	when it was done it, but let me give you an exhibit	09:54:17
21	that you cite in your report, which is Exhibit 2063.	09:54:23
22	(Previously marked Exhibit 2063 presented	09:54:23

1	to the witness.)	09:54:19
2	BY MR. ANSTAETT:	09:54:19
3	Q Do you see in paragraph 87 of your	09:54:29
4	declaration, you cite Exhibit 2063?	09:54:33
5	A One second. Let me see. I just want to	09:54:38
6	get this in the right order.	09:54:41
7	MR. BAUGHMAN: Counsel, just to clarify,	09:55:29
8	you want paragraph 87, not page 87?	09:55:30
9	MR. ANSTAETT: Yes.	09:55:34
10	Q I was referring to paragraph 87.	09:55:34
11	A Paragraph 87.	09:55:36
12	Q Yeah. I'm sorry about that.	09:55:37
13	(Cross-talk.)	09:55:40
14	Q And when you get there, just let me know.	09:55:47
15	A Sure.	09:55:49
16	Q Exhibit 2063 is one of the exhibits you	09:55:51
17	cite in paragraph 87 of your declaration, correct?	09:55:55
18	A I'm in paragraph 87. And so this is the	09:56:07
19	exhibit?	09:56:11
20	Q Yeah. Do you see how you have	09:56:12
21	Exhibit 2063 there at the end of paragraph 87?	09:56:15
22	A 2063, yeah.	09:56:17

1	Q	And then I've given you Exhibit 2063.	09:56:18
2	A	Correct.	09:56:20
3	Q	Okay. And Exhibit 2063 shows that	09:56:21
4		albiglutide wasn't withdrawn from the market until	09:56:25
5		2017, correct?	09:56:27
6	A	It is what it states, yeah.	09:56:34
7	Q	Okay. So a skilled artisan at the	09:56:36
8		priority date of the '462 patent would not have	09:56:38
9		known that albiglutide was withdrawn from the	09:56:41
10		market, correct?	09:56:43
11	A	This -- this argument is basically, as I	09:56:48
12		analyze Dr. Jusko's and Dr. Bantle's, when they	09:56:53
13		state that the GLP-1s -- long-acting GLP-1s, and the	09:57:02
14		longer they are long-acting are going to be more	09:57:08
15		acceptable and more tolerable was an argument just	09:57:13
16		to counteract that simple argument that being longer	09:57:15
17		acting and it's going to be approved, because that	09:57:18
18		was an argument to say that not necessarily all the	09:57:21
19		longer acting are going to be acceptable,	09:57:25
20		approvable, and so on.	09:57:32
21		This was approved, but actually was, as I	09:57:33
22		mentioned, for commercial reasons, as it states	09:57:35

here, because limited prescriber medicine.

So the fact that it's a long-acting, I was alluded in Dr. Jusko's statement in his declaration, that's no longer the case.

Q But you understand that obviousness and anticipation, which is what you're offering opinions on, those issues are judged based on what a skilled artisan at the priority date knew, correct?

A Again, you are telling me about anticipation and obviousness. I don't know exactly what you refer to. This is not prior art. This is an -- I can assume that this is something that if we go into more detail, this is expectation of success, and certainly, this is something that you have.

Q Well, you know an expectation of success is judged as of the priority date of the patent in question, correct?

A Understand.

Q Okay. And this Exhibit 2063 was not available to a skilled artisan at the priority date of the '462 patent, correct?

A In my declaration, I'm not using the

1 argument of albiglutide as a prior art. I'm using
2 this in my dissertation, in my scientific rigor of
3 the analysis, that the assumption that GLP-1 longer
4 acting is going to be more accepted and was going to
5 have less side effects.

6 So I'm using the albiglutide case there
7 not just in terms that it was discontinued. It was
8 also using the albiglutide case, which is prior art,
9 when I used that, it is for dosages given every two
10 weeks and once a month, and that was prior art.

11 Q Let me try to unpack that.

12 You referred to side effects but, of
13 course, you agree that albiglutide was not withdrawn
14 for any safety reasons or side effects, correct?

15 A But if we're going to discuss
16 specifically about albiglutide --

17 Q Doctor, this will go much faster if you
18 answer my question.

19 You agree with me that according to the
20 exhibit that you cited in your declaration,
21 Exhibit 2063, albiglutide was not withdrawn from the
22 market for any safety reason or anything to do with

1 side effects, right; it was a commercial decision,
2 correct?

3 MR. BAUGHMAN: Object to the form.

4 Q Do you agree with that?

5 A I did not use that exhibit as a prior
6 art.

7 Q Because it's not prior art, right?

8 A I used albiglutide as a prior art in my
9 statements relating to side effects. And related to
10 the administration of every two weeks, once a month,
11 and that was prior art. So I used albiglutide in
12 two separate occasions.

13 Q Okay. And we'll get to the use you're
14 referring to in a moment.

15 But with respect to Exhibit 2063, that's
16 your evidence of albiglutide being withdrawn from
17 the market, correct?

18 A That is the reason why the sponsor
19 decided to withdraw it.

20 Q All right. And that is -- that occurred
21 in 2017, correct?

22 A That is when it occurred for that.

1 Q Okay. And so the fact that albiglutide 10:00:58
2 was withdrawn from the market in 2017 could not 10:01:01
3 inform a skilled artisan's belief or a skilled 10:01:05
4 artisan's reasonable expectation of success with 10:01:10
5 respect to the dosing regimen claimed in the '462 10:01:15
6 patent as of 2012, correct? I mean, that's just a 10:01:18
7 matter of logic, right? 10:01:20

8 MR. BAUGHMAN: Object to the form. 10:01:22

9 A When I wrote my declaration, I did not 10:01:22
10 use this exhibit as a prior art. I did not use this 10:01:26
11 for that purpose. 10:01:31

12 Q Okay. 10:01:32

13 A I just used it only in terms of the 10:01:33
14 discussion of Dr. Jusko and his assertion that a 10:01:36
15 once weekly is going to be very well accepted and so 10:01:41
16 on, I put it as an example. I did use albiglutide 10:01:44
17 as a prior art in a different exhibit. 10:01:47

18 Q Okay. Let's talk about that. 10:01:49

19 You write in paragraph 89 of your 10:01:57
20 declaration that the use of higher monthly doses of 10:02:01
21 albiglutide was constrained by the higher frequency 10:02:08
22 of GI-related adverse events, correct? 10:02:11

1	A	In paragraph 89?	10:02:16
2	Q	Mm-hmm.	10:02:17
3	A	Yes, sir.	10:02:18
4	Q	Okay. And for that proposition, you cite	10:02:24
5		Exhibit 2062, correct?	10:02:27
6	A	Yep.	10:02:30
7		MR. ANSTAETT: I'm going to have to	10:02:56
8		locate that exhibit, so why don't we take a break.	10:02:57
9		(Recess from 10:03 a.m. until 10:12 a.m.)	10:12:52
10		(Previously marked Exhibit 2062 presented	10:12:52
11		to the witness.)	10:12:53
12		BY MR. ANSTAETT:	10:12:53
13	Q	So Doctor, we were discussing	10:12:54
14		albiglutide, and I was looking for an exhibit, which	10:13:00
15		I found.	10:13:03
16		But just to set the stage again, in	10:13:04
17		paragraph 89 of your report, you say that the use of	10:13:06
18		higher monthly doses of albiglutide was constrained	10:13:13
19		by the higher frequency of GI-related adverse	10:13:17
20		events, correct?	10:13:21
21	A	Yes, sir.	10:13:22
22	Q	And the dosing regimen that's claimed in	10:13:23

1 the '462 patent is not a monthly dosing regimen, 10:13:26
2 correct? 10:13:30

3 A No, it's weekly. 10:13:30

4 Q Let me give you what was previously -- 10:13:32
5 what's been marked as Exhibit 2062. 10:13:36

6 And Exhibit 2062 is an article that you 10:13:50
7 co-authored that was published in October 2009 10:13:53
8 before the priority date of the '462 patent, 10:13:57
9 correct? 10:14:00

10 A Yes. That's what I meant, that this is 10:14:01
11 the one for prior art. 10:14:03

12 Q And Exhibit 2062 reports on a clinical 10:14:05
13 trial in which patients were administered either a 10:14:09
14 weekly, a biweekly, or a monthly dose of albiglutide 10:14:11
15 or exenatide twice daily as an open-label active 10:14:15
16 reference, correct? 10:14:20

17 A Yes. 10:14:21

18 Q And the conclusion you report for this 10:14:21
19 study was that weekly albiglutide administration 10:14:25
20 significantly improved glycemic control and elicited 10:14:29
21 weight loss in type 2 diabetic patients with a 10:14:33
22 favorable safety and tolerability profile, correct? 10:14:39

1	A	What paragraph again?	10:14:45
2	Q	It's on the very first page, and you see	10:14:46
3		there's a bold heading that says, Conclusions?	10:14:49
4	A	Yes.	10:14:58
5	Q	And now, when this paper refers to	10:14:59
6		biweekly dosing, do I understand it correctly that	10:15:05
7		that's referring to dosing once every two weeks?	10:15:08
8	A	Correct.	10:15:11
9	Q	Okay. And you report in your paper at	10:15:12
10		page 6 -- and again using those page numbers at the	10:15:15
11		bottom of the page -- and here I'm looking in the	10:15:22
12		middle column. So there is a paragraph in the	10:15:35
13		middle column that starts, Albiglutide 30 milligram	10:15:38
14		weekly dosing.	10:15:42
15		Do you see that?	10:15:43
16	A	Yes, sir.	10:15:43
17	Q	All right. And then if you go down, and	10:15:44
18		what I'm looking at are the last two sentences in	10:15:46
19		that paragraph.	10:15:50
20		And in the last two sentences of that	10:15:53
21		paragraph, you reported that, An escalating-dose	10:15:55
22		titration for the biweekly regimen might have	10:16:00

1	resulted in a lower frequency of GI events.	10:16:03
2	Correct?	10:16:08
3	A Let me read it, please.	10:16:08
4	Q Sure.	10:16:09
5	A Yes. So what do you want me to read,	10:16:57
6	then?	10:16:59
7	Q I just want you to confirm. You reported	10:16:59
8	in your paper that, An escalating-dose titration for	10:17:01
9	the biweekly regimen might have resulted in a lower	10:17:05
10	frequency of GI events.	10:17:09
11	Correct?	10:17:10
12	A Might have, might have.	10:17:11
13	Q Correct.	10:17:13
14	A What I did report is -- in the previous	10:17:13
15	statements, it says, When dosed biweekly,	10:17:17
16	50 milligrams albiglutide also improved glycemic	10:17:21
17	indexes but with higher GI adverse events.	10:17:24
18	And that's a statement. The other is	10:17:27
19	just a possibility, might have.	10:17:30
20	Q And, in fact, also on page 6, in the	10:17:32
21	third column, in the first full paragraph there, you	10:17:37
22	describe limitations to the phase 2 study, right?	10:17:42

1	A	Where is it?	10:17:46
2	Q	In the third column on page 6.	10:17:47
3	A	There are limitations?	10:17:50
4	Q	Yes. You're describing limitations of	10:17:51
5		the phase 2 study reported in this paper. And one	10:17:54
6		of the limitations that you identify was the fact	10:17:56
7		that no escalating doses were tested for biweekly	10:17:58
8		and monthly dosing, which may have attenuated GI	10:18:01
9		adverse events and FPG fluctuations, correct?	10:18:04
10	A	Yeah, that was the fourth limitation.	10:18:34
11		But there were other limitations in terms of the	10:18:36
12		high dropout because of the GI adverse event.	10:18:38
13		That's why it's so important to balance efficacy	10:18:41
14		with safety.	10:18:44
15		I mean, if -- there were not enough	10:18:45
16		patients to analyze there, but there was high	10:18:47
17		dropout, and certainly -- that was one estimate.	10:18:49
18		But certainly, what was factual was with the higher	10:18:56
19		dosages, there were more GI adverse events.	10:19:00
20	Q	But you don't dispute, do you, Doctor,	10:19:03
21		that one of the limitations you identified with the	10:19:06
22		study was that there was no escalating dose -- no	10:19:09

1 titration that was used for the biweekly and monthly
2 dosing, and had it been, it may have attenuated some
3 of those GI side effects, correct?

4 A All clinical research studies have
5 limitations. I wish they all were perfect. But the
6 fact that I state that limitation doesn't
7 necessarily mean that high titrating was done.
8 Because you could still titrate and use very high
9 dosages, still would not do anything.

10 So it's one -- what I would say, it's one
11 option there, one possible limitation. That's why I
12 listed four different ones. And the one I listed as
13 the fourth was the possibility of titration.

14 Q The possibility of titration reducing GI
15 side effects?

16 A Possibility.

17 Q And in paragraph 198 of your expert
18 report -- I'll give you a moment to get there.

19 In paragraph 198, you criticize
20 Dr. Bantle and Dr. Jusko for what you characterize
21 as their broad generalizations that GLP-1 receptor
22 agonists will be effective in reducing glucose

1	levels embodiment.	10:20:53
2	Do you see that?	10:20:54
3	A 198?	10:20:54
4	Q Correct.	10:20:55
5	A Yes, sir.	10:20:56
6	Q Okay. And you criticize them because,	10:20:56
7	according to you, this was only partially true for	10:21:00
8	albiglutide.	10:21:04
9	Do you see that?	10:21:05
10	A I thought that that was a broad	10:21:08
11	generalization.	10:21:11
12	Q Okay. You write that, Albiglutide	10:21:11
13	improved glucose control and had some weight loss	10:21:14
14	but was considerably inferior to other GLP-1	10:21:17
15	receptor agonists and eventually GSK decided to	10:21:21
16	withdraw albiglutide from the market for commercial	10:21:24
17	reasons.	10:21:26
18	Correct?	10:21:27
19	A Yeah. That's at the last -- you referred	10:21:28
20	to the last paragraph of the 198 where it says, This	10:21:35
21	was only partially true for albiglutide?	10:21:39
22	Q Correct.	10:21:41

1 A That improved glucose control and had 10:21:42
2 some weight loss but was considerably inferior to 10:21:46
3 other GLP-1 and eventually GSK -- yeah, that was a 10:21:48
4 posteriority [sic] there. 10:21:52

5 Q Okay. But as we looked at earlier, your 10:21:53
6 conclusions in your 2009 paper was that albiglutide 10:21:55
7 was effective at reducing glucose levels and body 10:21:59
8 weight, correct? 10:22:04

9 A It was -- that was a phase 2A. It was 10:22:04
10 effective in the sense that the lower dose was 10:22:09
11 effective. The higher doses was a tolerability. 10:22:13

12 So when you looked at effectiveness, it's 10:22:16
13 a combination of a ratio between effectiveness and 10:22:18
14 safety. 10:22:23

15 So it was -- effective also has a range. 10:22:24
16 I mean, at that time, show efficacy. But certainly, 10:22:26
17 when GSK decided later on -- when there was evidence 10:22:32
18 of other GLP-1s is when they said they decided to 10:22:39
19 withdraw albiglutide because it was considered 10:22:43
20 inferior. 10:22:46

21 But at that time, in 2009, when only 10:22:47
22 exenatide was available, and exenatide being given 10:22:50

1 twice a day, it was consistent with exenatide. So 10:22:53
2 it was effective at that time. 10:22:58

3 But the point that I was trying to make 10:23:00
4 here is the generalization that a longer half-life 10:23:03
5 is going to be more tolerable, acceptable, and so on 10:23:05
6 in longer administration. And albiglutide study 10:23:12
7 that we did proved otherwise. 10:23:15

8 Q Well, what you say in paragraph 198 was 10:23:17
9 that it was only partially true that albiglutide 10:23:21
10 improved glucose control and had some weight loss, 10:23:24
11 right? 10:23:27

12 But then you go on to say, it was 10:23:27
13 inferior to other GLP-1 receptor agonists and 10:23:29
14 eventually GSK decided to take it off the market, 10:23:32
15 right? 10:23:36

16 MR. BAUGHMAN: Object to the form. 10:23:36

17 A What it says here is, Moreover, part of 10:23:52
18 Dr. Bantle's and Dr. Jusko's broad generalizations 10:23:56
19 were that GLP-1 receptor will be effective in 10:24:01
20 reducing glucose levels and body weight. 10:24:05

21 And I said that they would have known 10:24:08
22 that there were other GLPs being studied, each which 10:24:11

1 was known to be effective. And so a POSA would have 10:24:18
2 reasonably expected semaglutide to behave in 10:24:22
3 a generally consistent -- that was Dr. Jusko. But 10:24:27
4 what I'm saying is partially true for albiglutide, 10:24:27
5 was effective, but relatively to other, was 10:24:29
6 inferior. 10:24:32

7 Q Okay. And, of course, when you say 10:24:33
8 relative to others, it was withdrawn for commercial 10:24:35
9 reasons, as we discussed earlier, that happened in 10:24:38
10 2017, right? 10:24:42

11 A Yes. But I'm not stating that as a prior 10:24:44
12 art. I'm stating that -- 10:24:47

13 Q Understood. 10:24:48

14 A -- as a scientific rigor discussion in 10:24:49
15 terms of the statement that I make. 10:24:52

16 Q Sure. Because something that happens in 10:24:54
17 2017 isn't prior art to the '462 patent, right? 10:24:56

18 MR. BAUGHMAN: Object to the form and 10:25:01
19 foundation. 10:25:02

20 A The 2017 was a commercial decision. 10:25:02
21 We're talking here about efficacy and so on. 10:25:07

22 Q Right. 10:25:09

1 A That the arguments of 2017 -- the point 10:25:10
2 that I'm making is, I'm not using the 2017 as a 10:25:12
3 prior art. What I'm using as a prior art is the 10:25:15
4 2010 data that I have. 10:25:18

5 Q Right. And in this publication from 10:25:19
6 2009, which is prior art to the '462 patent, what 10:25:23
7 you reported was that, Weekly albiglutide 10:25:26
8 administration significantly improved glycemic 10:25:28
9 control and elicited weight loss in type 2 diabetic 10:25:31
10 patients with a favorable safety and tolerability 10:25:36
11 profile. 10:25:38

12 Correct? 10:25:38

13 A I did not quite say that. The conclusion 10:25:39
14 was a general conclusion. The conclusion was, 10:25:41
15 Weekly albiglutide administration significantly 10:25:44
16 improved glycemic control and elicited weight loss 10:25:46
17 in type 2 diabetes. 10:25:50

18 Q With a favorable safety and tolerability 10:25:51
19 profile, correct? 10:25:54

20 A In general. The conclusion -- when you 10:25:54
21 write a paper, you have limitations in the number of 10:25:56
22 words that you can do. The journals and the editors 10:25:59

1 are very, very serious in restricting the number of 10:26:02
2 words. This is basically refer in general. 10:26:07

3 But clearly, in the report, in the 10:26:10
4 results, and in the discussion says very clearly 10:26:13
5 that when you go to 50 milligrams and a hundred 10:26:15
6 milligrams, those were dosages that were 10:26:18
7 unacceptable and they were not tolerable. 10:26:21

8 So in general, you can conclude that it 10:26:23
9 was effective. It was favorable safety at that time 10:26:26
10 in 2009 compared to exenatide. 10:26:31

11 But the point that in 2017, I'm not 10:26:34
12 arguing there. I'm arguing of this one that 10:26:37
13 actually has some efficacy, has some effect on 10:26:40
14 weight loss, but certainly later on shown to be 10:26:45
15 inferior to others. 10:26:48

16 Q And so what I take you to be saying in 10:26:49
17 paragraph 198 is just that there are other GLP-1 10:26:52
18 receptor agonists that proved to be more effective 10:26:58
19 than albiglutide. 10:27:00

20 Is that right? 10:27:02

21 MR. BAUGHMAN: Object to the form. 10:27:03

22 A It says there that, This was only 10:27:04

1 partially true for albiglutide. Improved glucose
2 control and had some weight loss but was
3 considerably inferior to other GLP-1s and eventually
4 GSK took it out.

5 Q That's the criticism. While it reduced
6 HbA1c, while it reduced weight, it wasn't as
7 effective as other GLP-1 RAs.

8 Is that fair?

9 A But what I'm referring this is the
10 general statement that Dr. Bantle and Dr. Jusko says
11 that it says there the bottom of 198, Moreover, part
12 of Dr. Bantle, Dr. Jusko broad generalization was
13 that GLP-1 will be effective in reducing glucose
14 levels and body weight. I was referring to that.

15 Q As you report, albiglutide is effective
16 in reducing glucose levels and body weight; it's
17 just not as effective as certain other GLP-1
18 receptor agonists, fair?

19 MR. BAUGHMAN: Object to the form
20 foundation.

21 A It is well -- I can tell you that at that
22 time, it is -- was effective in relation to

1	exenatide.	10:28:07
2	Q Okay. And you understand, right, that	10:28:08
3	the claims of the '462 patent don't require any	10:28:11
4	particular level of efficacy, right? We agree on	10:28:15
5	that?	10:28:18
6	A I agree.	10:28:18
7	Q Okay. And you also understand that the	10:28:19
8	claims of the '462 patent don't require that the	10:28:20
9	claim treatment method using semaglutide is superior	10:28:24
10	or even noninferior to other GLP-1 receptor	10:28:27
11	agonists, correct?	10:28:31
12	A I'm not -- in my declaration, I'm not	10:28:31
13	making any assertions of superiority of semaglutide	10:28:34
14	and so on. I'm restricted to the claim 1 that goes	10:28:37
15	for the dose of 0.1.	10:28:42
16	Q And claim 1 doesn't require that dose of	10:28:43
17	0.1 milligrams of semaglutide be superior to other	10:28:46
18	GLP-1 receptor agonists, right?	10:28:49
19	MR. BAUGHMAN: Object to the form.	10:28:51
20	A It says 0.1 -- 1.0 milligrams. 1.0.	10:28:52
21	Q Right. And no requirement that it be	10:28:57
22	more effective than any other GLP-1 receptor	10:28:59

1	agonists, correct?	10:29:04
2	A I did not see that.	10:29:04
3	Q All right. In paragraph 90 of your	10:29:05
4	report, you write that the pegylated GLP-1 analog	10:29:07
5	LY2428757 was also abandoned during development,	10:29:16
6	correct?	10:29:22
7	A In what paragraph? Excuse me?	10:29:22
8	Q Paragraph 90.	10:29:24
9	A Yes, sir.	10:29:31
10	Q Okay. And you would agree with me, I	10:29:32
11	take it, that skilled artisans at the priority date	10:29:36
12	of the '462 patent would not have known that	10:29:41
13	LY2428757 was never commercialized, correct?	10:29:45
14	A Can you repeat that?	10:29:49
15	Q Sure. You would agree with me that at	10:29:50
16	the priority date of the '462 patent, a skilled	10:29:53
17	artisan would not have known that LY2428757 was	10:29:55
18	never commercialized, correct?	10:30:01
19	A When the -- I cannot recall exactly the	10:30:06
20	date when Eli Lilly make the decision to discontinue	10:30:09
21	that.	10:30:12
22	Q So you just don't know one way or the	10:30:13

1	other?	10:30:15
2	A Well, I don't recall. Can you point it	10:30:15
3	out, the date?	10:30:17
4	Q I don't think you pointed it out. And --	10:30:18
5	actually, I take that back. I think the only	10:30:23
6	document you cite for that proposition -- let me	10:30:27
7	give it to you.	10:30:31
8	(Previously marked Exhibit 2064 presented	10:30:31
9	to the witness.)	10:30:34
10	BY MR. ANSTAETT:	10:30:34
11	Q I think the only document you cite for	10:30:41
12	that proposition is Exhibit 2064.	10:30:44
13	Do you see in paragraph 90 you have a	10:30:57
14	citation at the end of Exhibit 2064?	10:30:59
15	A So what is your question?	10:31:59
16	Q In paragraph 90 you say, Additionally,	10:32:01
17	Lilly or LY2428757, a pegylated GLP-1 analog, was	10:32:04
18	also abandoned during development, and then you cite	10:32:10
19	Exhibit 2064.	10:32:13
20	Do you see that?	10:32:14
21	A Yes.	10:32:16
22	Q Okay. And I've given you Exhibit 2064.	10:32:17

1	And that's a document dated December 2023, right?	10:32:21
2	A Yeah. But it says, Discontinued.	10:32:28
3	Q Correct.	10:32:31
4	A It says, Discontinued 2023. And that was	10:32:31
5	discontinued prior to 2023.	10:32:38
6	Q Okay. But you don't say in your report	10:32:39
7	when LY2428757 was abandoned.	10:32:44
8	A I didn't state it, but it was most likely	10:32:53
9	public domain. I mean, it was in the public domain,	10:32:57
10	because it was known that Eli Lilly continued the	10:33:00
11	development of 265, which turned out to be	10:33:04
12	dulaglutide, but it was in the public domain.	10:33:09
13	Q But, Doctor, you don't cite anything to	10:33:11
14	show when it was abandoned, correct? The only thing	10:33:13
15	you cite is a publication from December 27, 2023,	10:33:16
16	right?	10:33:19
17	MR. BAUGHMAN: Object to the form.	10:33:19
18	A It was in the public domain.	10:33:26
19	Q What do you mean, it was in the public	10:33:28
20	domain? Where in the public domain was it? What's	10:33:27
21	your evidence of that?	10:33:30
22	A I didn't put a document, but it was in	10:33:33

1	the public domain.	10:33:35
2	Q The only document you put in as evidence	10:33:35
3	of that is dated December 2023, correct?	10:33:38
4	A Correct.	10:33:42
5	Q Okay. Now, you -- your declaration also	10:33:42
6	doesn't say why LY2428757 was never commercialized,	10:33:46
7	correct?	10:33:53
8	A I did not, no.	10:33:53
9	Q You didn't know why, right?	10:33:55
10	A I didn't know, and I don't think that I	10:33:57
11	needed to know because those are things that	10:33:59
12	pharmaceutical industry many times discontinue.	10:34:02
13	There are many, many compounds in the pipeline that	10:34:04
14	they discontinue.	10:34:07
15	Q For many different reasons, right?	10:34:08
16	A For many different reasons.	10:34:09
17	Q Could have been a commercial reason,	10:34:11
18	right?	10:34:12
19	A I don't think so at that stage.	10:34:12
20	Q Could have been because Eli Lilly had a	10:34:14
21	more promising GLP-1 receptor agonist candidate,	10:34:16
22	right?	10:34:20

1	A	I don't know.	10:34:20
2	Q	You just don't know one way or the other,	10:34:20
3		right?	10:34:22
4	A	I don't need to know.	10:34:22
5	Q	Okay. You also note in paragraph 93 of	10:34:24
6		your declaration that another Eli Lilly GLP-1	10:34:26
7		receptor agonist that was under investigation and	10:34:30
8		disclosed in the Lovshin reference, Lilly 2189265,	10:34:33
9		was later commercialized as dulaglutide, correct?	10:34:41
10		MR. BAUGHMAN: Object to the form.	10:34:44
11	A	Yes, sir.	10:34:45
12	Q	Okay. And dulaglutide was very	10:34:45
13		commercially successful for Eli Lilly, correct?	10:34:46
14		MR. BAUGHMAN: Object to the form,	10:34:50
15		foundation and scope.	10:34:51
16	A	At the time of 2009, that was unknown.	10:34:52
17	Q	Right. But dulaglutide was later	10:34:55
18		commercialized as Trulicity, correct?	10:34:57
19	A	That was later. But at the 2009 for	10:35:01
20		Lovshin, that was unknown.	10:35:04
21	Q	Correct. I agree with you on that.	10:35:06
22		But am I right that LY2189265 was later	10:35:08

1	commercialized as Trulicity by Eli Lilly?	10:35:15
2	MR. BAUGHMAN: Object to the form,	10:35:18
3	foundation.	10:35:20
4	A Yes, but that will not be prior art.	10:35:20
5	That was not known at that time.	10:35:24
6	Q Right. It wasn't commercialized at that	10:35:26
7	time?	10:35:28
8	A It was -- according to Lovshin, it says,	10:35:28
9	I, which means under investigation.	10:35:32
10	Q Right. And you also state in paragraph	10:35:34
11	91 of your report that CJC-1134-PC, which is also	10:35:40
12	identified in Lovshin, has not yet been approved	10:35:48
13	today despite being disclosed in Lovshin as being	10:35:52
14	under investigation, correct?	10:35:56
15	A Correct. That's -- I stated that this	10:35:57
16	Canadian compound CJC from ConjuChem was being	10:36:01
17	investigated, no data.	10:36:08
18	Q Okay. It was being investigated, no	10:36:10
19	data, and you say in your report that it has not yet	10:36:12
20	been approved, right?	10:36:15
21	A Yeah. We don't know if it was	10:36:16
22	discontinued. There is no data.	10:36:18

1	Q	But a skilled artisan at the priority	10:36:19
2		date wouldn't have known that it had not yet been	10:36:22
3		approved today, correct, to state the obvious?	10:36:25
4	A	In 2009, that was under investigation.	10:36:27
5	Q	Right. You say in your report at	10:36:31
6		paragraph 91, And CJC-1134-PC has not yet been	10:36:34
7		approved despite being disclosed as being	10:36:41
8		investigated in Lovshin, right?	10:36:45
9		MR. BAUGHMAN: Object to the form.	10:36:46
10	A	It says there that it's part of the list	10:36:47
11		in Table 1.	10:36:49
12	Q	Right. And you offer the opinion that	10:36:50
13		it's not been approved today as evidence that you	10:36:53
14		can't know whether something is going to be	10:36:57
15		approved, right?	10:37:00
16	A	That is a comment that I do. I'm	10:37:01
17		qualifying this. I'm analyzing this as I would	10:37:07
18		analyze any other grant or any paper, or in this	10:37:10
19		case, analyzing the declaration of Dr. Bantle and	10:37:15
20		Dr. Jusko.	10:37:22
21		I only can say that at that time, it was	10:37:23
22		not approved, and I can add a qualifying comment	10:37:25

1 that to my knowledge at this time, it hasn't been
2 approved.

3 Q And what a skilled artisan knew at the
4 priority date was that it was being investigated,
5 right?

6 A Just being investigated.

7 MR. ANSTAETT: Okay. Let's look at
8 another exhibit.

9 (Previously marked Exhibit 1014 presented
10 to the witness.)

11 BY MR. ANSTAETT:

12 Q So I've handed you what is marked as
13 Exhibit 1014. And this is the NCT773 clinical trial
14 protocol that you describe in paragraphs 99 to 105
15 of your declaration, correct?

16 A Yes, sir.

17 Q Okay. NCT773 describes the protocol for
18 a phase 1 trial to examine the safety, tolerability,
19 and profile of action of semaglutide NN9535 in
20 healthy male Japanese and Caucasian subjects,
21 correct?

22 A Yes, sir.

1	Q	And in paragraph 103 of your declaration,	10:39:09
2		you describe a portion of NCT773 that's dated	10:39:15
3		September 11, 2009, and that's at pages 11 to 12 of	10:39:20
4		Exhibit 2014, which identifies the once-weekly	10:39:26
5		semaglutide doses to be tested in the trial,	10:39:35
6		correct?	10:39:38
7	A	I'm sorry. You're referring to --	10:39:38
8	Q	Pages 11 and 12 of Exhibit 1014.	10:39:40
9	A	Yes, sir.	10:39:46
10	Q	Okay. And again, in your report, at	10:39:47
11		paragraph 103, where you're discussing pages 11 to	10:39:55
12		12, you describe one of the dosing regimens in the	10:40:01
13		trial as involving 0.4 milligrams for one week, 0.8	10:40:05
14		milligrams for one week, followed by unspecified	10:40:10
15		variable doses for six weeks, correct?	10:40:14
16	A	That's what I wrote, yeah.	10:40:19
17	Q	Okay. And then if we look at page 11 of	10:40:21
18		Exhibit 1014, I think what you're describing in	10:40:25
19		paragraph 103 of your declaration is experimental	10:40:29
20		Arm G in the trial protocol.	10:40:32
21		Is that right?	10:40:34
22	A	Let me just try to --	10:40:36

1	Yes, sir.	10:41:30
2	Q And experimental Arm G says that subjects	10:41:31
3	randomized to that trial arm will receive by	10:41:34
4	subcutaneous injection 0.4 milligrams once weekly	10:41:37
5	for one week, 0.8 milligrams once weekly for one	10:41:40
6	week, followed by once weekly injections for six	10:41:43
7	weeks, dose to be determined based on safety and	10:41:47
8	tolerability of previous dose steps.	10:41:50
9	Correct?	10:41:53
10	A Yes, sir.	10:41:53
11	Q And then experimental Arm G says, This	10:41:54
12	dose arm is optional and will only be implemented if	10:41:59
13	the 0.8 milligram dose is tolerated but the 1.6	10:42:03
14	milligram is not.	10:42:08
15	Correct?	10:42:08
16	A That's what it states.	10:42:09
17	Q And the 1.6 milligram was the highest	10:42:11
18	dose to be tested in the trial, right?	10:42:14
19	A Which dose?	10:42:16
20	Q The 1.6 milligram.	10:42:17
21	A Yes, sir.	10:42:18
22	Q And the study protocol contemplates the	10:42:19

1	possibility of the 1.6 milligram once-weekly dose	10:42:21
2	would not be tolerated, correct?	10:42:24
3	A Correct.	10:42:27
4	Q And according to this arm of the	10:42:28
5	protocol, if the 1.6 milligram dose were not	10:42:30
6	tolerated but the 0.8 milligram dose is tolerated,	10:42:33
7	then a dose greater than 0.8 milligrams and less	10:42:36
8	than 1.6 milligrams would be administered to	10:42:39
9	subjects.	10:42:43
10	Is that right?	10:42:43
11	MR. BAUGHMAN: Object to the form and	10:42:43
12	scope.	10:42:44
13	A Can you repeat it again?	10:42:44
14	Q Sure. So according to this arm of the	10:42:45
15	protocol, Arm G, if the 1.6 milligram dose were not	10:42:49
16	tolerated but the 0.8 milligram dose was tolerated,	10:42:53
17	then a dose greater than 0.8 but less than 1.6 would	10:42:57
18	be administered to subjects.	10:43:02
19	Is that right?	10:43:04
20	MR. BAUGHMAN: Same objections.	10:43:05
21	A Can you repeat it again?	10:43:05
22	Q Sure. In this arm, the protocol	10:43:07

1 contemplates that if the 1.6 dose were not tolerated 10:43:16
2 but the 0.8 milligram dose is tolerated, then a dose 10:43:20
3 greater than 0.8 but less than 1.6 would be 10:43:23
4 administered to patients. 10:43:26

5 Is that right? 10:43:28

6 MR. BAUGHMAN: Object to the form and 10:43:28
7 scope. 10:43:28

8 A It doesn't quite say that. 10:43:28

9 Q How do you read it? 10:43:30

10 A It said that, Subcutaneous injections 0.4 10:43:32
11 milligram once weekly for one week, 0.8 milligrams 10:43:37
12 once weekly for one week, followed by once weekly 10:43:40
13 injection for eight weeks. Dose to be determined 10:43:44
14 based on safety and tolerability of previous dose 10:43:49
15 steps. The dose arm is optional and will be 10:43:53
16 implemented if the 0.8 milligram is tolerated but 10:43:58
17 the 1.8 milligram is not. 10:44:03

18 So it could well be that they just stay 10:44:06
19 on the 0.8 milligram. 10:44:09

20 Q Well, if the -- that would be if the 0.8 10:44:11
21 milligram was not tolerated. 10:44:15

22 Is that right? 10:44:17

1	A	No, it does not say that.	10:44:17
2	Q	It says, The dose arm is optional and	10:44:19
3		will only be implemented if the 0.8 milligram is	10:44:21
4		tolerated.	10:44:24
5	A	Correct.	10:44:24
6	Q	So if the 0.8 milligram is tolerated --	10:44:25
7	A	But the 1.6 is not.	10:44:27
8	Q	-- but the 1.6 is not, in that	10:44:29
9		circumstance, then this dose arm is going to be	10:44:30
10		implemented, right?	10:44:32
11		MR. BAUGHMAN: Object to the form and	10:44:33
12		scope.	10:44:34
13	A	It states there that, This dose arm is	10:44:35
14		optional and will only be implemented if the 0.8	10:44:40
15		milligrams is tolerated but the 1.6 milligrams is	10:44:45
16		not.	10:44:48
17		So I can assume that the 0.8 milligrams	10:44:49
18		remains there.	10:44:52
19	Q	Right. And so if 0.8 is tolerated,	10:44:52
20		right, and 1.6 milligrams is not tolerated, then	10:44:58
21		this optional dose arm comes into play, right? It	10:45:02
22		will be implemented, it says.	10:45:05

1	Do you agree with me so far?	10:45:07
2	MR. BAUGHMAN: Object to the form and	10:45:09
3	foundation.	10:45:11
4	A Where does it say the optional?	10:45:11
5	Q It says this dose arm is optional.	10:45:12
6	Do you see that?	10:45:15
7	A Yes. What this option is is the 1.6.	10:45:15
8	Q What it says is the dose -- okay. I want	10:45:18
9	to understand how you understood this in reaching	10:45:21
10	your opinions in the case, okay? Because this is	10:45:24
11	dated September 9th -- September 11, 2009, right?	10:45:27
12	This is prior art. This is before the priority date	10:45:33
13	of the '462 patent, right?	10:45:36
14	A Yeah. This gives different dosages --	10:45:37
15	Q Right.	10:45:40
16	A -- 0.1, 0.2, 0.4, 0.4, 0.8, 0.4 titrated	10:45:41
17	up to 0.8. Then you go subcutaneous injection 0.4	10:45:46
18	milligrams once weekly for one week, 0.8 milligrams	10:45:53
19	once weekly for one week, followed by once weekly	10:45:56
20	injections for six weeks. Dose to be determined	10:45:59
21	based on safety and tolerability of previous dose	10:46:03
22	steps. This dose arm is optional and will only be	10:46:06

1 implemented if the 0.8 milligrams is tolerated but 10:46:11
2 the 1.6 milligram is not. 10:46:14

3 So I don't see there that it's telling me 10:46:19
4 going above 0.8. It's telling me there that if the 10:46:22
5 1.6 is not tolerated and the 0.8 milligram is 10:46:29
6 tolerated, you can remain on the 0.8. It doesn't 10:46:32
7 specify what other optional dose is given. 10:46:36

8 Q But it does say that a -- that -- strike 10:46:38
9 that. 10:46:43

10 It says that patients in experimental 10:46:44
11 Arm G, right, they'll get 0.4 milligrams once weekly 10:46:49
12 for a week, right? 10:46:53

13 A Yes, sir. 10:46:54

14 Q They'll get -- then they'll move to 0.8 10:46:55
15 milligrams. 10:46:57

16 A Yes, sir. 10:46:58

17 Q And they'll receive one injection of 10:46:58
18 that, right, 0.8 milligrams once weekly for one 10:47:01
19 week, right? And then they will get once weekly 10:47:04
20 injections for six weeks, right? 10:47:07

21 A Yes. 10:47:11

22 Q But it doesn't specify what dose they'll 10:47:11

1	be getting during that six-week period, correct?	10:47:14
2	A What is specified is 0.8 milligrams.	10:47:16
3	Q Well, it says, followed by once weekly	10:47:19
4	injections for six weeks. Dose to be determined	10:47:23
5	based on safety and tolerability of previous steps.	10:47:27
6	This dose arm is optional and will only be	10:47:30
7	implemented if the 0.8 milligrams is tolerated and	10:47:33
8	the 1.6 milligram is not.	10:47:37
9	A Yeah, but the determine is because it was	10:47:39
10	assumed there that you have the 0.8 and then you	10:47:42
11	escalate to 1.6. I understand, Counsel, that you	10:47:44
12	can interpret any way that you want, but that the	10:47:47
13	numbers here -- clearly the only numbers that they	10:47:50
14	refer to is the 0.4, 0.8, and 1.6. There is no	10:47:52
15	talking 0.9, 0.10, 0.11, 0.12. Those are the	10:48:00
16	things. In a clinical research study, you cannot	10:48:06
17	leave this totally open to decide what you're going	10:48:09
18	to do there.	10:48:12
19	What is referring here is the dose arm is	10:48:13
20	optional and will only be implemented if the 0.8	10:48:15
21	milligrams is tolerated but the 1.6 is not.	10:48:20
22	So you stay in the 0.8 milligrams.	10:48:22

1	Q	The way you read this is that you just --	10:48:26
2		if the 0.8 milligrams is tolerated -- and this is	10:48:27
3		your understanding in reaching your opinions in this	10:48:30
4		case. If the 0.8 milligram dose is tolerated and	10:48:33
5		the 1.6 milligram is not, then patients randomized	10:48:36
6		to experimental Arm G would stay at 0.8 milligrams.	10:48:40
7		Is that your understanding of this?	10:48:43
8	MR. BAUGHMAN:	Object to the form,	10:48:44
9		foundation and scope.	10:48:45
10	A	That is one interpretation.	10:48:46
11	Q	I'm interested in your interpretation,	10:48:47
12		Doctor. You're the expert here. You're the one who	10:48:50
13		is offering opinions in this case.	10:48:53
14		So what is your opinion? Is it your	10:48:54
15		opinion that under experimental Arm G, if the 0.8	10:48:56
16		dose is tolerated and the 1.6 milligram dose is not,	10:49:00
17		then patients randomized to that arm stay at 0.8	10:49:04
18		milligrams?	10:49:08
19	MR. BAUGHMAN:	Same objections.	10:49:08
20	A	What it says is, This dose is optional.	10:49:09
21		It will only be implemented if the 0.8 milligrams is	10:49:12
22		tolerated but the 1.6 is not. The dose arm refers	10:49:14

1 to the 1.6. That's what is optional. That is my
2 interpretation.

3 Q So your interpretation, so just so I have
4 it correct, is that in experimental Arm G, patients
5 randomized to that arm, if it's found that the 0.8
6 milligram dose is tolerable, and it's found that the
7 1.6 milligram dose is not tolerable, your reading of
8 experimental Arm G is that patients in that
9 situation will then take another six weeks of 0.8
10 milligram doses?

11 A Presumably. That's my interpretation. I
12 don't see any other numbers there.

13 Q Okay. You can set that aside.

14 Okay. Let's look at Exhibit 2006.

15 (Previously marked Exhibit 2006 presented
16 to the witness.)

17 BY MR. ANSTAETT:

18 Q Exhibit 2006 is an article that you rely
19 on for the proposition that skilled artisans would
20 have believed that from 2006 to 2007, 72 percent of
21 phase 2 clinical trials failed, and that from 2008
22 to 2009, 82 percent of phase 2 clinical trials

1	failed.	10:50:58
2	Is that right?	10:50:58
3	A That's what I stated. But can you remind	10:50:59
4	me where I stated there in my --	10:51:02
5	Q I think you state it in many places in	10:51:04
6	your declaration. But an example would be at	10:51:07
7	paragraphs 119 to 122.	10:51:09
8	A Yeah.	10:51:26
9	Q Okay. And Exhibit 2006 is a single-page	10:51:27
10	article, right?	10:51:32
11	A Yeah.	10:51:36
12	Q It consists in its entirety of three	10:51:37
13	paragraphs, correct?	10:51:41
14	A It's a news report.	10:51:41
15	Q There are no footnotes in this article,	10:51:44
16	correct?	10:51:46
17	A It is -- this report is analysis of X	10:51:56
18	number of trials being conducted in that -- in	10:52:01
19	phase 2 between 2008 and 2010. It's a collection of	10:52:04
20	those data.	10:52:08
21	Q So the answer to my question is, yes,	10:52:08
22	there are no footnotes cited in this article,	10:52:11

1	correct?	10:52:13
2	A There are no footnotes, but there were	10:52:13
3	analyzed all these studies that were done at that	10:52:17
4	time and how many make it and how many did not make	10:52:19
5	it.	10:52:21
6	Q All right. And none of the clinical	10:52:22
7	trials the article purports to analyze are	10:52:23
8	identified, correct?	10:52:26
9	A Say it again.	10:52:27
10	Q None of the clinical trials that the	10:52:27
11	article purports to analyze are identified, correct?	10:52:29
12	A It doesn't say that, but it's very	10:52:34
13	credible, because in my experience, phase 2 trials	10:52:37
14	fail all the time.	10:52:40
15	Q None of the drugs that were subject of	10:52:41
16	the clinical trials that the article purports to	10:52:44
17	analyze are identified, correct?	10:52:45
18	A They are analyzing general, cancer,	10:52:49
19	neuroscience, cardiovascular, and so on. That's	10:52:52
20	what the article makes.	10:52:55
21	Q So the answer to my question is, yes,	10:52:56
22	it's correct that none of the drugs that were	10:52:59

1 subject of the clinical trials that the article

10:53:01

2 purports to analyze are identified, correct?

10:53:02

3 MR. BAUGHMAN: Object to the form.

10:53:05

4 A I did not say that. That's not the words

10:53:06

5 that I'm saying. The words that I'm saying is that

10:53:09

6 they looked at the phase 2 trials in general, and

10:53:11

7 looked at the percentage of trials that don't make

10:53:14

8 it, as is very well-known in the industry, many

10:53:17

9 phase 2 trials do not make it.

10:53:20

10 Q Doctor, none of the drugs that were the

10:53:22

11 subject of this purported analysis are identified in

10:53:25

12 Exhibit 2006, correct?

10:53:27

13 A They are cardiovascular drugs,

10:53:29

14 neuroscience drugs, cancer drugs. They don't list

10:53:31

15 the specific drugs.

10:53:34

16 Q Okay. And the 72 percent and 82 percent

10:53:34

17 failure rates that you rely on come from the first

10:53:38

18 paragraph reporting on an analysis done by something

10:53:41

19 called the Centre for Medicines Research, correct?

10:53:43

20 A It states there, Phase II success rates

10:53:50

21 are lower than at any other phase of development.

10:53:53

22 Analysis by the Centre of Medicine Research of

10:53:57

1 projects from a group of 16 companies (representing
2 approximately 60 percent of global -- 60 percent of
3 R&D spending), which is in the public domain, where
4 the data was taken, in the CMR International Global
5 database.

6 So they looked at the database, and they
7 looked at a good number of phase, and they came up
8 with this, how many failed or did not go through.

9 Q What is the Centre for Medicines
10 Research?

11 A Center there is what it is there. It is
12 Centre for Medicines Research, projects from a group
13 of -- it's a company that analyzes data.

14 Q Are you familiar with that company?

15 A I rely on this thing.

16 Q Had you ever heard of that company before
17 you read Exhibit 2006?

18 A Perhaps, but I don't recall.

19 Q Do you know what it is today?

20 A I don't know.

21 Q You relied on the sentence in the first
22 paragraph of Exhibit 2006, I think you just said,

1 that says that based on information from the Centre
2 for Medicines Research, the Phase II success rate
3 for new development projects have fallen from 28
4 percent (2006-2007) to 18 percent (2008-2009).

5 Correct?

6 A Is what it says, yeah.

7 Q And that's how you come to your number
8 that 82 percent of all phase 2 Clinical trials
9 failed in 2008-2009, and 28 percent of all phase 2
10 clinical trials failed from 2006 to 2007, right?

11 A It's highly credible in terms of -- in
12 the experience in the pharma industry that a lot of
13 phase 1, phase 2 trials fail.

14 Q My question was -- I'm just trying to get
15 how you came to your numbers of 82 percent and
16 28 percent. You just --

17 A I rely on this data.

18 Q You rely on this data in the first
19 sentence?

20 A Which is a number that I can use. But
21 certainly, it is pretty much reflective of, in my
22 experience, conducting clinical trials for 35,

1 40 years, that we see a lot of phase 2 trials that 10:56:04

2 fail. 10:56:07

3 Q And Exhibit 2006 doesn't explain how and 10:56:07

4 where CMR got its data, correct? 10:56:10

5 A I presume that it was taken from the -- 10:56:14

6 what is in the public domain that the pharmaceutical 10:56:18

7 companies are obliged to report. 10:56:21

8 Q You have to presume because it doesn't 10:56:23

9 explain, right? 10:56:24

10 A It is well-known that all the companies 10:56:26

11 need to report on a quarterly basis what is going on 10:56:29

12 and what the studies are. It is a requirement that 10:56:35

13 the companies do. And that is in public domain. 10:56:38

14 Q Doctor, does Exhibit 2006 explain how and 10:56:40

15 where CMR got its data? 10:56:43

16 A It says there, To help understand these 10:56:47

17 trends, Thomson Reuters Life Science Consulting 10:56:56

18 analyzed the 108 reported Phase II failures from 10:57:00

19 2008 to 2010 for new drugs and major new indications 10:57:05

20 of existing drugs. 10:57:09

21 Drug News cites three there. 10:57:10

22 Out of these, 87 reported that the 10:57:14

1 reasons for failure were: 51 percent (44 out of 87) 10:57:16
2 were due to insufficient efficacy, 29 percent (25 of 10:57:20
3 87) were due to strategic reasons, and 19 percent 10:57:24
4 (17 to 87) were due to clinical or preclinical 10:57:28
5 safety reasons. Out of the 25 failures that were 10:57:32
6 determined for strategic reasons, 16 percent 10:57:35
7 involved validated targets such as PPAR alpha and 10:57:38
8 factor Xa. 10:57:44

9 And so I think that it is very credible 10:57:45
10 what it says with this data. 10:57:48

11 Q Doctor, you're confusing two different 10:57:49
12 things. First of all, you're just reading from the 10:57:51
13 article, right? 10:57:53

14 A That's what I did. 10:57:54

15 Q But you're confusing two different 10:57:55
16 things. You referred to an analysis by Thomson 10:57:57
17 Reuters Life Science Consulting. That's a different 10:58:00
18 analysis than the analysis that you rely on in 10:58:03
19 paragraph 1 by CMR that -- from which you derive 10:58:05
20 your 72 percent and 82 percent numbers, isn't it? 10:58:09

21 MR. BAUGHMAN: Object to the form. 10:58:12

22 A No. 10:58:13

1 Q You think these are the two same things? 10:58:13

2 A The CMR took some of that data. I mean, 10:58:16
3 when you do an analysis, they have different 10:58:19
4 sources. That's one of the sources they did. it's 10:58:22
5 perfectly valid. 10:58:25

6 Q Doctor, I don't think you understand this 10:58:25
7 article. The first paragraph where -- the numbers 10:58:28
8 that you rely on, the percentages you rely on, that 10:58:31
9 is from a study by CMR of clinical trials conducted 10:58:33
10 from 2006 to 2007 and 2008 to 2009, correct? 10:58:38

11 MR. BAUGHMAN: Object to the form. 10:58:43

12 A Again, they make this statement, and they 10:58:43
13 actually said the sources. One of the sources is 10:58:46
14 Thomson Reuters. I don't see the contradiction. 10:58:50
15 It's perfectly -- 10:58:53

16 Q Thomson Reuters is not a source for the 10:58:53
17 CMR study that's reported here, is it? Is that your 10:58:56
18 understanding of this? 10:58:59

19 A To help understand this trend, Thomson 10:59:00
20 Reuters and science analyzed the report. This is 10:59:04
21 one of the sources that they have. 10:59:07

22 Q One of the sources that who has? 10:59:08

1	A	CMR.	10:59:10
2	Q	No. CMR -- the CMR report that's	10:59:11
3		referred to in paragraph 1 is of studies from 2006	10:59:15
4		to 2007 and 2008 to 2009.	10:59:18
5		Do you agree with me on that?	10:59:20
6	A	That's what this article said.	10:59:23
7	Q	Okay. And then the Thomson Reuters	10:59:24
8		study, which is a different study, looks at phase 2	10:59:26
9		trials from 2008 to 2010, a different time period,	10:59:29
10		correct?	10:59:32
11	A	2008 to 2010. The Phase II failures:	10:59:35
12		2008-2010 in the title of the article.	10:59:41
13	Q	Correct. The 2008 to 2010 is the	10:59:44
14		analysis that Thomson Reuters Life Science did,	10:59:46
15		right, of clinical trials from 2008 to 2010.	10:59:49
16		What you rely on in your report is this	10:59:52
17		CMR study referred to in the first paragraph that	10:59:54
18		looked at trials from 2006 to 2007 and 2008 to 2009,	10:59:57
19		correct? Those are two different studies.	11:00:02
20		Do you agree with that?	11:00:05
21	A	It may be two different studies in your	11:00:05
22		interpretation. But the actual data is correct and	11:00:08

1 is consistent with what we see in clinical research. 11:00:10

2 This is one source that we chose to use, 11:00:13
3 but it's -- it doesn't -- whether it's 18 or 22, I 11:00:16
4 mean, those are some numbers. The numbers could 11:00:21
5 vary, depends on what the company is. 11:00:23

6 But what is true and the thrust of what I 11:00:25
7 wanted to say is not the specific numbers. The 11:00:28
8 thrust that I want to convey there is that most of 11:00:31
9 the phase 2 trials fail. Whether it's 18 percent or 11:00:35
10 22 percent, it doesn't matter, Counsel. What it 11:00:39
11 matters is that most of the phase 2 trials fail. 11:00:43

12 Q Doctor, the only thing you cite in your 11:00:46
13 declaration, the only article you cite, the only 11:00:51
14 literature you cite in your entire 137-page 11:00:54
15 declaration for the proposition that 80 or 70 11:00:59
16 percent of phase 2 trials fail is Exhibit 2006. 11:01:03

17 Right or wrong? 11:01:08

18 MR. BAUGHMAN: Object to the form. 11:01:09

19 A This is one example of what is commonly 11:01:11
20 known in the public domain in clinical research in 11:01:14
21 the pharmaceutical industry, that a lot of the 11:01:18
22 trials fail. 11:01:20

1	Q	Do you cite anything other than	11:01:21
2		Exhibit 2006 for that proposition?	11:01:23
3	A	It is in the public domain.	11:01:25
4		MR. BAUGHMAN: Object to the form.	11:01:27
5	Q	Where in your declaration do you cite	11:01:27
6		anything other than Exhibit 2006 for that	11:01:30
7		proposition? Please point me to it.	11:01:32
8		MR. BAUGHMAN: Object to the form.	11:01:35
9	A	In my proposition, I cited that, but I	11:01:36
10		also, as a person of skill in the art conducting	11:01:39
11		clinical trials for 35, 40 years, it is in my	11:01:43
12		experience that, indeed, phase 2 trials fail very	11:01:46
13		often.	11:01:49
14	Q	Now, according to Exhibit 2006, the CMR	11:01:49
15		analysis on which you rely was based on data from 16	11:01:52
16		unidentified companies, correct?	11:01:56
17	A	That's what it says there.	11:01:58
18	Q	And it doesn't say who determined whether	11:01:59
19		a trial was a success or a failure or how that was	11:02:03
20		done in the CMR report, correct?	11:02:06
21	A	It is what is written there.	11:02:10
22	Q	Okay. And then, as we talked about, the	11:02:12

1 article goes on to discuss an analysis by Thomson
2 Reuters Life Science Consulting, correct? That's
3 the second paragraph?

11:02:15

11:02:19

11:02:21

4 A Yes, sir.

11:02:22

5 Q Okay. And for the purpose of that
6 analysis, how is a failure of a phase 2 trial
7 defined in Exhibit 2006?

11:02:22

11:02:25

11:02:29

8 A Well, it doesn't specify with that
9 granularity, Counsel. That is a decision for each
10 pharmaceutical company to decide what parameters for
11 failure. I don't think that the article does.

11:02:31

11:02:35

11:02:38

11:02:40

12 The thrust of the article and the bottom
13 line, what is important here is that most of the
14 phase 2 trials fail, and just by having a phase 2
15 trial being done doesn't mean that is going to be
16 successful and infallible.

11:02:43

11:02:46

11:02:50

11:02:58

11:02:58

17 Q As defined by this article that you cite,
18 Exhibit 2006, failure includes a failure to move a
19 drug forward in development for strategic reasons,
20 correct?

11:03:00

11:03:03

11:03:05

11:03:07

21 A That's one of the reasons.

11:03:08

22 Q All right. But what constitutes a

11:03:10

1	strategic reason is not defined in the article,	11:03:12
2	correct?	11:03:15
3	A It is very much decided by the	11:03:15
4	pharmaceutical industry.	11:03:17
5	Q All right. And the definition of	11:03:18
6	"failure" in Exhibit 2006 also includes insufficient	11:03:19
7	efficacy, correct?	11:03:22
8	A As defined by the sponsor.	11:03:24
9	Q Because what qualifies as insufficient	11:03:26
10	efficacy is not defined in Exhibit 2006, correct?	11:03:28
11	A It doesn't need to be defined.	11:03:31
12	Q All right. And for many of the studies	11:03:33
13	deemed a failure in this analysis in Exhibit 2006,	11:03:35
14	there was no reason at all reported for why the	11:03:39
15	trial purportedly failed, correct?	11:03:44
16	A I don't know.	11:03:46
17	MR. BAUGHMAN: Object to the form,	11:03:46
18	foundation.	11:03:47
19	Q You don't know?	11:03:47
20	A Well, I don't need to know what the	11:03:48
21	reason is. I mean, sometimes there are many reasons	11:03:50
22	that the sponsor --	11:03:53

1	Q	So a phase 2 clinical trial that fails	11:03:56
2		for any reason is part of your analysis?	11:03:58
3	A	I did not say that, Counsel. I said that	11:04:03
4		I don't know the reasons for failure. They listed	11:04:06
5		those reasons, but I don't know what other	11:04:10
6		additional reasons could be.	11:04:12
7	Q	The article, Exhibit 2006, says that for	11:04:14
8		many of the clinical trials that purportedly failed,	11:04:18
9		there is no reason available, correct?	11:04:22
10		MR. BAUGHMAN: Object to the form.	11:04:24
11	A	I don't know.	11:04:24
12	Q	Okay. And the authors of Exhibit 2006	11:04:26
13		acknowledge that it's difficult to draw conclusions	11:04:31
14		from these data, correct?	11:04:33
15	A	Well, no data is definitive, Counsel.	11:04:35
16		But the thrust of the article is clear, that phase 2	11:04:39
17		trials are not infallible. Phase 2 trials are	11:04:42
18		clinical studies that are trying to ascertain	11:04:47
19		something very specific. But many of those fail.	11:04:51
20	Q	In fact, the authors of Exhibit 2006 say	11:04:55
21		that it is difficult to draw conclusions from these	11:04:59
22		data, but that some of the failures in the study	11:05:02

1 were due to inadequate differentiation for more 11:05:05

2 advanced drugs in the same class or from drugs with 11:05:08

3 similar indications in another mechanistic class, 11:05:11

4 correct? 11:05:15

5 A That's presumably one of the reasons, but 11:05:15

6 I don't know the reasons. 11:05:18

7 Q Okay. And for the purported failures 11:05:19

8 where no reason for the failure was reported, the 11:05:21

9 authors state that it's reasonable to conclude that 11:05:24

10 some of these failures were due to insufficient 11:05:27

11 evidence of an efficacy advantage over a more 11:05:29

12 advanced drug, correct? 11:05:32

13 A That is one of the reasons, Counsel. 11:05:34

14 Q Okay. And the authors conclude that the 11:05:35

15 finding that a substantial portion of phase 2 11:05:38

16 failures were due to strategic reasons suggests that 11:05:40

17 one important underlying factor could be overlapping 11:05:44

18 R&D activity between companies with drugs in phase 2 11:05:47

19 trials, correct? 11:05:50

20 A I don't know. 11:05:51

21 Q That's what the authors of this article 11:05:51

22 that you cite state, isn't it? 11:05:53

1	A	But I don't know. I don't know if this	11:05:55
2		is one of the reasons. This is one of the reasons,	11:05:57
3		but that's not the only reason.	11:05:59
4	Q	Are you relying on this article or not?	11:06:00
5	A	I cite this article. I think that the	11:06:02
6		article provides important evidence that provides a	11:06:06
7		number to what is very well-known, that phase 2	11:06:09
8		trials often fail.	11:06:13
9	Q	According to the authors, the finding	11:06:15
10		that a substantial portion of phase 2 failures were	11:06:17
11		due to strategic reasons suggests that one important	11:06:20
12		underlying factor could be overlapping R&D activity	11:06:24
13		between companies with drugs in phase 2 trials.	11:06:27
14		You don't disagree where that, right?	11:06:30
15		MR. BAUGHMAN: Object to the form.	11:06:32
16	A	This is one of the reasons.	11:06:32
17	Q	Okay. And you don't take any of these	11:06:34
18		factors into account in discussing Exhibit 2006 in	11:06:36
19		your expert declaration, correct?	11:06:39
20		MR. BAUGHMAN: Object to the form.	11:06:41
21	A	What do you mean by that?	11:06:42
22	Q	You never mention any of these factors	11:06:43

1 that the failures you're talking about could be for 11:06:46
2 strategic reasons, because there's a more 11:06:48
3 efficacious drug in the same class, for commercial 11:06:51
4 reasons; you never mention that in your expert 11:06:53
5 declaration, do you? 11:06:56

6 MR. BAUGHMAN: Object to the form. 11:06:57

7 A It doesn't make any difference for my 11:06:58
8 statement. The point that I want to rely, 11:07:02
9 regardless of the reason, whether it's efficacy, 11:07:05
10 whether it's safety, whether it's strategic reasons, 11:07:08
11 whether it's commercial reasons, many of the phase 2 11:07:11
12 trials fail. So that is the bottom line. 11:07:16

13 Q If we look at the authors' pie charts in 11:07:19
14 Exhibit 2006 identifying the reasons for the 11:07:23
15 purported phase 2 clinical trial failures in their 11:07:27
16 study -- 11:07:30

17 Do you see those pie charts? 11:07:30

18 A Yes, sir. 11:07:31

19 Q -- 80 percent of the failures were down 11:07:32
20 to either insufficient level of efficacy or 11:07:34
21 strategic reasons, correct? 11:07:37

22 A That's what it says, the pie is. 11:07:39

1	Q	And only 20 percent failed for reasons of	11:07:42
2		safety, pharmacokinetics, or bioavailability,	11:07:46
3		correct?	11:07:48
4	A	That's what the article says. But	11:07:49
5		certainly, there is not -- when a trial fails,	11:07:52
6		doesn't necessarily need to fail for one specific	11:07:56
7		reason. Could be a combination of all those	11:07:58
8		reasons.	11:08:01
9	Q	That's not in the article that you	11:08:01
10		brought into these proceedings, right?	11:08:03
11		MR. BAUGHMAN: Object to the form.	11:08:05
12	A	It makes no difference.	11:08:05
13	Q	All right. You can set that aside.	11:08:08
14		MR. BAUGHMAN: I don't want to interrupt	11:08:11
15		you.	11:08:12
16		MR. ANSTAETT: We can take a break now.	11:08:13
17		(Recess from 11:08 a.m. until 11:25 a.m.)	11:25:38
18		(Previously marked Exhibit 2065 presented	11:25:38
19		to the witness.)	11:25:39
20	BY MR. ANSTAETT:		11:25:39
21	Q	Doctor, I'm going to give you what has	11:25:39
22		been marked as Exhibit 2065.	11:25:41

1	Exhibit 2065 is Novo Nordisk's annual	11:26:03
2	report for 2010, correct?	11:26:07
3	A Yes, sir.	11:26:10
4	Q And you state in paragraph 124 of your	11:26:12
5	declaration that it was published on February 1st,	11:26:19
6	2011, correct?	11:26:24
7	A That's what I wrote, yeah.	11:26:26
8	Q And how did you determine the publication	11:26:28
9	date?	11:26:30
10	A It was given to me.	11:26:30
11	Q Okay. And that publication date is -- if	11:26:32
12	you look at page 111 of the exhibit, again, using	11:26:36
13	those numbers in the bottom right-hand corner, that	11:26:42
14	date is consistent with page 111, which shows that	11:26:48
15	the report is dated February 1st, 2011, correct?	11:26:55
16	MR. BAUGHMAN: Object to the form.	11:26:59
17	A It says February the 1st, 2011?	11:27:00
18	Q Yes.	11:27:07
19	A Yeah, here it is here.	11:27:09
20	Q Okay. And then in Exhibit 2065, you cite	11:27:11
21	a statement on page 26 of the document. In your	11:27:18
22	declaration, you cite that page and the statement on	11:27:35

1	it that identifies semaglutide as a once weekly	11:27:37
2	GLP-1 analog in Novo's pipeline, and it says,	11:27:43
3	Phase 3 initiation was postponed in June 2010	11:27:49
4	pending a long-acting portfolio development strategy	11:27:52
5	decision.	11:27:56
6	Correct?	11:27:57
7	MR. BAUGHMAN: Object to the form.	11:27:57
8	A I'm sorry. Can you point out where?	11:28:02
9	Q Yeah. So it's --	11:28:04
10	A On page 28?	11:28:07
11	Q You cite on page 26 --	11:28:08
12	A 26.	11:28:08
13	Q -- 26, you cite a statement on that page	11:28:10
14	that identifies semaglutide as a once weekly GLP-1	11:28:12
15	analog in Novo's pipeline and says, Phase 3	11:28:16
16	initiation was postponed to June 2010 pending a	11:28:19
17	long-acting portfolio development strategy decision.	11:28:23
18	Correct?	11:28:27
19	A Yes, sir.	11:28:28
20	Q And what do you understand that sentence	11:28:28
21	to be referring to as a long-acting -- or as Novo's	11:28:30
22	long-acting portfolio?	11:28:35

1	A	That they have a portfolio of options on	11:28:43
2		long-acting analogs.	11:28:46
3	Q	Long-acting GLP-1 analog?	11:28:48
4	A	Long-acting portfolio. I mean, it could	11:28:52
5		be any of the medication. It could include GLP-1	11:28:54
6		analog.	11:28:58
7	Q	And according to page 26 of Exhibit 2065,	11:28:58
8		that long-acting portfolio would include	11:29:06
9		semaglutide, correct?	11:29:08
10	A	It would have included semaglutide.	11:29:09
11	Q	And it would also include NN9924 that is	11:29:11
12		also listed there, which is identified in Exhibit	11:29:16
13		2065 as a long-acting oral GLP-1 analog for which a	11:29:21
14		first phase 1 study had been initiated in the first	11:29:26
15		quarter of 2010, correct?	11:29:28
16	A	It says long-acting oral.	11:29:32
17	Q	Right.	11:29:34
18	A	Yeah.	11:29:34
19	Q	So that would be part of the --	11:29:35
20		presumably part of the long-acting portfolio?	11:29:36
21	A	It is part of the same terminology.	11:29:39
22	Q	And in addition to NN9924, do you know	11:29:42

1	whether, before the priority date of the '462	11:29:48
2	patent, Novo Nordisk was also investigating a	11:29:51
3	long-acting depo formulation of liraglutide?	11:29:55
4	A I don't know.	11:29:58
5	Q All right. Then you state in paragraph	11:30:00
6	127 of your declaration that a skilled artisan would	11:30:03
7	have understood that postponing the initiation of	11:30:08
8	semaglutide phase 3 trials could have been due to	11:30:13
9	unfavorable trial outcomes in the then-completed	11:30:16
10	phase 1 and phase 2 trials of semaglutide.	11:30:19
11	Correct?	11:30:21
12	A Correct.	11:30:22
13	Q And what do you mean by "unfavorable	11:30:23
14	trial outcomes"?	11:30:25
15	A Well, it could be that once they analyzed	11:30:26
16	the data, it is not what they expected in terms of	11:30:31
17	efficacy. It could have been it had more toxicity.	11:30:35
18	It may have that they have a unknown, off-target	11:30:38
19	results, and so on. So there are multiple factors	11:30:45
20	that they may be there.	11:30:48
21	Q Okay. Is it your opinion that a skilled	11:30:49
22	artisan reading the sentence that you quote from the	11:30:55

1	2010 annual report would have concluded that the	11:30:58
2	phase 2 trial of semaglutide failed?	11:31:01
3	A I cannot say that it failed, but it	11:31:05
4	really raised a flag. Because if the trial was very	11:31:08
5	successful, there wouldn't have been any hesitation	11:31:14
6	or any reconsideration and so on. There was	11:31:19
7	something going on that needed to (inaudible). It	11:31:21
8	certainly raised a flag.	11:31:24
9	One of the options is that's unfavorable	11:31:25
10	and so on, and the unfavorable, it opens the room	11:31:28
11	for many different categories of not being	11:31:31
12	favorable. Could be efficacy, toxicity,	11:31:35
13	tolerability.	11:31:40
14	Q It could be less efficacy than they hoped	11:31:40
15	it would show?	11:31:44
16	A That is one of the options.	11:31:44
17	Q If the phase 1 and 2 trials of	11:31:46
18	semaglutide had failed, why would a decision on	11:31:48
19	moving semaglutide to phase 3 have been merely	11:31:50
20	postponed?	11:31:52
21	A Postponed is just a temporary, as I	11:31:56
22	interpret as a person of skill, is that a decision	11:32:00

1 to terminate or to move on and so on takes many
2 considerations.

3 So what I'm saying is that there were
4 reasons to reanalyze, to think about it, measure
5 what the pros and cons and so on. It could well be
6 that it is not what they expected. It could have
7 been that even commercial considerations could be
8 there, and so on.

9 So it could be efficacy, tolerability,
10 toxicity, and so on. It could be manpower. Many
11 options.

12 But the only thing that I can say is that
13 it raises a flag, and one of those is that this is
14 unfavorable.

15 Q Okay. All right. You can set that
16 aside.

17 MR. ANSTAETT: This is one exhibit we are
18 going to have to mark because it's not been marked
19 yet.

20 (Exhibit 1130 marked for identification
21 and attached to the transcript.)

22 BY MR. ANSTAETT:

1	Q	I'll hand you what's been marked as	11:33:28
2		Exhibit 1130.	11:33:29
3	MR. BAUGHMAN:	Counsel, I don't know if	11:33:38
4		we can agree. I'll preserve objections to this so I	11:33:40
5		don't clutter up the record now.	11:33:43
6	MR. ANSTAETT:	Sure, that's fine.	11:33:44
7	Q	Do you recognize what we've marked as	11:33:52
8		Exhibit 1130 to be Novo Nordisk's annual report for	11:33:54
9		2011?	11:33:58
10	A	For 2011? Yeah, I have it in my hand.	11:34:01
11	Q	And do you see on page -- and here I'm	11:34:06
12		using the page number. There are just page numbers	11:34:15
13		in the bottom right-hand corner. On page 109, do	11:34:17
14		you see that this annual report is dated the 1st of	11:34:22
15		February 2012?	11:34:25
16	A	Page 109?	11:34:33
17	Q	Yes, sir.	11:34:34
18	A	February 2012, yes, sir.	11:34:36
19	Q	And so this is the annual report for the	11:34:44
20		year after the report that you rely on in your	11:34:48
21		expert declaration, correct?	11:34:51
22	A	Correct.	11:34:52

1 Q And then if you turn to page 19, there's 11:34:53
2 a little blue box on that page in the first column 11:35:04
3 that says, Our goal is to offer treatments that are 11:35:08
4 as safe and convenient as possible. 11:35:11

5 And then if you look at the paragraph 11:35:15
6 right below that, it says, We are now building a 11:35:17
7 GLP-1 portfolio with the intention to provide an 11:35:22
8 even broader range of treatment options, including 11:35:24
9 longer-acting versions to improve convenience. Our 11:35:27
10 late-stage GLP-1 pipeline includes two new 11:35:31
11 treatments, a fixed combination of Victoza, with 11:35:35
12 degludec, which may offer the benefits of both 11:35:37
13 compounds in a convenient solution, and a novel 11:35:41
14 once-weekly GLP-1 analog, semaglutide. 11:35:43

15 Do you see that? 11:35:49

16 A Yes, sir. 11:35:50

17 Q So by February 2012, skilled artisans 11:35:51
18 would have known that once-weekly semaglutide was 11:35:57
19 part of Novo Nordisk's late-stage GLP-1 pipeline, 11:35:59
20 correct? 11:36:03

21 MR. BAUGHMAN: Object to the form. 11:36:03

22 A It says there that they're still building 11:36:03

1 a part of the pipeline. That's what they say that 11:36:08
2 they -- they talk about the combination of the 11:36:11
3 weekly -- of dulaglutide with the once-daily insulin 11:36:15
4 degludec and a Novo once-weekly GLP-1 analog, 11:36:23
5 semaglutide. 11:36:27

6 Q Okay. And then if you look at page 26 of 11:36:28
7 Exhibit 1130, on that page, we see the same kind of 11:36:37
8 pipeline overview that you relied on in the 2010 11:36:46
9 annual report, correct? 11:36:49

10 A Yes, sir. 11:36:51

11 Q Okay. And now one year later, there is 11:36:51
12 no reference to the phase 3 development of 11:36:54
13 semaglutide being postponed, right? 11:36:57

14 A It states that once-weekly GLP-1 phase 2 11:37:00
15 completed. But it doesn't say whether it's ongoing 11:37:03
16 or it's postponed. Just said completed without any 11:37:07
17 commitment. 11:37:11

18 Q And in the 2010 report that you relied 11:37:11
19 on, it said postponed. Here, it doesn't say 11:37:15
20 postponed, correct? 11:37:18

21 A In 2010, when it was postponed, Novo had 11:37:19
22 already the data on semaglutide. And based on the 11:37:24

1	data, they postponed.	11:37:27
2	In 2010, they just limit to say that it	11:37:28
3	was completed.	11:37:31
4	Q In 2011?	11:37:32
5	A In 2011.	11:37:33
6	Q Right. Excuse me. Right. So in 2010,	11:37:34
7	it says phase 3 initiation was postponed in June	11:37:40
8	2010 pending a long-acting portfolio development	11:37:43
9	strategy decision, right? That's in 2010, the one	11:37:46
10	you relied on?	11:37:50
11	A Yes, sir.	11:37:51
12	Q Okay. And then in 2011, the reference to	11:37:52
13	postponement no longer appears in the pipeline	11:37:56
14	overview.	11:37:59
15	Is that fair?	11:38:00
16	A It says that it's completed.	11:38:01
17	Q Okay.	11:38:02
18	A But can you point it out whether or not	11:38:05
19	there is that they are continuing with the	11:38:09
20	development there? I mean, let me just read this	11:38:14
21	just to see whether or not there is any mention of	11:38:18
22	initiation of phase 3 or anything like that.	11:38:25

1	Because I appreciate you giving me this. I wasn't	11:38:31
2	seeing -- I haven't seen it before. So can I have a	11:38:34
3	chance to examine it?	11:38:37
4	Q Yeah, no, absolutely. Anytime I show you	11:38:38
5	an exhibit today, you should feel free to take as	11:38:40
6	much time as you want to look at it.	11:38:43
7	A May I point out something here, Counsel?	11:39:16
8	Q Sure.	11:39:18
9	A In that statement, I'm just --	11:39:20
10	Q Just so the record is clear, which	11:39:22
11	statement are you referring to?	11:39:24
12	A In the statement that you mentioned that	11:39:25
13	we are now building a GLP-1 portfolio, where you	11:39:27
14	mentioned that a fixed combination of Victoza with	11:39:33
15	degludec, which may offer the benefits of compounds	11:39:37
16	in a convenient solution in a novel once-weekly	11:35:41
17	GLP-1, when I looked in page 27, I can see that,	11:39:43
18	indeed, in the third -- in the third row, I can see	11:39:50
19	that at that time, Novo Nordisk have continued with	11:39:58
20	the phase 3 basal insulin degludec and liraglutide	11:40:04
21	as they stated. But I can see that they have not	11:40:09
22	moved from the clinical benefit of GLP-1 with less	11:40:12

1 frequent injections -- 11:40:15

2 (Reporter interruption.) 11:40:15

3 A I'm just saying that -- I'm seeing this 11:40:28

4 for the first time, and as I looked, paraphrased, 11:40:29

5 the previous in page 19, that Novo is building a 11:40:38

6 GLP-1 portfolio with intention to provide a broader 11:40:43

7 range of treatments, and they state that late-stage 11:40:47

8 GLP-1 pipeline of new treatments, fixed combination 11:40:52

9 of Victoza or liraglutide with degludec, and also 11:40:56

10 Novo once-weekly. 11:41:02

11 When I looked at page 27, in the blue, 11:41:03

12 which means diabetes agents, I can see that, indeed, 11:41:08

13 Novo has gone on to phase 3 developing basal insulin 11:41:14

14 degludec and liraglutide. 11:41:23

15 But when they refer to GLP-1 analog with 11:41:26

16 least frequent injections, I assume that maybe 11:41:33

17 semaglutide still is stuck in phase 2. 11:41:34

18 So they say that phase 2 is completed but 11:41:36

19 I don't see that they have moved. So I can 11:41:39

20 interpret this as a person in the art that it still 11:41:42

21 this is on hold. 11:41:46

22 Q Well, it says phase 2 completed, right? 11:41:47

1	That's on page 26.	11:41:53
2	A Correct.	11:41:55
3	Q And on page 19, as you said, Novo Nordisk	11:41:56
4	says that semaglutide, a novel once-weekly GLP-1	11:42:01
5	analog, is part of the GLP-1 portfolio that it's	11:42:06
6	building, correct?	11:42:12
7	A Correct.	11:42:13
8	Q In the 2010 report, you put some	11:42:13
9	significance on the fact that it said that the	11:42:16
10	phase 3 trials had been postponed, right?	11:42:18
11	A Correct.	11:42:20
12	Q And in the 2011 annual report, Novo	11:42:22
13	Nordisk says, in fact, semaglutide is part of our	11:42:25
14	GLP-1 portfolio, and that that language about	11:42:30
15	phase 3 trials being postponed has been removed,	11:42:35
16	correct?	11:42:37
17	MR. BAUGHMAN: Object to the form.	11:42:37
18	A What I'm saying -- what I'm saying,	11:42:39
19	Counsel, is that the phase 2 trial finished in 2009.	11:42:43
20	The phase 2 trials were -- they finished in 2009.	11:42:49
21	Novo chose the language in 2010, knowing that these	11:42:57
22	studies were completed in 2009, to put the studies	11:43:01

1 on hold.

11:43:04

2 One year later, when they report there,
3 they just say, phase 2 completed. But when I looked
4 at page 27, I can see that after one year, which is
5 a lot of time in the pharmaceutical industry, they
6 have not made the decision to go to phase 3.

11:43:06

11:43:10

11:43:13

11:43:17

11:43:20

7 So as a person in the art, I can
8 interpret this that remains on hold. Whether or not
9 they stated that it's on hold remains on hold. What
10 is true and is factual is that the phase 2
11 completed. That doesn't invalidate that it's still
12 on hold, because I don't see in the table, 27, that
13 has moved on to phase 3.

11:43:22

11:43:25

11:43:27

11:43:32

11:43:35

11:43:38

11:43:41

14 Q It doesn't say it's moved on to phase 3,
15 Doctor, but what do you make of the language in the
16 very same annual report that says, We are now
17 building a GLP-1 portfolio with the intention to
18 provide an even broader range of treatment options
19 including longer-acting versions to improve
20 convenience including a novel once-weekly GLP-1
21 analog semaglutide?

11:43:43

11:43:46

11:43:50

11:43:52

11:43:55

11:43:59

11:44:02

11:44:05

22 A You said it, Counsel. With intention.

11:44:06

1	Q	Okay.	11:44:06
2	A	With intention. That doesn't mean that	11:44:09
3		they are doing it. And since they are not doing it,	11:44:11
4		I can see that they have not moved.	11:44:14
5		So in my interpretation as a skilled	11:44:17
6		person of the art, I can see that it's still in	11:44:20
7		2011, I don't see that Novo has moved to phase 3.	11:44:24
8	Q	Agreed. I'm not arguing that they've	11:44:28
9		moved to phase 3. But if the phase 2 trial, which	11:44:30
10		is completed, according to Exhibit 1130, right?	11:44:33
11	A	Yes, sir.	11:44:38
12	Q	If the phase 2 trial had failed, would	11:44:39
13		Novo have said in its 2011 annual report that	11:44:44
14		semaglutide was part of its GLP-1 long-acting	11:44:50
15		portfolio?	11:44:55
16	MR. BAUGHMAN:	Object to the form and	11:44:56
17		foundation.	11:44:57
18		You can answer.	11:44:58
19	A	They have an intent. "Failure" has	11:44:58
20		different definitions. If the study was an absolute	11:45:03
21		success or would have -- they wouldn't have two	11:45:08
22		years to move to phase 3.	11:45:13

1	So they only say they have the intent.	11:45:14
2	That means that it's still at this point, in 2011,	11:45:18
3	that you showed me this new thing, they are still	11:45:22
4	considering, it's part of the hold.	11:45:25
5	I can only, as a person skilled in the	11:45:27
6	art, having done hundreds of clinical trials, been	11:45:31
7	involved in phase 2, phase 3, I can say that if in	11:45:36
8	2009 the phase 2 have concluded, and still in 2011	11:45:41
9	they have not started on phase 3, I can interpret as	11:45:46
10	a person in the art that the study remains on hold	11:45:49
11	in 2011. That is --	11:45:53
12	(Cross-talk.)	11:45:57
13	Q When you say the study remains on hold --	11:45:57
14	A I'm sorry. Not the study. The drug	11:45:57
15	remains on hold, the development of the drug.	11:45:59
16	Q Right. And as you said, that could be	11:46:01
17	for a variety of reasons.	11:46:03
18	A Correct.	11:46:05
19	Q Correct? Commercial reasons, strategic	11:46:05
20	reasons. But Novo wouldn't have -- if the phase 2	11:46:07
21	trial had failed in the sense that the drug had	11:46:12
22	unacceptable toxicity or it didn't reduce HbA1c or	11:46:16

1 it caused weight gain, Novo wouldn't have told their 11:46:23
2 shareholders in 2011 that semaglutide was part of 11:46:26
3 its long-acting portfolio. 11:46:30

4 Is that fair? 11:46:32

5 MR. BAUGHMAN: Object to the form and 11:46:33
6 foundation. 11:46:34

7 A Novo has the obligation to be transparent 11:46:34
8 in all the declarations. This study is on hold. 11:46:37
9 That means it's under consideration. I don't think 11:46:40
10 that -- it depends on what failure is. It could 11:46:43
11 well be that Novo is considering doing more phase 2 11:46:46
12 studies, and they don't do that. 11:46:49

13 But they don't say that. They just say 11:46:53
14 that the study was completed. So it's under 11:46:55
15 analysis, under consideration. 11:46:57

16 In my book, in my interpretation as a 11:46:59
17 person of the art, I don't think that just by 11:47:01
18 stating that the phase 2 was completed, that means 11:47:04
19 that the hold was lifted. 11:47:08

20 Q Right. And I guess what the only 11:47:11
21 distinction I'm trying to make is, we agree that, 11:47:14
22 you know, a hold can be for a whole variety of 11:47:18

1 reasons; commercial, strategic, efficacy. 11:47:20

2 What I'm trying to understand if you 11:47:25

3 agree with me is that if the phase 2 data that Novo 11:47:27

4 had since 2009, as you say, right? 11:47:32

5 A Yes, sir. 11:47:35

6 Q -- if that showed that semaglutide was 11:47:35

7 unacceptable for reasons of no efficacy in reducing 11:47:42

8 HbA1c, toxicity, they wouldn't tell their 11:47:46

9 shareholders in 2011 that it was still in the 11:47:51

10 pipeline and part of the portfolio because as you 11:47:57

11 say, they have an obligation to be transparent, 11:47:59

12 right? 11:48:01

13 MR. BAUGHMAN: Object to the form and 11:48:01

14 foundation. 11:48:02

15 A First of all, I don't know the data. I 11:48:02

16 cannot make any comments about the data. I cannot 11:48:06

17 say that it's failure or other things. I have no 11:48:09

18 doubts that if it was, as you -- you actually put 11:48:11

19 the extreme scenario. You gave me the extreme 11:48:15

20 scenario of failure in efficacy and toxicity. 11:48:19

21 There are many reasons why Novo is 11:48:22

22 considering. They had the data. The data was not 11:48:24

1 available at all in the public domain. The data was 11:48:27
2 available in 2009. In 2010, they decided to put it 11:48:30
3 on hold. In 2011, they have not moved yet. What is 11:48:35
4 going on, I cannot assert there. 11:48:40

5 Q Okay. 11:48:43

6 A But I can certainly conclude that as of 11:48:45
7 2011, a person in the art would have seen that the 11:48:49
8 study -- the drug is not moving, so there is a flag 11:48:53
9 there. It could be unfavorable and so on. But many 11:48:57
10 reasons. 11:49:00

11 Q Many reasons? 11:49:00

12 A And I can say that that means that the 11:49:02
13 study is -- the drug is still on hold. It hasn't 11:49:04
14 been lifted, from what you just showed me in this 11:49:08
15 new exhibit. 11:49:11

16 Q You say in paragraph 164 of your expert 11:51:29
17 report -- you're talking about -- there, you're 11:51:33
18 discussing the Lund article? 11:51:35

19 A The Lund article? 11:51:39

20 Q Lund, yeah. And you see in paragraph -- 11:51:40
21 I'll start you off with paragraph 159. You have a 11:51:44
22 table there from Lund. 11:51:47

1	A	Yes.	11:51:51
2	Q	And you note that Lund says that in terms	11:51:52
3		of ongoing trials, it says with respect to	11:51:55
4		semaglutide, on hold.	11:51:58
5		Do you see that?	11:52:00
6	A	Yes, sir.	11:52:00
7	Q	Okay. And then in paragraph 164, you	11:52:00
8		say, I do not agree with Dr. Jusko that a POSITA	11:52:09
9		would have understood from Lund that Novo Nordisk	11:52:13
10		was actively investigating semaglutide in phase 1	11:52:15
11		and phase 2 trials. To the contrary, a POSITA would	11:52:18
12		have understood that Novo Nordisk had halted or	11:52:22
13		potentially abandoned development of semaglutide,	11:52:24
14		and this could have been due to unfavorable results	11:52:27
15		in the then-completed phase 1 and phase 2 trials	11:52:30
16		discussed by Lund.	11:52:33
17		Do you see that?	11:52:34
18	A	Yes, sir.	11:52:34
19	Q	Would you at least agree with me that	11:52:35
20		based on the 2011 annual report, it would not be a	11:52:37
21		fair inference to draw that Novo Nordisk had	11:52:40
22		abandoned semaglutide?	11:52:43

1	MR. BAUGHMAN:	Object to the form.	11:52:44
2	A	Halted or potentially. I did not say	11:52:49
3		that abandoned it. I said potentially. When	11:52:53
4		something is on hold, there is consideration to	11:52:56
5		abandon it.	11:52:59
6	Q	But why would a skilled artisan who reads	11:53:00
7		the 2011 report in which semaglutide is described as	11:53:03
8		being part of Novo Nordisk's GLP-1 long-acting	11:53:07
9		portfolio, why would they determine that Novo	11:53:12
10		Nordisk had potentially abandoned that molecule?	11:53:17
11	MR. BAUGHMAN:	Object to the form.	11:53:20
12	A	Because there are many considerations. I	11:53:21
13		mean, as we discussed, has to do with efficacy, has	11:53:23
14		to do with side effects, has to do with	11:53:27
15		tolerability, and off-target effects and so on.	11:53:31
16		They are being very conscientious in	11:53:36
17		making a decision. Clearly, the study was halted.	11:53:40
18		And when something is halted, has the potential --	11:53:42
19	Q	What study was halted?	11:53:45
20	A	I'm sorry. Not a study. I rectify. The	11:53:46
21		compound was halted. Semaglutide was on hold. The	11:53:51
22		clinical development of semaglutide was on hold.	11:53:57

1	Q	Well, Doctor, I think -- I'm just trying	11:53:59
2		to understand. You say that a skilled artisan	11:54:01
3		would, you know, reading Lund --	11:54:05
4	A	Yes.	11:54:05
5	Q	-- would have understood that Novo	11:54:09
6		Nordisk had potentially abandoned semaglutide,	11:54:15
7		right?	11:54:18
8	A	It says, had halted. That is an	11:54:18
9		affirmation. And then I said, potentially	11:54:22
10		abandoned.	11:54:25
11	Q	Right. Potentially abandoned, right?	11:54:26
12	A	Potentially.	11:54:30
13	Q	And my question for you is, is that	11:54:31
14		really your opinion of what a skilled artisan would	11:54:36
15		believe? Because Lund is published in September	11:54:40
16		2011, right?	11:54:48
17	A	Correct.	11:54:49
18	Q	Okay. And in this report that we're	11:54:49
19		looking at was published in February 2011, right?	11:54:54
20	A	Yeah.	11:54:58
21	Q	Okay. And what this report from February	11:54:59
22		2011 says is that semaglutide is very much a part of	11:55:03

1	Novo Nordisk's portfolio of long-acting GLP-1	11:55:09
2	analogs.	11:55:13
3	Do you agree with that?	11:55:14
4	MR. BAUGHMAN: Object to the form.	11:55:16
5	A I don't think it says "very much a part."	11:55:17
6	I don't think that that language is there.	11:55:19
7	Q Let me read the exact language.	11:55:20
8	We are now building a GLP-1 portfolio	11:55:23
9	with the intention to provide an even broader range	11:55:25
10	of treatment options, including longer-acting	11:55:27
11	versions to improve convenience.	11:55:30
12	And then they talk about the combo	11:55:32
13	product with liraglutide and degludec.	11:55:35
14	And then they say, and a novel	11:55:38
15	once-weekly GLP-1 analog, semaglutide.	11:55:41
16	Now, a skilled artisan reading that, you	11:55:43
17	would agree, wouldn't come to the conclusion that	11:55:45
18	semaglutide had been abandoned by Novo Nordisk.	11:55:49
19	Is that fair?	11:55:52
20	MR. BAUGHMAN: Object to the form.	11:55:53
21	A There is a critical word of intent. In	11:55:53
22	the 2011, and the authors of this article, including	11:56:00

1 Filip Knop and Tina Vilsboll, were very, very 11:56:04
2 experts in GLP-1. They would have known that they 11:56:08
3 are in phase 3. 11:56:10

4 So in September, there was not in the 11:56:11
5 public domain. They have this, you give me this 11:56:14
6 reference, September 11 when they publish, it's 11:56:17
7 still on hold. 11:56:20

8 So when something is on hold, after two 11:56:21
9 years of being finished, there is a potential that 11:56:24
10 at one point the sponsor may decide to abandon the 11:56:28
11 development. So it's a potential. 11:56:33

12 The only thing I'm putting of fact is 11:56:35
13 that it had halted, and the study was -- I'm 11:56:38
14 sorry -- the drug development of semaglutide had 11:56:42
15 halted, and it was stuck in phase 2. 11:56:44

16 Q The fact that it hadn't moved to phase 3 11:56:48
17 didn't mean it was abandoned. 11:56:51

18 Is that fair? 11:56:53

19 A At that time, in this report, it hasn't 11:56:54
20 moved to phase 3. When it moves to phase 3, that 11:57:00
21 means it's not abandoned. That means it's continued 11:57:03
22 development. That means it's not on hold. 11:57:06

1	The authors were highly respectable, and	11:57:08
2	I know them. They put in very clear in that	11:57:11
3	table -- where is the table that -- you showed me	11:57:14
4	the table that Lund --	11:57:17
5	Q It's in your report.	11:57:20
6	A Yes, in my report. What paragraph was	11:57:21
7	that?	11:57:26
8	Q I think just maybe a little earlier from	11:57:27
9	where you're looking.	11:57:29
10	A Yeah, that's right. So it's clear. And	11:57:30
11	actually, I even put it in red, it's on hold. For	11:57:41
12	me, as a skillful person in the art, that is highly	11:57:45
13	indicative of a concern.	11:57:48
14	Q I think we've agreed that that concern	11:57:50
15	could encompass any number of things, right?	11:57:52
16	A But it's still a concern.	11:57:55
17	Q Well, it could be a concern for	11:57:57
18	commercial reasons, right?	11:57:58
19	A But it's a concern.	11:57:59
20	Q It could be a concern for strategic	11:58:00
21	reasons, right?	11:58:02
22	A But it's a concern related to success.	11:58:02

1	Q	Why couldn't it be a concern related to	11:58:05
2		the fact that they've decided to develop oral	11:58:07
3		semaglutide, which is also in the pipeline?	11:58:10
4	A	I don't know.	11:58:12
5	Q	You don't know, right, and the skilled	11:58:12
6		artisan doesn't know?	11:58:15
7	A	A skilled artisan will know that there's	11:58:15
8		a red flag or yellow flag, or just a flag.	11:58:17
9	Q	A flag?	11:58:20
10	A	There is a flag, a concern that the drug	11:58:21
11		is not in development.	11:58:25
12		So when I see that, I said, there's	11:58:27
13		something there that I don't know, but it may be an	11:58:30
14		unfavorable result.	11:58:33
15	Q	It may be?	11:58:34
16	A	Correct.	11:58:35
17	Q	Or it may be -- as I think you	11:58:36
18		acknowledge, it could be a commercial concern. It	11:58:39
19		could be that Novo Nordisk is trying to decide,	11:58:41
20		should we prioritize oral semaglutide, right?	11:58:45
21	MR. BAUGHMAN:	Object to the form and	11:58:48
22		foundation.	11:58:49

1	Q	That's fair, isn't it?	11:58:50
2	A	I don't know, Counsel. I just don't	11:58:51
3		know.	11:58:53
4	Q	You don't know and a skilled artisan	11:58:53
5		doesn't know, right?	11:58:54
6	A	Doesn't know. But a skilled artisan will	11:58:55
7		know that there is data in phase 2 in 2009, and two	11:58:58
8		years later, the drug has not moved. So that is a	11:59:02
9		concern.	11:59:06
10	Q	Okay. And --	11:59:06
11		MR. ANSTAETT: It's noon. Why don't we	11:59:11
12		do our lunch break, and I'll see if lunch is here.	11:59:13
13		But we can go off the record.	11:59:17
14		(Recess from 11:59 a.m. until 12:58 p.m.)	12:58:53
15		(Exhibit 1131 marked for identification	12:58:53
16		and attached to the transcript.)	12:58:53
17		BY MR. ANSTAETT:	12:58:53
18	Q	So Doctor, I'm going to hand you what	12:58:54
19		we're marking now as Exhibit 1131.	12:58:56
20		MR. BAUGHMAN: Can I preserve objections	12:59:01
21		to that if there are any?	12:59:02
22		MR. ANSTAETT: Absolutely.	12:59:04

1	Q	And do you see that Exhibit 1131 is a	12:59:06
2		Form 6-K that Novo Nordisk filed with the U.S.	12:59:12
3		Securities and Exchange Commission?	12:59:17
4	A	Yes, sir.	12:59:19
5	Q	Okay. And you see it's dated	12:59:20
6		February 2nd, 2011?	12:59:23
7	A	Yes, sir.	12:59:24
8	Q	Okay. And then if you turn to -- it's	12:59:25
9		page 14, and then the page numbers are kind of	12:59:28
10		weird. They're kind of in the middle of the page in	12:59:31
11		the bottom right-hand corner. But it says page 14	12:59:34
12		of 29.	12:59:37
13	A	Oh, yeah, here, I see it.	12:59:41
14	Q	Okay. And about halfway through the text	12:59:42
15		on that page, there's a little heading that says,	12:59:46
16		Once-weekly GLP-1 portfolio decision now expected	12:59:50
17		mid-2012.	12:59:52
18		Do you see that?	12:59:54
19	A	Yes, sir.	12:59:55
20	Q	Okay. And here, Novo Nordisk reported	12:59:55
21		that, As previously communicated in June 2010, Novo	12:59:59
22		Nordisk has an intent to select among the two	13:00:03

1	primary once-weekly GLP-1 candidates in the	13:00:06
2	development portfolio, semaglutide and once-weekly	13:00:10
3	liraglutide. To allow for a more complete	13:00:14
4	characterization of once-weekly liraglutide,	13:00:22
5	including data from a clinical multiple-dose study,	13:00:22
6	this decision is now expected mid-2012.	13:00:26
7	Do you see that?	13:00:28
8	A Yes, sir.	13:00:35
9	Q Okay. So as of February 2nd, 2011, based	13:00:35
10	on this exhibit, skilled artisans would know that	13:00:47
11	Novo Nordisk had an intent to select among its two	13:00:52
12	primary once-weekly GLP-1 candidates in the	13:00:59
13	development portfolio, either semaglutide or	13:01:02
14	once-weekly liraglutide.	13:01:05
15	Is that fair to say?	13:01:07
16	MR. BAUGHMAN: Object to the form.	13:01:08
17	A That's what it states.	13:01:10
18	Q Okay. You can set that aside.	13:01:18
19	A Is there any specific question about it?	13:01:22
20	Q No. That was the question I had for you.	13:01:24
21	A Can I make a comment?	13:01:27
22	Q I'm going to let your -- if your counsel	13:01:28

1	wants to ask you about it, he can certainly have the	13:01:30
2	opportunity to do that. And if he does, then I may	13:01:34
3	have more questions about it.	13:01:37
4	A Okay. That's fine.	13:01:38
5	Q Okay. Let's turn to another topic.	13:01:40
6	You're familiar with the W0421 prior art	13:01:46
7	reference that petitioners contend anticipates the	13:01:51
8	'462 patent claims, correct?	13:01:55
9	A I'm aware of the 421.	13:01:58
10	Q Right. That's one of the prior art	13:02:02
11	references that you discuss in your declaration?	13:02:06
12	A Correct.	13:02:08
13	Q And that reference discloses a	13:02:09
14	once-weekly semaglutide dose range of 0.1 to	13:02:13
15	1.6 milligrams to treat type 2 diabetes, correct?	13:02:19
16	A It's part of the 421 that provides that	13:02:21
17	information, the range of 0.1 to 1.6.	13:02:25
18	Q Okay. And the Lovshin reference also	13:02:28
19	discloses once-weekly semaglutide, subcutaneous dose	13:02:34
20	range of 0.1 to 1.6 milligrams to treat type 2	13:02:38
21	diabetes, correct?	13:02:42
22	A Yeah.	13:02:43

1	MR. BAUGHMAN: Object to the form.	13:02:44
2	A In the Lovshin describes the NN9535, 0.1	13:02:44
3	to 1.6.	13:02:52
4	Q Okay. And then starting at paragraph 209	13:02:53
5	of your report, you discuss your opinions concerning	13:02:58
6	that once-weekly semaglutide dose range of 0.1 to	13:03:12
7	1.6 milligrams, correct?	13:03:19
8	A In the 209?	13:03:22
9	Q Starting at 209. That's where you're	13:03:23
10	discussing your opinions with respect to that dose	13:03:28
11	range of 0.1 to 1.6 milligrams?	13:03:30
12	MR. BAUGHMAN: Object to the form.	13:03:35
13	A Yes, I do.	13:03:45
14	Q Okay. And then in paragraph 210 in your	13:03:46
15	declaration, you state that in your opinion, a	13:03:50
16	skilled artisan would have looked to Novo Nordisk's	13:03:54
17	then ongoing NCT657 clinical trial which was testing	13:03:56
18	certain doses of semaglutide once weekly for the	13:04:02
19	treatment of type 2 diabetes to understand W0421's	13:04:05
20	range.	13:04:10
21	Correct?	13:04:11
22	A What I wrote there is what they describe	13:04:12

1 in the study, the dose range of 0.1, 0.2, 0.4, 0.8, 13:04:17
2 the one dose titrated, 1.6 titrated, but did not 13:04:24
3 disclose the 1.0. 13:04:30

4 Q Right. And based on the NCT657 trial 13:04:32
5 protocol, it's your opinion that a skilled artisan 13:04:39
6 would have understood W0421's range to include only 13:04:41
7 the following -- or the doses that you just recited, 13:04:46
8 right, the 0.1, the 0.2, the 0.4, the 0.8, and the 13:04:50
9 1.6 milligram? 13:04:56

10 A Those are the doses that were described. 13:04:58

11 Q And all of those doses are measured in 13:05:00
12 tenths of a milligram, correct? 13:05:04

13 A The dosages that they tested there were 13:05:06
14 0.1, 0.2, 0.4, 0.8, 1.6, doubling the dose at each 13:05:10
15 point. 13:05:18

16 Q And all of those doses that you just 13:05:18
17 recited that were tested, those are all measured in 13:05:21
18 tenths of a milligram, correct? 13:05:24

19 A And that specifically is what it shows. 13:05:26

20 Q In paragraph 220 of your declaration, you 13:05:29
21 take issue with Dr. Bantle and Dr. Jusko's opinion 13:05:40
22 that the prior art semaglutide dose range of 0.1 to 13:05:44

1	1.6 milligram discloses 16 discrete doses, correct?	13:05:48
2	A Correct.	13:05:53
3	Q And your opinion is that there are at	13:05:54
4	least 320 possible doses in that range, right?	13:05:56
5	A It could easily be 320.	13:05:59
6	Q And based on that, it's your opinion that	13:06:01
7	a POSA would not have once envisioned the claimed	13:06:03
8	1.0 milligram dose when looking at that 0.1 to 1.6	13:06:09
9	range, right?	13:06:14
10	MR. BAUGHMAN: Object to the form.	13:06:15
11	A There's no way that the POSA will only	13:06:15
12	look at the 1.0 because there are multiple array of	13:06:17
13	options of adjustments that don't necessarily only	13:06:21
14	be adjustment by 0.1 milligram.	13:06:25
15	Q But would 1.0 milligrams be one of the	13:06:28
16	doses that the skilled artisan would envisage when	13:06:31
17	looking at that dose range of 0.1 to 1.6?	13:06:33
18	MR. BAUGHMAN: Object to the form.	13:06:37
19	A Well, if you go by increments of 0.5, or	13:06:37
20	if you go by increments of 0.25, or if you go by	13:06:42
21	increments of 0.1, 0.01, or 0.05, you know, the 1.0	13:06:47
22	milligram will be somewhere there, but in the midst	13:06:56

1	of 320 or even more. So there is no way that you	13:06:58
2	can envision, by looking at that, boom, I have the	13:07:02
3	1.0 milligram.	13:07:07
4	Q It's one of the ones that you would	13:07:08
5	envision, but it's surrounded by lots of other ones.	13:07:10
6	Is that your point?	13:07:13
7	MR. BAUGHMAN: Object to the form.	13:07:14
8	A It's one of 300 or -- I mean, easily,	13:07:15
9	there is no way that I can say that the only options	13:07:20
10	are 16 options if you go by 0.1. If you go by 0.05,	13:07:24
11	you go by 32. If you go by 0.025, you have 64. And	13:07:30
12	if you go by 0.0005 and look at 5 or 10 micrograms,	13:07:36
13	you end up with 3200 -- even 320 or 3200.	13:07:41
14	So by looking at this range, I -- as a	13:07:46
15	person of skill in the art, I cannot say it is	13:07:53
16	apparent to me. I can envision the 1.0. It will	13:08:01
17	not hit on my --	13:08:07
18	Q You gave the example that if you look at	13:08:09
19	dosing in amounts including five-hundredths of a	13:08:14
20	milligram?	13:08:20
21	A Correct.	13:08:21
22	Q You said if you did that, then that dose	13:08:22

1 range of 0.1 to 1.6 would give you 32 doses, right? 13:08:24

2 A I'm saying that if you go 1.5, you 13:08:29

3 multiply by 2 to 16. If you go by 0.025, you have 13:08:33

4 64. 13:08:41

5 And as you can see there in my 13:08:43

6 statement -- let me see where I wrote that. You can 13:08:45

7 see there that it -- if we look at the dose-response 13:08:52

8 curve that was reported in 2004 by -- it ranges of 13:08:57

9 0.05, 0.225, 0.45, 0.60, that's one of the dose 13:09:07

10 responses that were previously reported, and it was 13:09:12

11 basically a failure. 13:09:16

12 But you can see that if we looked at the 13:09:17

13 third digit, then you can see that we can go up to 13:09:20

14 increments of 5 micrograms there. That will give me 13:09:24

15 320. 13:09:28

16 And so there are multiple there. So when 13:09:29

17 I looked at this, 1 milligram is just one of 320 or 13:09:32

18 even more. So I cannot envision that it will -- 13:09:37

19 Q Let me try to use an example that you 13:09:41

20 gave in your declaration, okay? 13:09:43

21 A Yes. 13:09:45

22 Q So in paragraph 226, you say, dosing in 13:09:45

1	amounts including five-hundredths of a milligram	13:09:50
2	(i.e., 0.05 milligrams) was common in this field at	13:09:54
3	the time.	13:09:59
4	Do you see that?	13:09:59
5	A At that time, it's fair. But not	13:10:02
6	necessarily so because you can see that is all the	13:10:05
7	0.25, 0.025.	13:10:08
8	Q Just bear with me for a second.	13:10:12
9	Then in that paragraph 226, you	13:10:14
10	illustrate how you would identify every dose in that	13:10:16
11	range, 0.1 to 1.6, if you were looking at increments	13:10:22
12	of five-hundredths of a milligram, correct? You	13:10:27
13	say, e.g., 0.1, 0.15, 0.2, 0.25, 0.3, 0.35,	13:10:30
14	et cetera.	13:10:39
15	Right?	13:10:39
16	A In that example. But that's one of the	13:10:42
17	examples that I gave. This is just one example.	13:10:44
18	Q Understood.	13:10:48
19	A I went on and on and on.	13:10:48
20	Q Bear with me, Doctor.	13:10:50
21	So going by five-hundredths of a	13:10:52
22	milligram, if that's the increment, and you look at	13:10:55

1 that dose range, then a person of skill in the art 13:10:59
2 can certainly identify every dose between 0.1 and 13:11:02
3 1.6 if the increment is five-hundredths of a 13:11:07
4 milligram, right? That's a simple exercise. 13:11:10

5 A If. You said "if." The truth of the 13:11:14
6 matter is we don't know. There are multiple 13:11:16
7 options. That's just one example. There are other 13:11:18
8 options. 13:11:20

9 Q I'm giving you an example. And you gave 13:11:21
10 us the example. This was your example in paragraph 13:11:24
11 226, correct? 13:11:27

12 A I gave you another example there. 13:11:28

13 Q Well, Doctor, I'm just going to ask, that 13:11:30
14 was your example in paragraph 226, right? We'll 13:11:33
15 talk about other examples. 13:11:35

16 A That was one of the examples that I gave 13:11:36
17 in my declaration. 13:11:38

18 Q That was one of the examples that you 13:11:39
19 gave. 13:11:41

20 And in that example -- 13:11:42

21 A And my job was, as I looked at the 13:11:43
22 declaration of Dr. Bantle and Dr. Jusko, they only 13:11:46

1 gave one option, increment of 0.1, which is not 13:11:49
2 correct. 13:11:54

3 Q Understood. But you gave then -- you 13:11:54
4 took it to the next level. You said, rather than 13:11:56
5 use tenths of a milligram, let's use amounts 13:11:59
6 including five-hundredths of a milligram, right? 13:12:02
7 That's what you did in paragraph 226, and you 13:12:06
8 identified, using that increment, what every dose in 13:12:08
9 the range would be, correct? 13:12:11

10 MR. BAUGHMAN: Object to the form. 13:12:12

11 A In that specific example. But I had 13:12:14
12 other examples. 13:12:16

13 Q Right. So let's take another example. 13:12:17
14 Then you say -- the way you get to 320 doses is by 13:12:20
15 applying increments of five thousandths of a 13:12:26
16 milligram to the dose range of 0.1 to 1.6, correct? 13:12:29

17 A By getting to that, I can tell you that I 13:12:33
18 use some fact which is in the data from the dose 13:12:36
19 response with liraglutide from 2004, which can be 13:12:43
20 regarded as a failed phase 2 trial, as we recall our 13:12:50
21 discussions of phase 2 failures. 13:12:54

22 So in that case, it was tested 0.05, 13:12:57

1 0.225, 0.45, 0.60, 0.75. And we looked at the digit 13:13:02
2 of 5 there. This is literally 20 times smaller than 13:13:09
3 the 0.1. So that's another example I can give you, 13:13:14
4 because the truth of the matter, Counsel, I don't 13:13:16
5 know the data. So the options for increments are 13:13:19
6 huge. 13:13:22
7 Q Just, again, bear with me, because your 13:13:23
8 example -- you say repeatedly in your declaration -- 13:13:26
9 you identify, you know, 320. That's a number you 13:13:29
10 use repeatedly in your declaration, right? 13:13:34
11 A Correct. 13:13:36
12 Q And you reach 320 doses by applying 13:13:37
13 increments of five-thousandths of a milligram to the 13:13:41
14 range 0.1 to 1.6, and that's how you come up with 13:13:46
15 320, right? 13:13:50
16 A I'm applying a 0.05 increments. 13:13:51
17 Q Right. And a person of skill in the art 13:13:54
18 could tell you, using five thousandths of a 13:13:57
19 milligram increments, exactly what doses exist in 13:14:04
20 the range from 0.1 to 1.6, correct? That would be a 13:14:10
21 simple exercise for a skilled artisan? 13:14:14
22 A You need to write down the 320. You're 13:14:16

1 going to write down 320. And the truth of the 13:14:19
2 matter, we don't know the data. We don't know where 13:14:21
3 the data is going to look efficacious, tolerable, 13:14:24
4 and safe. 13:14:28

5 Q I completely agree. And I'm not asking 13:14:29
6 whether any one of those doses -- 320 doses would be 13:14:32
7 safe or tolerable or effective. But you agree, I 13:14:36
8 think, at least that a skilled artisan could 13:14:39
9 identify all 320 doses in the range of 0.1 to 1.6 13:14:41
10 using five-thousandths of a milligram as the 13:14:46
11 increment. 13:14:52

12 Is that fair? 13:14:53

13 A That's what I wrote, and actually, you 13:14:53
14 can go even further. If you add another digit, as 13:14:55
15 we discuss before, then we add up with 3200 options. 13:14:58

16 Q And you can identify all the 3200 doses. 13:15:02
17 Your point is that you wouldn't know if they were 13:15:06
18 efficacious or tolerable? 13:15:08

19 A The bottom line, Counsel, is, I don't 13:15:09
20 know. And by looking at that, I cannot envision a 13:15:12
21 1.0. 13:15:17

22 Q Well, you can, right? I mean, you don't 13:15:18

1 know if it will be effective or tolerable, but you 13:15:20
 2 can certainly identify using a tenth of a milligram 13:15:23
 3 increment, we can all sit here today and say, that 13:15:26
 4 would be 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, et cetera, 13:15:29
 5 right? 13:15:33

6 A No, sir. 13:15:34

7 Q You think a skilled artisan can't figure 13:15:35
 8 out what the doses are in the range of 0.1 to 1.6 13:15:37
 9 using a tenth of a milligram increment? They can do 13:15:40
 10 that, right? 13:15:43

11 A But that's not the scientific basis of a 13:15:44
 12 study is where you are trying to identify a dose, 13:15:47
 13 because those are the doses there, and obviously, 13:15:51
 14 when you have the dose -- I mean, there could be 13:15:54
 15 many increments. We don't know if this stops at 13:15:57
 16 0.8. I don't know if you can -- 13:16:01

17 Q When you say "this stops," what are you 13:16:02
 18 talking about? The efficacy? 13:16:03

19 A The efficacy or the tolerability. 13:16:05

20 Q I just want to take this out. I want to 13:16:07
 21 set efficacy and tolerability aside, if I may. 13:16:09
 22 Okay. I'm not disagreeing with you. My question is 13:16:13

1 not suggesting that by identifying what doses are in 13:16:16
2 the range, you would know that any given dose is 13:16:20
3 safe, efficacious, or tolerable. But you could 13:16:24
4 certainly identify what the doses are in that range, 13:16:27
5 right? 13:16:31

6 A Counsel, there are multiple options. 13:16:31
7 There are more than 300 options. There are more 13:16:35
8 than a thousand options. I understand that claim 1 13:16:39
9 does not specify efficacy or safety. But in 13:16:42
10 choosing the dose, when you look at those range, you 13:16:48
11 need to look at what is effective and tolerable. 13:16:52

12 And if you get to a dose, as Dr. Jusko 13:16:57
13 states somewhere in his declaration, that he assumed 13:17:02
14 that a 1.6 is going to be toxic, for instance, or he 13:17:06
15 assumed that it's going to be effective because 13:17:10
16 there's a little bit of a contradiction there. At 13:17:13
17 one point he says it's toxic; another place it will 13:17:16
18 be effective. 13:17:20

19 But it may well be, Counsel, that you 13:17:21
20 cannot get higher than 0.8 because is not effective. 13:17:22
21 And in that case, the titration goes to 1.22, very, 13:17:27
22 very small there. 13:17:34

1	So I cannot envision the 1.0 milligram	13:17:35
2	even on an option because I don't know the data. I	13:17:43
3	don't know if people can get to 1.0.	13:17:46
4	Q Everything you've just said deals with	13:17:49
5	whether or not a particular dose will be, in your	13:17:52
6	words, safe, efficacious, or tolerable, right?	13:17:54
7	A The claim doesn't specify that.	13:17:57
8	Q I understand that.	13:18:00
9	A But in choosing the dose, you actually	13:18:00
10	when you looked at the -- I don't have the data,	13:18:02
11	Counsel.	13:18:05
12	Q I understand that. But what you do have	13:18:05
13	from the prior art, I think we agreed, is a dose	13:18:07
14	range.	13:18:10
15	A Correct.	13:18:10
16	Q Okay. And you can identify every	13:18:11
17	possible dose within that range, whether it's you	13:18:14
18	use a tenth of a milligram or five-hundredths of a	13:18:19
19	milligram or five-thousandths of a milligram,	13:18:22
20	correct?	13:18:25
21	MR. BAUGHMAN: Object to the form.	13:18:26
22	A You can identify multiple there. What	13:18:26

1 I'm saying, a person of skill in the art will not 13:18:29
2 just use 0.1 increments, and a person skilled in the 13:18:32
3 art will not envision that a 1.0 dose is going to be 13:18:36
4 the sweet spot there, to pick it there. It's not 13:18:41
5 the one that comes to me. 13:18:45

6 Q They won't envision that it's going to be 13:18:46
7 the sweet spot in terms of it's tolerable, it's 13:18:49
8 efficacious? 13:18:52

9 A Or whatever the criteria is to decide 13:18:52
10 there. But I don't see it. 13:18:55

11 Q Okay. 13:18:55

12 A That was not tested as we discussed 13:18:56
13 initially. 13:18:58

14 Q Okay. You also say in paragraphs 237 to 13:18:58
15 239 of your declaration, you state your opinion that 13:19:14
16 the prior art semaglutide dose range of 0.1 to 1.6 13:19:17
17 does not disclose doses in exactly tenths of a 13:19:21
18 milligram increments because that understanding is 13:19:25
19 contradicted by the dosing of semaglutide itself 13:19:26
20 later approved by the FDA, correct? 13:19:29

21 A For liraglutide? 13:19:32

22 Q For I believe you're referring to 13:19:33

1	semaglutide.	13:19:37
2	A Yes. They use 0.25.	13:19:37
3	Q Right.	13:19:40
4	A That's as a starting dose.	13:19:42
5	Q But that wasn't approved until 2017,	13:19:44
6	correct?	13:19:46
7	A That's when it was approved, yeah.	13:19:46
8	Q All right. And okay. Let's look at --	13:19:49
9	I'm going to talk to you about your opinions that	13:19:58
10	you have or that you express in paragraphs 240 to	13:20:00
11	258 of your declaration. And you're discussing in	13:20:04
12	that section your opinion that the 1 milligram	13:20:08
13	once-weekly semaglutide dose claimed in the '462	13:20:11
14	patent is critical, correct?	13:20:15
15	A What I claim is that the dosages were all	13:20:18
16	different. And certainly they were different there,	13:20:21
17	they will not behave the same.	13:20:26
18	Q Okay. And your criticality opinion is	13:20:28
19	based on certain data that's disclosed in the '462	13:20:30
20	patent specification, correct?	13:20:34
21	A Yeah. I can see that in the disclosure	13:20:35
22	there is that -- I can see that the dosages behave	13:20:38

1	differently.	13:20:43
2	Q Okay. And you have -- you've got Exhibit	13:20:43
3	1001 there, which is the '462 patent, so I want to	13:20:46
4	ask you some questions about that.	13:20:50
5	A Yes, sir.	13:20:52
6	Q Starting in paragraph 244 of your	13:20:52
7	declaration, you discuss the efficacy data from the	13:20:58
8	'462 patent specification, correct?	13:21:02
9	A In the 244?	13:21:09
10	Q In paragraph 244, yeah, of your	13:21:12
11	declaration, you discuss certain efficacy data from	13:21:14
12	the '462 patent specification.	13:21:20
13	Is that right?	13:21:21
14	A Yeah. It does say -- that's what I refer	13:21:23
15	to, that they operate different. I say that, In my	13:21:26
16	opinion, the '462 patent itself confirmed that a	13:21:29
17	1 milligram once-daily dose operate different than	13:21:32
18	large portions of the 421 range, that the	13:21:36
19	1 milligram was different because not all doses of	13:21:39
20	the 421, 0.1 to 1.6 were effective of reducing A1c.	13:21:43
21	Q And in that paragraph, you state, For	13:21:51
22	example, 0.1 milligrams --	13:21:52

1	A	Correct.	13:21:52
2	Q	-- did not reduce HbA1c from baseline as	13:21:53
3		compared to placebo, correct?	13:21:55
4	A	Correct.	13:21:56
5	Q	All right. And for that proposition, you	13:21:57
6		cite Figure 1 from the patent specification,	13:21:59
7		correct?	13:22:01
8	A	It does not at the 0.1 milligram and also	13:22:02
9		the 0.2, 0.4 did not have any changes in weight.	13:22:06
10		But in regards to the A1c that you asked, the	13:22:12
11		Figure 1, which Figure 1 --	13:22:15
12	Q	It's not reproduced in your declaration.	13:22:16
13	A	You mean --	13:22:16
14	Q	But you cite Figure 1 --	13:22:19
15		(Cross-talk.)	13:22:19
16	A	This one?	13:22:19
17	Q	-- in paragraph 244. That one, exactly.	13:22:21
18		You're looking at Figure 1 --	13:22:25
19	A	Correct.	13:22:25
20	Q	-- in Exhibit 1001, okay, and that's what	13:22:26
21		I want to ask you about.	13:22:30
22	A	Yes.	13:22:31

1	Q	Figure 1 shows that the 0.2 milligram	13:22:31
2		once-weekly semaglutide dose reduced HbA1c from	13:22:34
3		baseline in a statistically significant fashion	13:22:39
4		compared to placebo, correct?	13:22:43
5	A	Correct.	13:22:44
6	Q	All right. Figure 1 also shows that 0.4	13:22:44
7		milligrams once-weekly semaglutide reduced HbA1c	13:22:48
8		from baseline in a statistically significant manner	13:22:48
9		compared to placebo, correct?	13:22:52
10	A	And liraglutide. And liraglutide 1.2	13:22:53
11		milligrams. So they actually behaving differently.	13:22:56
12	Q	Doctor, I need you to focus on my	13:22:59
13		question, okay? I've given you a lot of leeway in	13:23:01
14		giving very lengthy answers, but I really -- this is	13:23:04
15		supposed to be a cross-examination. I need you to	13:23:06
16		answer my questions.	13:23:08
17		Figure 1 shows that the 0.4 milligram	13:23:10
18		once-weekly semaglutide dose reduced HbA1c from	13:23:13
19		baseline in a statistically significant fashion as	13:23:16
20		compared to placebo, correct?	13:23:19
21	A	Correct.	13:23:20
22	Q	Okay. That's also true of the 0.8	13:23:21

1	milligram dose, the 0.8 milligram titrated dose, and	13:23:24
2	the 1.6 milligram titrated dose, correct?	13:23:24
3	A Correct, but there's also differences	13:23:32
4	with liraglutide that was also a comparator.	13:23:33
5	Q Okay, we'll get to that.	13:23:33
6	So aside from the 0.1 milligram dose,	13:23:34
7	every dose tested reduced HbA1c from baseline in a	13:23:37
8	statistically significant fashion as compared to	13:23:42
9	placebo, correct?	13:23:44
10	A There are differences of statistics and	13:23:45
11	power of statistics.	13:23:48
12	Q Right. But you agree that the reduction	13:23:49
13	compared to placebo for every dose, other than 0.1	13:23:54
14	milligrams, was statistically significant reduction	13:23:57
15	of HbA1c, correct?	13:24:01
16	A Statistically significant versus placebo	13:24:04
17	but with different magnitudes. So there are	13:24:06
18	differences there in the magnitude of the reduction,	13:24:09
19	which also counts and is difference in the magnitude	13:24:12
20	of the statistical power.	13:24:15
21	Q And you would also agree that the	13:24:17
22	specification itself -- if you look at column 22.	13:24:25

1	A	Which column?	13:24:31
2	Q	It's in the patent. So the numbers at	13:24:32
3		the very top of the page -- on top of each column,	13:24:36
4		there's a number.	13:24:39
5	A	Oh, okay.	13:24:40
6	Q	And I'm looking at column 22.	13:24:41
7	A	Yes, sir.	13:24:50
8	Q	Okay. And you would agree with me that	13:24:50
9		there in column 22 the patent specification there's	13:24:55
10		a heading there that says Results.	13:24:58
11		Do you see that?	13:25:00
12	A	Yes, sir.	13:25:00
13	Q	And it reports that, In the full analysis	13:25:00
14		set, semaglutide, greater than or equal to 0.2	13:25:03
15		milligrams, dose-dependently reduced HbA1c from	13:25:07
16		baseline, Figure 1, and increased the likelihood of	13:25:12
17		achieving HbA1c less than 7 percent, correct?	13:25:14
18	A	That's what it says.	13:25:17
19	Q	And in paragraph 245 of your expert	13:25:18
20		report, you state that, only doses of 0.8 milligrams	13:25:22
21		and above brought subjects HbA1c to the level	13:25:28
22		recommended by the American Association of Clinical	13:25:33

1	Endocrinologists as compared to placebo.	13:25:36
2	Correct?	13:25:39
3	A In what paragraph?	13:25:40
4	Q 245.	13:25:42
5	A Yes, you can see that in the figure.	13:25:45
6	Q And the figure you're referring to is	13:25:51
7	Figure 3A from the patent specification, correct?	13:25:53
8	A Correct.	13:25:56
9	Q Okay. And do I understand correctly that	13:25:56
10	the HbA1c level recommended by the American	13:25:59
11	Association of Clinical Endocrinologists, that you	13:26:02
12	refer to as less than or equal to 6.5 percent?	13:26:05
13	A Correct.	13:26:09
14	Q And you agree that the '462 patent	13:26:10
15	claims, though, don't require treating type 2	13:26:13
16	diabetes with any particular level of efficacy,	13:26:17
17	right?	13:26:19
18	A They don't require it. But I'm just	13:26:20
19	referring how the different doses behave differently	13:26:22
20	in terms not just of the A1c compared to placebo, I	13:26:26
21	also referring to compared to liraglutide that was	13:26:31
22	the other comparator --	13:26:34

1	Q	Okay.	13:26:34
2	A	-- and also in reference to A1c reduction	13:26:35
3		and reaching targets of 7 and 6.5.	13:26:39
4		So there were clear differences in the	13:26:42
5		dosages there.	13:26:45
6	Q	But the claims themselves don't require	13:26:45
7		reaching a level of HbA1c reduction as recommended	13:26:48
8		by the American Association of Clinical	13:26:54
9		Endocrinologists or the American Diabetes	13:26:56
10		Association or anyone else, right?	13:26:58
11	A	The claim doesn't do that. But there is	13:27:01
12		criticality there in the differences of response of	13:27:03
13		each of the different dose. There are very clear	13:27:06
14		differences between the different dosages.	13:27:11
15	Q	And to support -- now looking at	13:27:13
16		paragraph 246.	13:27:17
17		To support your criticality opinion, you	13:27:19
18		also state that the '462 patent discloses that, 0.1	13:27:22
19		milligram, 0.2 milligram, and 0.4 milligram did not	13:27:26
20		result in statistically significant weight loss in	13:27:31
21		subjects with type 2 diabetes as compared to	13:27:34
22		placebo.	13:27:37

1	Correct?	13:27:38
2	A Correct.	13:27:38
3	Q All right. And we agreed earlier that	13:27:38
4	the '462 patent claims don't require weight loss	13:27:41
5	much less any specific amount of weight loss,	13:27:44
6	correct?	13:27:46
7	A That is what the claim says. When I	13:27:46
8	looked at the data, I see criticality that the	13:27:48
9	dosages were different, not just in reference to	13:27:51
10	placebo but also in reference to liraglutide. Not	13:27:53
11	just in reference to Alc. I see differences in	13:27:55
12	weight. All those are criteria for assessing	13:27:58
13	differences in response.	13:28:03
14	Q And you think those are all relevant to	13:28:04
15	criticality, notwithstanding the fact that the	13:28:07
16	patent claims themselves don't require any level of	13:28:10
17	efficacy, any weight loss, any tolerability.	13:28:13
18	Is that -- do I understand your opinion	13:28:16
19	correctly?	13:28:17
20	MR. BAUGHMAN: Object to the form and	13:28:18
21	foundation.	13:28:19
22	A The claim asks for 1.0 milligram. The	13:28:21

1 claim does not talk about efficacy or safety. I'm 13:28:26
2 analyzing this from the criticality point of view, 13:28:29
3 and I can see that there are differences there in 13:28:33
4 the dosages. So I cannot, without knowing the data, 13:28:35
5 envision one dose that is going to be effective. I 13:28:38
6 cannot say that the 1 milligram is going to be 13:28:40
7 effective at all. 13:28:43

8 Q Well, Doctor, I don't understand why 13:28:44
9 you're saying without knowing the data. Your whole 13:28:47
10 criticality opinion is based on the data in the 13:28:50
11 patent specification, right? 13:28:53

12 A I'm talking about if I'm going to be 13:28:53
13 challenging this patent, if I am -- when I looked at 13:28:57
14 the -- I looked at the declaration of Dr. Bantle and 13:29:01
15 Dr. Jusko. Without knowing the data, they 13:29:06
16 challenged the claim 1. 13:29:10

17 I'm here to tell you that I don't see 13:29:11
18 that the argument that they have is strong enough to 13:29:13
19 claim the data for the 1 milligram because I don't 13:29:17
20 see the 1 milligram. 13:29:20

21 Q I understand -- I kind of feel like 13:29:21
22 you're just giving me your opinion writ large 13:29:23

1	without focusing on what we're talking about. We're	13:29:26
2	talking about your opinion about criticality, right?	13:29:28
3	A Yeah.	13:29:31
4	Q That's what I'm asking you about now.	13:29:31
5	MR. BAUGHMAN: Object to the form.	13:29:33
6	Q And your opinion about criticality is	13:29:34
7	based on data in the patent specification, right?	13:29:36
8	A My opinion in terms of criticality, now	13:29:41
9	that I have the data on hand, I can see that the	13:29:46
10	dosages behave differently. So if I'm a person of	13:29:49
11	skill looking only at 0.1, 0.2, 0.4, 0.8, and 1.6, I	13:29:54
12	cannot see the 1.0 milligrams because the dosages	13:30:03
13	are different.	13:30:07
14	Q Okay. But again, I'm focused on your	13:30:08
15	criticality opinions. And your criticality opinions	13:30:12
16	rely on data in the patent specification, okay. So	13:30:15
17	that's what we're talking about now.	13:30:17
18	A Yes.	13:30:19
19	Q Okay. And for example, in paragraph 248	13:30:20
20	of your report, you state that, the criticality of	13:30:26
21	the 1 milligram dose is also supported by the fact	13:30:29
22	that only weekly doses of 0.8 milligrams or greater	13:30:33

1	offered significant improvement over once-daily	13:30:38
2	liraglutide in terms of HbA1c reduction, right?	13:30:42
3	A Correct.	13:30:45
4	Q And that's based on data in the patent	13:30:45
5	specification?	13:30:48
6	A When I looked at the data --	13:30:48
7	Q Right.	13:30:48
8	A -- when I have it in hand --	13:30:49
9	Q Right.	13:30:49
10	A -- the data in the 416, and I see the	13:30:51
11	numbers, when I see the figures, I can see that the	13:30:54
12	dosages behave differently, and I can say that the	13:30:56
13	dosage of 0.8 milligrams and above are able to show	13:31:00
14	superiority of A1c reduction, also in targets, and	13:31:03
15	also, in terms of weight, they look surprise --	13:31:08
16	there was a surprisingly positive weight reduction.	13:31:13
17	So it was unexpected robustness on the weight there.	13:31:17
18	So there's criticality in the sense that	13:31:21
19	the dosages behaved differently. And more	13:31:23
20	differently from 0.8 and above.	13:31:27
21	Q So the 0.8 dose is critical?	13:31:29
22	MR. BAUGHMAN: Object to the form.	13:31:32

1	A	There are differences in the dosages.	13:31:34
2	Q	Is the 0.8 dose critical?	13:31:37
3	A	It's critical --	13:31:39
4		MR. BAUGHMAN: Sorry, just a second.	13:31:41
5		Object to the form, scope, and	13:31:42
6		foundation.	13:31:43
7		You can answer.	13:31:43
8	A	I mean, my understanding is criticality	13:31:44
9		is based on differences of the dosages. 0.8 and	13:31:50
10		above show differences there that are both	13:31:52
11		statistically significant in Alc and weight that are	13:31:56
12		surprisingly greater than the others and so on.	13:31:59
13		Yes, it's critical.	13:32:03
14	Q	Okay. The 0.9 milligram dose would be	13:32:04
15		critical, in your opinion?	13:32:07
16		MR. BAUGHMAN: Same objections.	13:32:08
17	A	I don't have the data on 0.9.	13:32:09
18	Q	You don't have the data on 1.0 either,	13:32:11
19		right?	13:32:13
20	A	I did not have the data. Novo had the	13:32:14
21		data.	13:32:16
22	Q	Doctor, your criticality opinion is based	13:32:17

1 on data in the patent specification, right? Every 13:32:20
2 place throughout your report where you discuss 13:32:23
3 criticality, you reference the patent specification. 13:32:26
4 In paragraph 244, you reference Figure 1. In 13:32:29
5 paragraph 245, you reference Figure 3A. On the next 13:32:33
6 page, you reference Figure 5. 13:32:33

7 Your criticality opinion is based on data 13:32:37
8 in the patent specification. Do you understand 13:32:40
9 that? 13:32:41

10 MR. BAUGHMAN: Object to the form. 13:32:42

11 A I understand, Counsel. And I already 13:32:43
12 answered the question. There is criticality there. 13:32:46
13 The dosages behave differently. The 1 milligram, it 13:32:49
14 does not stay there. Novo had that information. I 13:32:53
15 did not have it. 13:32:56

16 Q But your opinion on criticality is based 13:32:57
17 on the data in the patent specification. 13:32:59

18 A Correct. 13:33:01

19 Q Based on that, is the 0.9 milligram dose, 13:33:02
20 would it be critical? 13:33:07

21 A I don't see that -- 13:33:08

22 MR. BAUGHMAN: Sorry. Just a second. 13:33:08

1	Object to the form, scope, and	13:33:09
2	foundation.	13:33:10
3	A I don't see the 0.9 there, Counsel.	13:33:10
4	Q You don't see the 1.0 milligram dose in	13:33:12
5	the patent specification either, right?	13:33:16
6	A It was not tested, Counsel.	13:33:16
7	Q Correct. So you can't offer an opinion,	13:33:18
8	then. If you can't tell me whether 0.9 would be	13:33:20
9	critical, you can't tell me whether 1.0 would be	13:33:23
10	critical, correct?	13:33:27
11	MR. BAUGHMAN: Objection to the form,	13:33:27
12	scope, and foundation.	13:33:29
13	A I am stating that 0.8 and above is	13:33:30
14	critical, have differences from the rest. The	13:33:33
15	dosages behave differently.	13:33:36
16	Q So 0.8 is critical?	13:33:37
17	MR. BAUGHMAN: Objection to the form, scope,	13:33:40
18	and foundation.	13:33:41
19	A In my opinion -- it says, In my	13:33:41
20	opinion -- in 244 -- the '462 patent itself	13:33:44
21	confirmed that the 1.0 once-weekly dose operates	13:33:49
22	differently than large portion of the 421 range	13:33:53

1	because not all dosages in 421, 0.1 to 1.6 range,	13:33:56
2	were effective at reducing Alc.	13:34:03
3	I'm stating that they are different.	13:34:07
4	For example, 0.1 milligram did not reduce	13:34:09
5	Alc from baseline as compared to placebo.	13:34:11
6	And then, if I may continue there.	13:34:14
7	Q Doctor, with all due respect, I don't	13:34:19
8	need you to read your report to me. I have the	13:34:20
9	benefit of your report. The board has the benefit	13:34:23
10	of your report. They're going to be able to read	13:34:25
11	it. They're going to be able to read this	13:34:27
12	deposition transcript.	13:34:29
13	My question to you is, is the 0.8	13:34:30
14	milligram dose, in your opinion, based on the data	13:34:33
15	in the patent specification critical?	13:34:35
16	MR. BAUGHMAN: Object to the form, scope,	13:34:36
17	and foundation.	13:34:37
18	A The 0 point -- if I may, I think that I	13:34:38
19	can write what I -- I can read what I wrote. May I?	13:34:40
20	Q If you think it's necessary, but I mean,	13:34:44
21	at the end of the day, I'm going to ask you to	13:34:48
22	answer my question.	13:34:50

1 A I think I did, Counsel. I already 13:34:51
2 mentioned that the dosages from 0.1 to 1.6 are 13:34:54
3 different. And my understanding is that meets the 13:34:58
4 criticality. 13:35:02

5 I also said that the 0.8 and above 13:35:03
6 behaves differently. And Novo, when they had the 13:35:07
7 data for the patent, they chose the 1 milligram that 13:35:11
8 was not tested. 13:35:15

9 Q So would you agree with me that the doses 13:35:16
10 between point -- in your opinion, the doses 13:35:18
11 between -- based on the data in the patent 13:35:22
12 specification that you cite and that you rely on, 13:35:23
13 doses between 0.8 milligrams and 1.6 milligrams, 13:35:26
14 which is the highest dose that was tested in the 13:35:29
15 specification, are critical? 13:35:32

16 A It could well be -- 13:35:34

17 MR. BAUGHMAN: Sorry. You need to give 13:35:34
18 me a second. 13:35:34

19 Object to the scope, form, and 13:35:37
20 foundation. 13:35:40

21 Go ahead. 13:35:40

22 A It could well be, Counsel. I don't have 13:35:41

1 the data. I don't have the data because I don't 13:35:43
2 know if above the 1.0 could be toxic, it could be 13:35:45
3 side effects and so on. It's critical to be into 13:35:52
4 the thing. The 1.0 is data that Novo had in their 13:35:55
5 hands when they analyzed and decided to do the -- 13:36:00
6 Q So even though it's not in the patent 13:36:07
7 specification, it's not tested in the patent 13:36:09
8 specification, you're relying on the fact that 13:36:11
9 because Novo had data, according to you on a -- 13:36:13
10 (Reporter interruption.) 13:36:35
11 Q You're assuming because the 1 milligram 13:36:35
12 dose is not one of the doses for which there is data 13:36:41
13 in the patent specification, right? 13:36:44
14 A I did not have -- I don't see it. Novo 13:36:46
15 had that data. 13:36:48
16 Q Novo had that data. And so you're 13:36:49
17 assuming is Novo had that data, the 1.0 milligram 13:36:51
18 dose must be critical? 13:36:57
19 A I assume so. 13:36:58
20 Q I want to ask you a few more questions 13:37:05
21 about the patent specification. Would you agree 13:37:07
22 with me that -- well, in paragraph 250 of your 13:37:20

1	declaration, you quote the observation in the '462	13:37:33
2	patent specification that, the effect of semaglutide	13:37:38
3	0.4 milligram on glycemic control and body weight	13:37:40
4	was comparable to that of liraglutide 1.2	13:37:45
5	milligrams, while semaglutide greater than or equal	13:37:48
6	to 0.8 milligrams appeared to bring more subjects to	13:37:51
7	target and provide the better weight loss than	13:37:55
8	liraglutide 1.8 milligrams.	13:37:58
9	Correct?	13:38:00
10	A Yes, sir.	13:38:01
11	Q And so according to the specification,	13:38:01
12	the 0.4 milligram dose of semaglutide and the 1.2	13:38:04
13	milligram dose of liraglutide were comparable in	13:38:09
14	terms of glycemic control and weight loss, correct?	13:38:11
15	MR. BAUGHMAN: Object to the form.	13:38:15
16	A Correct.	13:38:16
17	Q And the 1.2 milligram dose of liraglutide	13:38:16
18	was FDA-approved for treating type 2 diabetes before	13:38:17
19	the priority date of the '462 patent, correct?	13:38:21
20	A Can you repeat that again.	13:38:23
21	Q Sure. The 1.2 milligram dose of	13:38:26
22	liraglutide was FDA-approved for treating type 2	13:38:30

1	diabetes before the priority date on the '462	13:38:33
2	patent?	13:38:36
3	MR. BAUGHMAN: Object to the form.	13:38:36
4	A Let me remember -- remind me. When was	13:38:37
5	liraglutide approved? Was it 2017 that it was	13:38:42
6	approved?	13:38:51
7	Q You may be thinking of Ozempic in 2017.	13:38:52
8	A No. Liraglutide came -- okay, let me --	13:38:57
9	the thing is that the 1.2 milligram data was tested	13:38:59
10	as a comparator. So it's right there. So rather	13:39:03
11	than rely on other studies, I mean, it's there. So	13:39:06
12	it's a valid comparator there. It was an	13:39:10
13	open-label, but it was a valid comparator.	13:39:13
14	So when I looked at the A1c reduction of	13:39:15
15	the 0.4 and the weight reduction, they looked	13:39:18
16	similar.	13:39:21
17	Q Okay. In paragraph 248 of your	13:39:21
18	declaration, you cite figures 3A and 3B from the	13:39:26
19	patent specification.	13:39:31
20	Do you see that?	13:39:32
21	A Yes, sir.	13:39:40
22	Q And you say there that, in those figures,	13:39:40

1	Figures 3A and 3B, only semaglutide once-weekly	13:39:45
2	doses of 0.8 milligrams or greater, groups E through	13:39:48
3	G, showed numerical improvement over once-daily	13:39:52
4	liraglutide.	13:39:57
5	Do you see that?	13:39:57
6	MR. BAUGHMAN: Object to the form.	13:39:58
7	Q Just do you see that you wrote that in	13:39:59
8	your declaration?	13:40:01
9	A In 248, yes. I just want to -- it's	13:40:04
10	numerical in regards to the A1c lower than 6.5	13:40:11
11	percent.	13:40:16
12	Q And what did you mean by "numerical	13:40:17
13	improvement"?	13:40:19
14	A Well, the thing is you can see the	13:40:19
15	differences there. "Numerical" is when you do a	13:40:21
16	clinical study, depends on the power you have. If	13:40:24
17	you have enough numbers there to show a statistical	13:40:27
18	significance.	13:40:31
19	"Numerical" means that it's in the right	13:40:31
20	direction close to establish a statistical	13:40:33
21	significance.	13:40:36
22	But for a person of skill in the art, you	13:40:36

1 can say that you are numerically better. 13:40:40

2 Q So you're numerically better but not 13:40:43

3 statistically significantly better? 13:40:47

4 A It is not -- but that is driven basically 13:40:49

5 by the number of subjects analyzed, conceivably, 13:40:52

6 that you put more at a side is there. But it's a 13:40:55

7 very valid thing to assume that it's better. 13:40:57

8 Q The numerical difference? 13:40:59

9 A Yes. 13:41:02

10 Q Okay. And Figure 3B in the patent -- you 13:41:02

11 may want to look at Exhibit 1001, if we just look at 13:41:07

12 that, and if you look at Figure 3B. 13:41:10

13 Am I right that Figure 3B shows that 13:41:15

14 treatment with every dose of semaglutide tested from 13:41:27

15 0.1 milligrams to 1.6 milligrams resulted in an 13:41:31

16 increased number of subjects reaching the American 13:41:36

17 Diabetes Association criteria for glycemic control 13:41:40

18 compared to placebo? 13:41:42

19 A Let me see the footnote, just to remind 13:41:43

20 me about that. 13:41:45

21 Q Are you talking about the little 13:41:51

22 asterisk? 13:41:53

1	A	Yeah. 3B.	13:41:54
2	Q	I think if you look at column 2, lines 21	13:41:57
3		through 33.	13:42:04
4	A	21?	13:42:07
5	Q	Column 2, lines 21 through 33, where	13:42:08
6		they're describing Figures 3A and 3B.	13:42:11
7		MR. BAUGHMAN: Column 2 -- sorry to	13:42:16
8		interrupt, Counsel.	13:42:17
9		MR. ANSTAETT: No, go ahead.	13:42:17
10		MR. BAUGHMAN: Column 2 has a 2 at the	13:42:18
11		top. I think you're at 22.	13:42:19
12	A	21 or 22 --	13:42:22
13	Q	Column 2.	13:42:22
14	A	Oh, yeah. We're talking about 3B?	13:42:42
15	Q	Correct.	13:42:44
16	A	So that's what I was trying to look,	13:43:29
17		Counsel. These asterisks of Figure 3B is in	13:43:31
18		comparison with placebo only, not in comparison with	13:43:37
19		liraglutide. But it's not indicated here. This is	13:43:42
20		only in comparison versus placebo. This is not --	13:43:46
21		But you can see that -- for a person	13:43:49
22		skilled in the art, you can see that those dosages	13:43:53

1 of 0.8 and above look better than the liraglutide 13:43:56
2 doses in reaching a target A1c of less than 7 13:43:59
3 percent. 13:44:03

4 Q Okay. But my question was slightly 13:44:03
5 different. Would you agree with me that figure -- 13:44:05
6 we were talking about -- we started this 13:44:07
7 conversation by talking about the difference between 13:44:11
8 numerical improvements and statistically significant 13:44:14
9 improvements. Do you recall that? 13:44:19

10 A Yeah. 13:44:20

11 Q Okay. Figure 3B shows that treatment 13:44:21
12 with every dose of semaglutide tested, from 0.1 13:44:23
13 milligrams to 1.6 milligrams, resulted in an 13:44:26
14 increased number of subjects reaching the American 13:44:29
15 Diabetes Association criteria for glycemic control 13:44:31
16 compared to placebo, correct? 13:44:35

17 A If I -- the 0.1 did not reach a 13:44:39
18 statistical difference. So it was different, the 13:44:45
19 0.1. 13:44:49

20 Q Well, the 0.1, according to Figure 3B, 13:44:50
21 did reach statistical significance, right? 13:44:52

22 A I'm sorry. I don't see an asterisk here. 13:44:54

1	In the 3B here?	13:44:54
2	Q Well, A is -- A is placebo, right?	13:44:56
3	A Oh, A is placebo. Yeah.	13:44:58
4	Q So B is the 0.1 milligram dose.	13:44:58
5	Is that right?	13:45:02
6	A Well, let me -- A is placebo?	13:45:03
7	Q Yes.	13:45:06
8	A Yes, correct. A is placebo.	13:45:07
9	Well, oh, what is in the baseline is the	13:45:10
10	baseline A1c. That's what it is.	13:45:13
11	So what I can see here for a person	13:45:16
12	skilled in the art is, yes, it reached statistical	13:45:20
13	significance. But as you can see, there is	13:45:25
14	difference of statistical power and percentage of	13:45:27
15	people who actually reach.	13:45:29
16	I mean, to have a 28 percent of people	13:45:31
17	reaching A1c, any person of skill in the art would	13:45:35
18	have regarded this as a very poor response. Same	13:45:40
19	even 45. But you can see from 0.8 and above, people	13:45:43
20	reaching more than 70 percent.	13:45:47
21	So you can see that you are correct in	13:45:49
22	the sense that it reaches statistical significance.	13:45:51

1	But the significance is also related to the power of	13:45:54
2	significance. And three asterisks versus one, in my	13:45:57
3	estimation, a person of skill, this is behaving	13:46:03
4	differently.	13:46:07
5	Q Is it your understanding that, without	13:46:08
6	regard to what is claimed, any difference between	13:46:15
7	the way two doses of semaglutide behave can show	13:46:23
8	criticality?	13:46:28
9	MR. BAUGHMAN: Object to the form.	13:46:31
10	A Can you explain?	13:46:33
11	Q Sure. I think we've agreed the claims	13:46:34
12	don't require any level of efficacy, right?	13:46:38
13	MR. BAUGHMAN: Objection to form.	13:46:40
14	A The claim 1 said 1.0 milligram.	13:46:46
15	Q I'm not talking about the dose. I'm	13:46:51
16	talking about claim 1, I think we've agreed, doesn't	13:46:53
17	require any particular level of efficacy. You know	13:46:56
18	the board has found that, right?	13:46:59
19	MR. BAUGHMAN: Object to the form.	13:47:00
20	Q Do you agree with that?	13:47:03
21	A What is your question?	13:47:05
22	Q Do you agree that claim 1 does not	13:47:06

1 require any particular level of efficacy in treating 13:47:09
2 type 2 diabetes? 13:47:14

3 A I agree. 13:47:14

4 Q And my question for you is, 13:47:15
5 notwithstanding that, is it your belief that if you 13:47:17
6 can identify any difference in efficacy between two 13:47:20
7 doses of semaglutide, that the dose that is more 13:47:23
8 efficacious is, therefore, critical? 13:47:29

9 A Well, Counsel, that is the definition of 13:47:32
10 behaving differently. I mean, just because you 13:47:34
11 reduce it, that means that this is the only 13:47:38
12 qualifying thing. I mean, the difference is 13:47:42
13 behaving differently. 13:47:44

14 And getting 70 percent of people getting 13:47:46
15 to the target Alc versus 25, any person of skill 13:47:49
16 will see that's a different response and will behave 13:47:56
17 differently. 13:48:00

18 Q For instance we talked -- thank you, 13:48:00
19 that's helpful to get your understanding. 13:48:02

20 We were talking in paragraph 248 about 13:48:05
21 Figure 3B where you said that only doses of 0.8 13:48:08
22 milligrams or greater showed numerical improvement 13:48:13

1 over liraglutide in number of subjects reaching

13:48:16

2 HbA1c, correct?

13:48:19

3 A You know, the thing is, if we looked at
4 that, you can appreciate that in the dose response,
5 presumably -- well, I -- the statistical plan, when
6 you do a phase 2 dose response, the statistical plan
7 probably was defined testing the doses of
8 semaglutide versus placebo.

13:48:23

13:48:27

13:48:34

13:48:40

13:48:47

13:48:49

9 Q Doctor, I'm just -- I'm literally asking
10 you if you agree with what you've written in your
11 own expert report. You wrote in your expert
12 report -- as part of your criticality opinion, you
13 cited Figure 3B, and you said -- and I'm reading
14 from paragraph -- your paragraph 248, only doses 0.8
15 milligram or greater showed numerical improvement
16 over liraglutide in number of subjects reaching
17 HbA1c less than or equal to 7 percent, correct?

13:48:51

13:48:54

13:48:57

13:48:59

13:49:01

13:49:04

13:49:08

13:49:11

13:49:14

18 A This is what I wrote. If I may explain
19 why I used this term.

13:49:18

13:49:21

20 Q Well, your counsel can ask you for your
21 explanations. That's not my job.

13:49:23

13:49:26

22 You wrote that, and you found that that

13:49:28

1	numerical difference, not -- it's not statistically	13:49:30
2	significant but because it's numerically different,	13:49:36
3	you thought that supports your criticality opinion.	13:49:39
4	Is that right?	13:49:41
5	MR. BAUGHMAN: Object to the form.	13:49:41
6	A I need to explain, Counsel, if I may?	13:49:42
7	Because --	13:49:44
8	Q Doctor, this is not how this works. This	13:49:44
9	is cross-examination.	13:49:47
10	A It's just that you are assuming that Novo	13:49:48
11	analyzes statistically. Because -- if you allow me	13:49:50
12	to explain.	13:49:54
13	A dose-response study, they have a	13:49:54
14	statistical assessment plan, an SAP, that is	13:49:57
15	predefined how the statistics is going to be done.	13:50:01
16	And here, the statistics were done versus placebo.	13:50:04
17	The liraglutide was used as a reference.	13:50:07
18	And on purpose, as you can see in the figures, you	13:50:12
19	don't see any asterisks because Novo did not analyze	13:50:14
20	statistically there. So you can see that	13:50:20
21	pictorially, numerically, any way you want to	13:50:23
22	define, you can see differences in behavior.	13:50:26

1	By study design, I don't see there any	13:50:28
2	statistical analysis versus liraglutide. That's	13:50:31
3	what I try to explain, Counsel.	13:50:34
4	Q Are you finished?	13:50:37
5	A And that's why I said numerical, yes,	13:50:38
6	sir.	13:50:41
7	Q Okay. But you nonetheless found that	13:50:41
8	numerical difference -- where there was no	13:50:44
9	statistical analysis, you found that to be evidence	13:50:47
10	of criticality of the doses you discuss, correct?	13:50:51
11	A There are differences in criticality in	13:50:54
12	Alc reductions, Alc reductions. There are	13:50:57
13	differences in criticality also in target Alcs. And	13:51:02
14	also, since there was no statistical difference, any	13:51:07
15	person skilled in the art looking at the bars of	13:51:11
16	liraglutide versus semaglutide, it is clear that is	13:51:16
17	a numerical difference.	13:51:19
18	I use the term "numerical" because	13:51:21
19	statistics were not performed.	13:51:23
20	Q And you agree with me that where	13:51:27
21	statistics were performed in Figure 3B, every dose	13:51:29
22	of semaglutide tested, including the 0.1 milligram	13:51:36

1 dose, resulted in improvements in HbA1c compared to 13:51:39
2 placebo, correct? 13:51:46

3 A Statistics were performed versus placebo. 13:51:47
4 There are differences in the magnitudes of the 13:51:50
5 changes. And, therefore, a person skilled in the 13:51:52
6 art is a different behavior of response. 13:51:54

7 Q And if we look at Figure 3A, in terms of 13:51:58
8 a numerical response or a numerical improvement, 13:52:15
9 that figure shows that every semaglutide dose tested 13:52:20
10 from 0.1 to 1.6 improved the percentage of subjects 13:52:24
11 reaching the AACE criteria for glycemic control as 13:52:29
12 compared to placebo, correct? 13:52:33

13 MR. BAUGHMAN: Object to the form. 13:52:35

14 A Let me read in the column 2. Is that the 13:52:36
15 description of the footnotes of 3A, just to make 13:52:39
16 sure that this is, again, only statistics versus 13:52:43
17 placebo? 13:52:46

18 We're talking about 3A, right, Counsel? 13:52:46

19 Q Correct. 13:53:10

20 A Yeah, it's statistics versus placebo. 13:53:11

21 Q Okay. But my question dealt with 13:53:14
22 numerical superiority. Like you were referring to 13:53:16

1	with liraglutide, where there was not a statistical	13:53:18
2	analysis done, right?	13:53:21
3	A In the 3A?	13:53:22
4	Q Right.	13:53:25
5	A I think that this, if I may, Counsel,	13:53:25
6	this actually strengthens the point that I was	13:53:29
7	trying to make, that there are difference of	13:53:32
8	behavior.	13:53:34
9	You can see here that the semaglutide	13:53:35
10	dose of 0.1, 0.2, and 0.4 did not reach a	13:53:39
11	statistical significance versus placebo. And only	13:53:45
12	the 0.8 and above.	13:53:48
13	And as I looked at the liraglutide two	13:53:50
14	last columns, it says no statistical difference. If	13:53:55
15	I want to be transparent and scientifically correct,	13:54:00
16	I cannot claim statistical difference because they	13:54:03
17	were not performed.	13:54:07
18	But it is obvious that -- it is clear, it	13:54:07
19	is clear that it is numerically different. I wish I	13:54:09
20	could stay statistically, but it was not performed.	13:54:15
21	Q Why is it clear that it is numerically	13:54:18
22	different? Is that because in terms of the percent	13:54:22

1 of subjects; 34 percent and 36 percent of subjects 13:54:25
2 on liraglutide saw an HbA1c reduction to less than 13:54:28
3 or equal to 6.5 percent? 13:54:37

4 A I think that the person skilled in the 13:54:39
5 art will look at these dosages and looked at the 0.8 13:54:41
6 and 1.6 having 45 or 50 percent of people versus 34, 13:54:45
7 this is look different. They behave different. 13:54:50

8 Q It's numerically different? 13:54:55

9 A Because it was not tested statistically, 13:54:57
10 but it was -- but if I am allowed to guess, which I 13:55:00
11 should not guess, I should not guess, but had a 13:55:02
12 statistical been done, there is a chance that it 13:55:07
13 would have shown statistically significance. But 13:55:10
14 the comparator was placebo. 13:55:13

15 MR. BAUGHMAN: Counsel, I don't want to 13:55:16
16 interrupt, if you have a couple more questions, but 13:55:18
17 I would like to take a break when you have a moment, 13:55:20
18 just for a second. 13:55:22

19 MR. ANSTAETT: Yeah, no, we can do that. 13:55:23
20 Sure. 13:55:24

21 (Recess from 1:55 p.m. until 2:02 p.m.) 13:57:21

22 BY MR. ANSTAETT: 14:02:54

1	Q	With respect to criticality, you also	14:02:57
2		discuss tolerability of the 1 milligram dose,	14:02:58
3		correct?	14:03:01
4	MR. BAUGHMAN:	Object to the form.	14:03:02
5	A	Can you point out where?	14:03:07
6	Q	I think it's in paragraphs 254 to 258 of	14:03:09
7		your declaration.	14:03:15
8	A	Yes, sir.	14:03:15
9	Q	Why is the 1.0 milligram dose of	14:03:16
10		semaglutide critical in terms of tolerability?	14:03:22
11	MR. BAUGHMAN:	Object to the form, scope,	14:03:24
12		foundation.	14:03:25
13	A	Why what?	14:03:25
14	Q	Why is the 1.0 milligram dose of	14:03:27
15		semaglutide critical in terms of tolerability?	14:03:31
16	MR. BAUGHMAN:	Same objection.	14:03:33
17	A	Well, when you looked at the differences	14:03:34
18		there, I mean, there is a report of -- depends of	14:03:36
19		how -- when you looked at the dose response, as the	14:03:42
20		dose varied, you may have differences in nausea and	14:03:48
21		vomiting. And so you look always at the ratio	14:03:52
22		between efficacy and tolerability and safety.	14:03:55

1	Q	And what are you looking at when you say,	14:03:59
2		"when you look at"? What are you referring to?	14:04:01
3	A	Well --	14:04:03
4	Q	Are you referring to something in the	14:04:04
5		patent specification or...	14:04:06
6	A	You looked at adverse events.	14:04:06
7	Q	In the patent specification?	14:04:09
8	A	I'm sorry?	14:04:10
9	Q	In the patent specification?	14:04:11
10	A	Well, the patent -- the patent in the	14:04:13
11		claim 1, 2, and 3, it doesn't talk about that. I	14:04:18
12		mean, talks about the 1 milligram. Novo, when they	14:04:23
13		had the data, they probably looked at that.	14:04:26
14	Q	So again, you're relying on data that	14:04:28
15		Novo may have had for your opinion that tolerability	14:04:31
16		of the 1 milligram dose is critical?	14:04:35
17	A	I rely on the fact that the dose that	14:04:38
18		Novo chose was a very careful analysis because they	14:04:41
19		have the data -- I don't -- to look at the	14:04:46
20		percentage of nausea, vomiting and so on so forth.	14:04:50
21	Q	In paragraph 281 of your report, you	14:04:54
22		reference the '462 patent's multiple statements	14:05:12

1 showing that the claimed once-weekly 1 milligram
2 dose operates differently than at other doses within
3 the 0.1 to 1.6 milligram range endpoints as to both
4 efficacy, as to HbA1c reduction and weight loss, and
5 tolerability, which supports criticality of that
6 dose.

7 Do you see that?

8 A Well, I respond to this because
9 Dr. Bantle and Dr. Jusko says that the 1 milligram
10 dose is not critical. And I said that in '462, the
11 claimed once-weekly 1 milligram operates differently
12 than the other dosages within 0.1, 1.6, both
13 efficacy, A1c reduction, and weight loss. And
14 tolerability. That's data that Novo had.

15 Q Okay. Yeah, that's the --

16 A And the data that I have is the A1c
17 and -- can you point that out in the reference for
18 tolerability in the --

19 Q No, Doctor.

20 A -- '462?

21 Q I mean, that's why I'm asking you.
22 Because I don't know what you're referring to. You

1 have this sentence in red, in your expert report 14:06:38
2 in -- I don't know if the copy we gave you is a 14:06:39
3 color copy. But in paragraph 281 that says, '462's 14:06:42
4 multiple statements showing that the claimed 14:06:47
5 once-weekly 1 milligram dose operates differently 14:06:49
6 than at other doses within the 0.1 to 1.6 milligram 14:06:51
7 range endpoints as to both efficacy, as to HbA1c 14:06:55
8 reduction and weight loss, and tolerability, which 14:06:59
9 supports the criticality of that dose. 14:07:01

10 And my question for you is just going to 14:07:03
11 be, what are the multiple statements in the '462 14:07:06
12 patent that you're referring to? 14:07:10

13 A Well, let me read it then. Let me find 14:07:11
14 it then. 14:07:14

15 Q Doctor, I want to be fair and give you as 14:13:09
16 much, you know, time as you need to look. But do 14:13:11
17 you -- have you been able to determine what the 14:13:13
18 multiple statements in the '462 patent are showing 14:13:16
19 that the 1 milligram dose is critical? 14:13:23

20 A I did show that it's critical based on 14:13:27
21 the behavior that behaved differently in terms of 14:13:29
22 A1c reduction, body weight, and target. Obviously, 14:13:33

1 that has the decision of choosing the 1 milligram is 14:13:40
2 based on the tolerability and safety, and that the 14:13:43
3 degree of granularity, Novo has that. And based on 14:13:47
4 that, Novo made that decision. 14:13:50

5 Q So you're relying on data that Novo had 14:13:52
6 or that you presume that Novo had that led them to 14:13:54
7 make the choice to claim a 1 milligram dose. 14:13:57

8 Is that right? 14:14:01

9 A Novo looked at the dose response. Novo 14:14:01
10 had the data. Novo looked at the A1c reduction, the 14:14:03
11 weight. They saw the criticality of 0.8 and above. 14:14:07
12 They decided to base on that data, which is the dose 14:14:11
13 that has the least amount of side effects 14:14:15
14 presumably. 14:14:18

15 So I'm trying to find -- you asked me to 14:14:18
16 find it. I'm trying to find there. But that level 14:14:21
17 of granularity for the decision is based on the 14:14:24
18 amount of the ratio between efficacy, tolerability, 14:14:28
19 and safety. And that's how Novo came up with a 14:14:34
20 1 milligram. 14:14:38

21 You asked me to find the places, and I 14:14:39
22 found it here. Here it is. There were no reports 14:14:43

1	of pancreatitis related to --	14:14:49
2	(Cross-talk.)	14:14:52
3	Q Just for the record, Doctor, can you tell	14:14:52
4	us where you're reading from, the column and line	14:14:54
5	number?	14:14:56
6	A Of course. You can read in column 23.	14:14:56
7	Q And which line? Where are you starting?	14:15:00
8	A Let me see. In column 23.	14:15:04
9	Q And the line numbers are just kind of	14:15:10
10	down the middle of the columns.	14:15:13
11	A Yes. In the top of column 23, it says,	14:15:39
12	There were no reports of pancreatitis or	14:15:43
13	treatment-related changes in blood calcitonin.	14:15:46
14	Proportion of subjects with nausea and vomiting	14:15:49
15	increased with dose but were originally mild or	14:15:53
16	moderate and ameliorated with titration.	14:15:56
17	Withdrawals due to GI adverse events were 4.7 to	14:15:56
18	27.7 for semaglutide and 2.2 to 10 percent for	14:16:04
19	liraglutide. Few subjects reported minor	14:16:04
20	hypoglycemia; semaglutide, 5, liraglutide, 3; no	14:16:07
21	major hypoglycemia. Injection site reactions were	14:16:07
22	reported by 7 subjects: Semaglutide, 2; liraglutide,	14:16:07

1 5. One subject with semaglutide 1.6 developed low
2 titer non-neutralizing.

3 So based on that -- and those are what is
4 in the report, but obviously, they have all the
5 data. And based on that and the difference of
6 behavior of Alc and weight, and of course, here,
7 that's what they report. And they looked at the
8 different dosages, and that's how they decided to
9 get to 1 milligram.

10 Q And just to be clear, everything you said
11 in column 23 there, that was based on the testing of
12 doses other than 1.0 milligrams, correct?

13 A You look at the whole spectrum, Counsel.
14 You look at the whole spectrum. They're not
15 specifying which specific dose. They had the data.
16 I don't have the data. But they knew what the
17 incidents and the frequency and the rates were for
18 0.4, 0.8, titrated or non-titrated, 1.6.

19 So based on that is the combination of
20 all is how they came up with tolerability.

21 Q Okay.

22 A And thank you for giving me the time to

1	read it.	14:17:29
2	Q Sure. No. And anytime today if you need	14:17:29
3	time to read something, you may certainly do that.	14:17:32
4	So let's look at another exhibit.	14:17:36
5	(Previously marked Exhibit 1012 presented	14:17:36
6	to the witness.)	14:17:58
7	BY MR. ANSTAETT:	14:17:58
8	Q This has been marked as Exhibit 1012.	14:17:59
9	Exhibit 1012 is the Lovshin publication.	14:19:07
10	Do you recognize that?	14:19:19
11	A Yes, sir.	14:19:19
12	Q And in paragraph 288 of your expert	14:19:20
13	report, you discuss Lovshin, and you contend that,	14:19:28
14	Dr. Bantle failed to identify in Lovshin disclosures	14:19:40
15	of administration of semaglutide to a subject in	14:19:43
16	need thereof.	14:19:46
17	Do you see that?	14:19:46
18	A Yes, sir.	14:19:47
19	Q All right. Now, in the '462 patent	14:19:48
20	claims, a subject in need of treatment with	14:19:50
21	semaglutide is someone with type 2 diabetes,	14:19:53
22	correct?	14:19:56

1	A	Yes, sir.	14:19:56
2	Q	And Lovshin is titled, Incretin-based	14:19:56
3		therapies for type 2 diabetes mellitus.	14:20:02
4		Is that right?	14:20:05
5	A	Yes, sir.	14:20:05
6	Q	All right. And the first sentence of the	14:20:06
7		Lovshin abstract identifies GLP-1 receptor agonists	14:20:08
8		as incretin-based drugs, correct?	14:20:12
9	A	Yes.	14:20:17
10	Q	And the abstract also says that GLP-1	14:20:18
11		receptor agonists are now routinely used to treat	14:20:21
12		type 2 diabetes mellitus, correct?	14:20:24
13	A	Yeah, including GLP-1 receptor agonists	14:20:27
14		at that time exenatide and DPP-4.	14:20:30
15	Q	Okay. And then Table 1 in Lovshin, which	14:20:34
16		is on page 2, that identifies NN9535, which is	14:20:37
17		semaglutide, as a GLP-1 receptor agonist	14:20:44
18		administered to patients by subcutaneous injection,	14:20:47
19		correct?	14:20:50
20	A	I'm sorry. Say it again?	14:20:52
21	Q	Sure. Table 1 in Lovshin on page 2, it	14:20:53
22		identifies NN9535, which is semaglutide, as a GLP-1	14:20:59

1	receptor agonist that's administered to patients by	14:21:05
2	subcutaneous injection, correct?	14:21:07
3	A It doesn't say subcutaneous. It only	14:21:08
4	says 0.1, 1.6, once-weekly, and investigation. I	14:21:12
5	don't see -- where do you see "subcutaneous,"	14:21:15
6	Counsel?	14:21:18
7	Q Just at the very top. It says GLP-1 --	14:21:18
8	A Oh, I see.	14:21:20
9	(Cross-talk.)	14:21:22
10	A I see.	14:21:22
11	Q -- subcutaneous injection.	14:21:22
12	And then Table 1 also says that	14:21:23
13	semaglutide is being investigated, correct?	14:21:26
14	A It says "I," that 9535 was I,	14:21:29
15	investigated.	14:21:34
16	Q Okay. And Lovshin -- and then at the top	14:21:35
17	of column 5 -- I'm sorry. On the top of the second	14:21:38
18	column on page 5 of the article, it says there that	14:21:43
19	semaglutide is under active clinical investigation	14:21:54
20	in phase 1 and phase 2 studies, correct?	14:21:56
21	A It says, Similarly, multiple once-weekly	14:21:59
22	GLP-1 therapies are under active clinical	14:22:05

1 investigation, phase 1, 2 studies, NN9535, and then 14:22:08
2 the LY, but few data are available on the structure 14:22:15
3 or efficacy of these molecules. 14:22:20

4 That's his statement. 14:22:22

5 Q Right. And based on those disclosures, 14:22:23
6 the skilled artisan reading Lovshin would understand 14:22:25
7 that semaglutide was being investigated as a 14:22:30
8 potential treatment to be administered to patients 14:22:32
9 with type 2 diabetes, correct? 14:22:34

10 A What it says there, that NN9535 is being 14:22:35
11 investigated in phase 1 and phase 2 studies. At 14:22:42
12 that point, not necessarily in type 2 diabetes. 14:22:46

13 Q What do you think the phase 1 and -- 14:22:49
14 based on Lovshin, what do you think a skilled 14:22:51
15 artisan would think semaglutide was being studied 14:22:54
16 for in phase 1 and phase 2 clinical trials? 14:22:57

17 A In healthy individuals, to see whether -- 14:23:00
18 I mean, phase 1 could be just a study to looking at 14:23:02
19 multiple ascending dose, isolated ascending dose in 14:23:09
20 healthy individuals. It could be looking at PK, PD, 14:23:15
21 pharmacokinetics -- 14:23:17

22 Q In phase 1, right? 14:23:17

1 A In phase 1. Even in phase 2, you can 14:23:18
2 have in -- if there are some specific scientific 14:23:21
3 questions in terms of mechanism of action, you can 14:23:23
4 still test it in healthy individuals. 14:23:25

5 Q So your opinion as a person of skill in 14:23:27
6 the art reading this article -- or your opinion is 14:23:30
7 that a person of skill in the art reading this 14:23:32
8 article, at the priority, date would not understand 14:23:34
9 that semaglutide was being investigated by Novo 14:23:38
10 Nordisk as a treatment for patients with type 2 14:23:42
11 diabetes? 14:23:44

12 MR. BAUGHMAN: Object to the form. 14:23:44

13 A What the article says is that NN9535 is 14:23:46
14 being investigated in phase 1 and phase 2 studies. 14:23:56
15 I mean, in phase 1 and phase 2 studies, at that 14:24:00
16 time, was given to healthy individuals. I cannot 14:24:03
17 assert that they were given to type 2 diabetes. 14:24:07

18 Whether or not that has the potential to 14:24:11
19 be type 2 diabetes, that's one thing. But to say 14:24:15
20 that it was given to people with type 2 diabetes, I 14:24:17
21 have no basis to make that assumption. 14:24:20

22 Q But your understanding is that it was 14:24:24

1	being investigated as a potential treatment for	14:24:26
2	type 2 diabetes based on this article, I take it?	14:24:29
3	A It had the potential, but I cannot say	14:24:31
4	that was given to people with type 2 diabetes.	14:24:33
5	Q Okay. But that's what this article, the	14:24:35
6	Lovshin article is all about, right, is treating	14:24:40
7	patients with type 2 diabetes?	14:24:42
8	A Well, the article --	14:24:44
9	MR. BAUGHMAN: Just a second.	14:24:45
10	Object to the form.	14:24:46
11	You can answer.	14:24:47
12	A The article also says, This review	14:24:47
13	highlights our current understanding, understanding	14:24:50
14	of the mechanism of action of incretin-based	14:24:54
15	therapies, with emphasis on the emerging clinical	14:24:58
16	profile of new agents.	14:25:01
17	So it also emphasizes understanding. And	14:25:02
18	that means mechanism of action. I don't know if at	14:25:05
19	that time 9935 was with the purpose of type 2	14:25:08
20	diabetes. It could have other purposes. But also,	14:25:12
21	emerging clinical profile, the clinical profile	14:25:17
22	could be very positive; it could be very negative.	14:25:19

1	Q	Now, you said with respect to WO421 that	14:25:21
2		a skilled artisan would look to the NCT657 clinical	14:25:26
3		trial protocol to understand the disclosures in	14:25:32
4		WO421.	14:25:36
5		Do you recall that, writing that in your	14:25:37
6		declaration?	14:25:39
7	A	Where?	14:25:39
8	Q	Look at paragraph 210.	14:26:12
9	A	Yes, sir.	14:26:29
10	Q	In 210 you write, In my opinion, a	14:26:29
11		skilled artisan would have looked to Novo Nordisk's	14:26:32
12		then-ongoing NCT657 clinical trial, which was	14:26:35
13		testing certain doses of semaglutide once-weekly for	14:26:37
14		the treatment of type 2 diabetes, to understand	14:26:40
15		WO421's range.	14:26:44
16		Do you see that?	14:26:45
17	A	Yes.	14:26:45
18	Q	Would a person reading Lovshin have	14:26:46
19		looked to Novo Nordisk's then-ongoing NCT657	14:26:49
20		clinical trial to understand whether or not	14:26:54
21		semaglutide was being used to treat patients with	14:26:59
22		type 2 diabetes?	14:27:03

1	A	That was in 2009. That's a possibility,	14:27:05
2		but I cannot assert. I cannot -- I'm not certain	14:27:07
3		that that was the case with Lovshin.	14:27:10
4	Q	Well, why did you -- why would a person	14:27:12
5		trying to understand WO421 look to NCT657, but with	14:27:15
6		Lovshin, are you saying they wouldn't do that?	14:27:21
7	A	It could do it, yeah, the same thing.	14:27:23
8	Q	They could do the same thing?	14:27:26
9	A	Yeah.	14:27:27
10	Q	And if they did that, they would see that	14:27:28
11		semaglutide was being administered to patients in	14:27:30
12		need of treatment for type 2 diabetes, correct?	14:27:34
13	A	Lovshin does not say that.	14:27:37
14	Q	But WO -- excuse me.	14:27:39
15		But NCT657 does, right?	14:27:41
16	A	But Lovshin does not say that. Lovshin	14:27:44
17		only refers to phase 1 and phase 2. And I cannot be	14:27:47
18		certain that those phase 1 and phase 2 refers to	14:27:51
19		that study.	14:27:54
20	Q	But if you looked to NCT657 or the person	14:27:54
21		of skill in the art did, you would know that, right?	14:27:59
22	A	I don't know if he did that or they did	14:28:00

1	that.	14:28:03
2	Q Well, it's a hypothetical. You don't	14:28:03
3	know if the person -- a hypothetical person of	14:28:06
4	ordinary skill in the art looked to NCT657 to	14:28:08
5	understand W0421 either, right?	14:28:13
6	A No, I understand that they could do that.	14:28:15
7	Lovshin could have done that.	14:28:17
8	Q Okay. So a --	14:28:18
9	A But --	14:28:18
10	Q -- person reading Lovshin could have seen	14:28:19
11	the reference to phase 2 clinical trials of	14:28:21
12	semaglutide and if they wanted to understand what	14:28:23
13	those phase 2 trials encompassed, they could have	14:28:25
14	looked to understand that to NCT657.	14:28:28
15	Is that fair?	14:28:32
16	A That's fair. The only point is they did	14:28:32
17	phase 1 or phase 2, not necessarily that one.	14:28:35
18	Q Okay. But NCT657 is phase 2, right?	14:28:37
19	A Yeah.	14:28:41
20	Q All right. Take a look at paragraph 302.	14:28:43
21	This is in the section of your report where you're	14:29:11
22	talking about the grounds related to obviousness.	14:29:16

1 And you state in paragraph 302 that, In 14:29:20
2 my opinion, the mere existence of both ongoing 14:29:26
3 phase 1 trials, in healthy volunteers, and ongoing 14:29:28
4 phase 2 trials, with efficacy still under 14:29:31
5 investigation, does not show the claimed once-weekly 14:29:35
6 1.0 milligram semaglutide dose for treating type 2 14:29:39
7 diabetes was safe, effective, and tolerable. 14:29:43
8 Instead, the existence of trials designed to explore 14:29:47
9 safety, tolerability, and efficacy confirms, to the 14:29:50
10 contrary, that those had not yet been established? 14:29:50
11 Do you see that? 14:29:54
12 A Yes, sir. 14:29:54
13 Q All right. For a claimed dosing regimen 14:29:55
14 to be obvious, does the prior art need to establish 14:29:59
15 that that regimen has been proven to be safe and 14:30:02
16 tolerable, in your opinion? 14:30:06
17 MR. BAUGHMAN: Object to the form and 14:30:07
18 foundation. 14:30:08
19 A There was absolutely no data -- there's 14:30:08
20 no data to base anything. So I mean, proven or not, 14:30:10
21 there was no data to look into that. There's -- no 14:30:13
22 data was available on semaglutide. 14:30:19

1 Q My question was just a little bit 14:30:21
2 different. For a claimed dosing regimen to be 14:30:23
3 obvious, is it your view that the prior art has to 14:30:27
4 establish that the regimen has been proven to be 14:30:31
5 safe, effective, and tolerable? 14:30:33

6 A Well, to be -- what do you mean by "to 14:30:35
7 establish to be obvious"? 14:30:39

8 Q Well, you say -- what I'm trying to 14:30:40
9 understand is, you say that safety, efficacy, and 14:30:47
10 tolerability had not yet been established. That's 14:30:49
11 your word, right? And so what I'm trying to 14:30:54
12 understand is, for -- just trying to understand what 14:30:56
13 you believe with respect to whether or not for a 14:31:03
14 dosing regimen to be obvious. 14:31:05

15 Because you're offering the opinion that 14:31:07
16 the dosing regimen was not obvious, right? That the 14:31:09
17 claimed dosing regimen of 1.0 milligram once-weekly 14:31:11
18 semaglutide in the '462 patent was nonobviousness? 14:31:16

19 MR. BAUGHMAN: Object to the form. 14:31:18

20 A There was no obviousness to pursue the 14:31:18
21 1 milligram there. I don't see -- without knowing 14:31:21
22 any data, I don't see any motivation to look for the 14:31:24

1 1.0 milligram. 14:31:27

2 Q And my question is, in this paragraph 14:31:28

3 302, you say that the safety and efficacy and 14:31:33

4 tolerability -- well, let me just read it again. In 14:31:41

5 your opinion, the existence of the ongoing phase 1 14:31:46

6 and phase 2 trials doesn't show that the claimed 14:31:48

7 once-weekly 1 milligram semaglutide dose for 14:31:52

8 treating type 2 diabetes was safe, effective, and 14:31:56

9 tolerable. Instead, the existence of the trials 14:31:59

10 designed to explore safety, tolerability, and 14:32:01

11 efficacy confirms that these have not yet been 14:32:04

12 established. 14:32:07

13 And my question to you is simply, do you 14:32:07

14 believe that, for that dosing regimen to be obvious, 14:32:11

15 the prior art would have to establish that it is 14:32:14

16 actually safe, effective, and well tolerated? 14:32:16

17 A What I believe, Counsel, is at that 14:32:19

18 point, when you have 0.1, 0.2, 0.4, 0.8, and 1.6, 14:32:22

19 without knowing the data, I don't see any motivation 14:32:29

20 to look for the 1.0. So it's not obvious to me that 14:32:33

21 I will have any motivation to go to the 1.0. 14:32:37

22 Q How are you -- in that paragraph 302, how 14:32:41

1 are you defining "effective"?

14:32:49

2 A I mean, effectiveness, as we already
3 discussed, in regards to the parameters that we
4 mentioned, was A1c, was weight, it was also targets
5 and so on, and so on. But there was no data
6 available for me to have the motivation to look for
7 a 1.0 without knowing if the 0.8 is going to work or
8 the 1.6 is going to work or anything like that. I
9 don't see any obviousness there.

14:32:55

14:32:57

14:33:00

14:33:06

14:33:09

14:33:14

14:33:17

14:33:20

10 Q In paragraph 354 of your declaration, you
11 criticize Dr. Bantle and Dr. Jusko for their failure
12 to show that there were any data suggesting that
13 semaglutide at any dose, let alone 1 milligram,
14 would be more effective or more tolerable than other
15 GLP-1 analogs.

14:33:30

14:33:42

14:33:45

14:33:48

14:33:51

14:33:56

16 Do you see that?

14:33:57

17 A 354?

14:33:57

18 Q Yes.

14:34:00

19 A Let me read it.

14:34:00

20 Q Sure.

14:34:01

21 A Yeah. They didn't have any data
22 available. Based on what they presented, they don't

14:34:07

14:34:09

1	have any data. There was no data available.	14:34:13
2	Q What you wrote was that they failed to	14:34:16
3	show that there were any data suggesting that	14:34:20
4	semaglutide had at any dose, let alone 1 milligram,	14:34:22
5	would be more effective or more tolerable than other	14:34:26
6	GLP-1 analogs, right?	14:34:29
7	MR. BAUGHMAN: Object to the form.	14:34:30
8	A They did not have the data.	14:34:31
9	Q Yes, Doctor. Are you disputing that you	14:34:33
10	wrote, would be more effective or more tolerable	14:34:36
11	than other GLP-1 analogs?	14:34:38
12	A No. I'm referring that they -- when I	14:34:40
13	looked at that, I analyzed their declaration, I took	14:34:44
14	what I did, because I have the data. Dr. Bantle	14:34:50
15	also do not show that there were any data suggesting	14:34:52
16	that any dose were effective.	14:34:55
17	They did not have --	14:34:56
18	(Cross-talk.)	14:34:58
19	Q You stop reading the sentence right at	14:34:58
20	the words I'm asking about.	14:35:01
21	A Or more tolerable than other GLP-1	14:35:02
22	analog.	14:35:04

1	Q	Okay. You understand that the claims	14:35:04
2		don't require the dosing regimen to be more	14:35:05
3		effective or more tolerable than any other GLP-1	14:35:10
4		analog, right?	14:35:14
5	A	That I understand, but what I'm referring	14:35:15
6		to is they did not have any data. There was no data	14:35:17
7		in the public domain at all to make any suggestion,	14:35:20
8		and we didn't have any data for any of those	14:35:24
9		specific data, let alone a 1.0 milligram.	14:35:27
10	Q	I'm going to refer you back to Exhibit	14:35:34
11		1001.	14:35:40
12	A	1001 is?	14:35:40
13	Q	That's the patent. That's the --	14:35:42
14	A	Okay.	14:35:42
15	Q	-- '462 patent.	14:35:43
16		And starting at column 20, line 56.	14:35:52
17	A	Column 20...	14:36:08
18	Q	You see line 56, there's a heading there	14:36:09
19		that says Examples?	14:36:12
20	A	Yes, sir.	14:36:15
21	Q	And then if you just -- you don't have to	14:36:15
22		read all this, but I think this will be	14:36:16

1	uncontroversial. But if you then go to column 23,	14:36:19
2	where it says, Conclusion.	14:36:25
3	A Yes.	14:36:26
4	Q And then there's a paragraph that ends	14:36:26
5	around line 26. That's where the patent	14:36:28
6	specification is describing the results of a	14:36:36
7	clinical trial, correct?	14:36:38
8	MR. BAUGHMAN: Object to the form and	14:36:39
9	foundation.	14:36:40
10	A I'm sorry. Say it again, Counsel?	14:36:40
11	Q That section of the patent specification	14:36:43
12	is describing the results of a clinical trial.	14:36:45
13	A In the conclusion?	14:36:47
14	Q Just the whole, that -- from, you know,	14:36:48
15	the bottom of column 20 to the top of column 23,	14:36:50
16	essentially, that's describing --	14:36:53
17	A Oh, from 20 to 23?	14:36:55
18	Q Yes.	14:36:57
19	A You mean from Examples?	14:37:00
20	Q Yes. Starting at Examples, going to	14:37:02
21	column 23, line 26, that is the description of the	14:37:06
22	results of a clinical trial.	14:37:10

1	A	You mean 20, 21, 22, 23, 24, 26. Okay.	14:37:12
2	Q	Yeah. To column 23, line 26.	14:37:16
3	A	Yeah.	14:37:20
4	Q	That section of the patent specification	14:37:21
5		describes the results of a clinical trial, right?	14:37:24
6		The design and the results of a clinical trial?	14:37:26
7		MR. BAUGHMAN: Object to the form.	14:37:28
8	Q	Do you agree with that?	14:37:29
9	A	That design -- it is design -- has the	14:37:31
10		examples. You mean includes the conclusion -- so	14:37:36
11		what do I need to agree that you asked me?	14:37:42
12	Q	Is it your understanding that what	14:37:45
13		appears at that part of the patent specification are	14:37:46
14		the design and results of Novo Nordisk's phase 2	14:37:49
15		clinical trial of semaglutide that's described in	14:37:53
16		NCT657?	14:37:56
17	A	Well, I believe so.	14:37:57
18	Q	Okay. Yeah. That's all I was trying to	14:37:58
19		establish.	14:38:00
20		My question for you is, if that -- what	14:38:01
21		appears in those parts of the specification were in	14:38:06
22		the prior art, okay, would the results that are	14:38:10

1 described there in the patent specification be 14:38:14
2 sufficient to give a skilled artisan a reasonable 14:38:17
3 expectation that a dosing regimen of 1 milligram 14:38:20
4 once-weekly of semaglutide could successfully be 14:38:25
5 used to treat type 2 diabetes? 14:38:27

6 MR. BAUGHMAN: Object to the form, 14:38:29
7 foundation and scope. 14:38:30

8 A Without the data, I don't think a person 14:38:32
9 of skill in the art could have guessed that it's 14:38:38
10 going to be 1.0. I mean, if you allow me to read 14:38:40
11 it, which you probably won't. 14:38:43

12 Q No, I will allow you to read it. 14:38:45

13 A But it is a lot of formulation and so on 14:38:48
14 and so forth. But the bottom line, a person of 14:38:51
15 skill in the preceding this had no data whatsoever 14:38:57
16 to come with a 1.0. 14:38:59

17 Q Okay. Well, I just want -- I want to be 14:39:01
18 clear. In that portion of the specification we've 14:39:03
19 been talking about, there is data about certain 14:39:04
20 doses of semaglutide, right, the ones you've 14:39:08
21 mentioned? The 0.1, 0.2, 0.4, 0.8, 1.6? 14:39:11

22 A No. That was only described in the 14:39:15

1	clinical trial, that cutoff, where the study was	14:39:18
2	reported to the government of the study design.	14:39:20
3	There's no data, there's no results.	14:39:24
4	Q In the patent specification?	14:39:27
5	A No. In the patent specification, yeah,	14:39:29
6	we reviewed the data.	14:39:31
7	Q That's what I'm talking about. I'm	14:39:32
8	talking about in the patent specification, from the	14:39:34
9	bottom of column 20 to the top of column 23, okay,	14:39:36
10	that's what I'm going to question you about now.	14:39:39
11	That's what I want to focus my questioning on.	14:39:41
12	A All right.	14:39:43
13	Q So if you were to assume that the	14:39:44
14	information that appears in that part of the patent	14:39:47
15	specification was prior art -- I understand that	14:39:51
16	it's not, but if you were to assume that it was,	14:39:52
17	okay, would that be sufficient to give a skilled	14:39:55
18	artisan a reasonable expectation that a dosing	14:40:02
19	regimen of 1 milligram once-weekly semaglutide could	14:40:04
20	be successfully used to treat type 2 diabetes?	14:40:08
21	MR. BAUGHMAN: Object to the form,	14:40:11
22	foundation and scope.	14:40:12

1 A You know, Counsel, you are making a very 14:40:13
2 hypothetical thing in the sense that -- my 14:40:20
3 understanding is that the data was not present. 14:40:22
4 Whether or not there is prior art in terms of how 14:40:25
5 you make the formulation, how you do different 14:40:30
6 things, which was not the subject of my test to 14:40:33
7 analyze claims 4 and above. So that prior art might 14:40:35
8 have nothing to do with the actual numbers on this 14:40:40
9 study. 14:40:43

10 Is that what you're referring to. 14:40:44

11 Q I'm not referring to that; I'm really 14:40:45
12 not. This section of the patent specification 14:40:48
13 describes the results of the NCT657 clinical trial, 14:40:49
14 right? 14:40:53

15 A Yeah. 14:40:53

16 Q And I know your criticism of Dr. Bantle 14:40:54
17 and Dr. Jusko, a lot of it is, there was no data -- 14:40:57

18 A Correct. 14:41:01

19 Q -- on semaglutide in the prior art, 14:41:01
20 right? And -- but there is data on semaglutide in 14:41:03
21 the patent specification in these columns. We have 14:41:08
22 the results from the NCT657 clinical trial, right? 14:41:10

1 Do you understand that?

14:41:15

2 A I understand that, but that's a July 1st,
3 2012.

14:41:16

14:41:19

4 Q Understand. It's not prior art. It's
5 not prior art. But I'm asking you a hypothetical.
6 You were right. Let's assume that that data was in
7 the prior art, okay? It's a hypothetical. I'm not
8 saying that it was, right?

14:41:19

14:41:22

14:41:24

14:41:28

14:41:30

9 But if you assume that it was, in your
10 opinion, would that data be sufficient to give a
11 skilled artisan a reasonable expectation that a
12 dosing regimen of 1 milligram once-weekly of
13 semaglutide could be successfully used to treat
14 type 2 diabetes?

14:41:32

14:41:36

14:41:39

14:41:41

14:41:45

14:41:47

15 A Well --

14:41:48

16 MR. BAUGHMAN: Object to the form,
17 foundation and scope.

14:41:48

14:41:49

18 A -- I cannot assume, Counsel. I'm
19 referring to my declaration. I did not look at that
20 this way. I cannot assume on that. And certainly,
21 it is a very hypothetical thing. I'm just basing it
22 on the actual data that was presented July 2012,

14:41:50

14:41:54

14:41:57

14:42:01

14:42:04

1	which was not in the prior art.	14:42:07
2	Q Okay.	14:42:09
3	MR. ANSTAETT: We're getting close to the	14:42:17
4	end. I'm guessing probably about a half an hour,	14:42:18
5	you know, depending how long the answers are. Do	14:42:21
6	you want to take a break before we eat lunch --	14:42:23
7	THE WITNESS: No, I'm good.	14:42:23
8	MR. ANSTAETT: -- or do you want to keep	14:42:25
9	going?	14:42:26
10	THE WITNESS: I'm good.	14:42:27
11	MR. ANSTAETT: Okay. All right.	14:42:40
12	MR. BAUGHMAN: Can you pause for a second	14:42:40
13	while I grab a cup of coffee?	14:42:40
14	MR. ANSTAETT: Yes. I actually need to	14:42:40
15	try to find something, too, so that's fine.	14:42:40
16	We can actually go off the record for a	14:42:40
17	second.	14:42:43
18	(Recess from 2:42 p.m. until 2:45 p.m.)	14:45:53
19	(Previously marked Exhibit 2075 presented	14:45:53
20	to the witness.)	14:45:54
21	BY MR. ANSTAETT:	14:45:54
22	Q So let me give you another reference.	14:45:54

1	This has been marked as Exhibit 2075.	14:46:06
2	A Thank you.	14:46:09
3	Q So this is an article that you discuss in	14:46:30
4	paragraph 322 and elsewhere in your declaration.	14:46:33
5	This is a 2004 publication by Madsbad and	14:46:57
6	colleagues. And you say in paragraph 322 that,	14:47:03
7	Madsbad 2004 reported a liraglutide dosing study in	14:47:14
8	which no weight loss was observed with the tested	14:47:21
9	doses of liraglutide.	14:47:24
10	Do you see that?	14:47:26
11	A In page 322?	14:47:26
12	Q Paragraph 322 of your declaration,	14:47:29
13	correct.	14:47:31
14	A Yes, sir.	14:47:35
15	Q Okay. Now, look at page 4 of	14:47:35
16	Exhibit 2075, okay? And do you see there in the	14:47:41
17	first column there's a heading that says Effect on	14:47:50
18	body weight?	14:47:55
19	A Yep.	14:47:56
20	Q And that says, Treatment with liraglutide	14:47:56
21	did not increase body weight, Figure 2.	14:47:58
22	Furthermore, the 0.45 milligram liraglutide dosage	14:48:02

1	group, table 2 -- excuse me. Let me start that	14:48:06
2	over.	14:48:09
3	Furthermore, for the 0.45 milligram	14:48:09
4	liraglutide dosage group, Table 2, a statistically	14:48:13
5	significant decrease compared with placebo was	14:48:16
6	observed.	14:48:19
7	Do you see that?	14:48:19
8	A Yes, sir.	14:48:20
9	Q So weight loss was observed with the 0.45	14:48:20
10	milligram liraglutide dose, correct?	14:48:24
11	A Not necessarily. One dose was positive.	14:48:26
12	The maximum doses that were tested, the 0.6 and	14:48:30
13	0.75, were not. So there is inconsistency in the	14:48:35
14	dose response.	14:48:38
15	Q Right.	14:48:39
16	A But there is only one dose that was	14:48:40
17	effective. The other dosages was not. I mean, it	14:48:43
18	says that -- it said that the 0.4 milligram dosage.	14:48:46
19	But the other dosages were not.	14:48:50
20	Q I understand that, Doctor, and I'll get	14:48:51
21	to that. But you wrote in paragraph 322 -- and I	14:48:53
22	think you're just wrong -- that Madsbad 2004	14:48:56

1 reported a liraglutide dose-finding study in which 14:48:59
2 no weight loss was observed with the tested doses of 14:49:03
3 liraglutide. 14:49:06

4 It was observed with one of the tested 14:49:07
5 doses, was it not? 14:49:09

6 A With all due respect, Counsel, this is 14:49:10
7 basically, if you look at -- you asked me before to 14:49:13
8 look at title. It says -- where it says improved -- 14:49:17
9 it says, Improved Glycemic Control With No Weight 14:49:23
10 Increase in Patients with Type 2 Diabetes After 14:49:28
11 Once-Daily Treatment. It doesn't say that there was 14:49:31
12 weight loss. 14:49:33

13 What it is important, the dose response, 14:49:35
14 it is clear that one dose was -- showed a very 14:49:37
15 modest weight loss. But most importantly, the 14:49:43
16 subsequent two higher dosages of 0.6 and 0.7 did not 14:49:47
17 show weight loss. 14:49:54

18 So any skilled person in the art will see 14:49:55
19 that as a spurious effect that is not sustained. I 14:49:58
20 mean, you show the statistical significance, but you 14:50:02
21 cannot conclude that the drug caused weight loss. 14:50:05

22 Now, if you want to hang up on the one 14:50:10

1 dose and not the subsequent doses, it's your 14:50:12
2 interpretation. But any person skilled in the art 14:50:16
3 will see that the dose of 0.6 and 0.75 were the same 14:50:19
4 and did not show weight loss, only the dose of 0.45, 14:50:23
5 which is a little bit inconsistent with what we 14:50:26
6 understand of GLP-1s. 14:50:29

7 Q Well, I think what you just said was, 14:50:31
8 only the dose of 0.45. What did you mean by that? 14:50:37
9 Only that dose showed weight loss, right? 14:50:42

10 A Yeah. 14:50:44

11 Q Okay. 14:50:44

12 A And this is -- that is enough to regard 14:50:45
13 this as a negative study. That -- as we were 14:50:48
14 discussing before, a phase 2 study, that it looks at 14:50:51
15 dose response -- I mean, the purpose of bringing 14:50:54
16 this is one of the contentions from -- when I 14:50:58
17 reviewed the -- if I may -- 14:51:01

18 Q Doctor, I -- 14:51:04

19 A If I may. 14:51:04

20 Q No, you may not. I'm sorry. But I've 14:51:05
21 given you an absolute ton of leeway. This is 14:51:08
22 cross-examination. And if there were a judge 14:51:11

1 sitting here, they would strike your answer, okay? 14:51:13

2 Because you're not answering my question. 14:51:16

3 Mr. Baughman will have the opportunity, 14:51:18

4 if he wants to elicit testimony from you about this, 14:51:20

5 he'll ask you an open-ended question and you can go 14:51:23

6 on all day about it, okay? But you have an 14:51:26

7 obligation to answer my questions now, okay? 14:51:28

8 And I don't say this to be rude. I have 14:51:31

9 a tremendous amount of respect for you. But you 14:51:33

10 really, in fairness, have to answer my questions. 14:51:36

11 A I will be happy to answer it. 14:51:38

12 Q Okay. So you agree, at least, that 14:51:40

13 the -- or you don't disagree that the authors of 14:51:44

14 Madsbad 2004 reported that, for the 0.45 milligram 14:51:49

15 liraglutide dosage group, a statistically 14:51:54

16 significant decrease in weight, compared with 14:51:58

17 placebo, was observed. They say that at page 4, 14:52:00

18 right? 14:52:02

19 A In my interpretation on this study, when 14:52:04

20 you looked at the dosages, I mean, and you look at 14:52:07

21 the dose response, the interpretation in general of 14:52:12

22 the study is that there was no weight loss. There 14:52:15

1 was an isolated weight loss in one of the dosages. 14:52:17

2 If this is what you want to say. 14:52:20

3 Q Okay. 14:52:20

4 A But in general -- 14:52:22

5 Q And you state in that paragraph that, In 14:52:23

6 fact, only the intermediate dose of liraglutide in 14:52:29

7 the study reported by Madsbad 2004 showed any weight 14:52:31

8 loss, and you say, This also contradicts Dr. Jusko's 14:52:35

9 opinion that the skilled artisan would have expected 14:52:39

10 the highest dose used in this type of study to have 14:52:41

11 provided the maximum effect. 14:52:44

12 Correct? 14:52:45

13 A Thank you very much. That's exactly what 14:52:46

14 I wanted to say before. 14:52:48

15 Q All right. Now, weight loss was not the 14:52:49

16 primary endpoint in the study reported in Madsbad 14:52:51

17 2004, correct? 14:52:56

18 A It was Alc. 14:53:13

19 Q Reduction in Alc was the primary endpoint 14:53:15

20 of the study, correct? 14:53:18

21 A And it was used, glimepiride, as a 14:53:22

22 comparator, and it was not superior to glimepiride. 14:53:29

1	So again, even in terms of the Alc, this study is	14:53:33
2	considered a failure.	14:53:35
3	Q Okay. We'll come on to your opinion that	14:53:36
4	the study was considered a failure.	14:53:38
5	But the primary endpoint, you agree, was	14:53:39
6	HbA1c after 12 weeks, right?	14:53:44
7	A Yes.	14:53:46
8	Q Okay. And weight loss was one of eight	14:53:46
9	secondary endpoints in the trial, correct?	14:53:50
10	A I didn't count them, but I assume so.	14:53:56
11	Q Okay. And the Madsbad 2004 article	14:53:59
12	reports at page 3 that, After 12 weeks of treatment,	14:54:05
13	HbA1c was decreased in all groups except the lowest	14:54:10
14	liraglutide dosage group. Treatment with the two	14:54:14
15	highest dosages reduced HbA1c significantly more	14:54:17
16	than placebo.	14:54:21
17	Correct?	14:54:21
18	A Where are you reading this?	14:54:22
19	Q So that's on page 3 and it's -- do you	14:54:23
20	see there's a heading there that says, Effect on	14:54:29
21	glycemic control?	14:54:32
22	A Yep.	14:54:39

1	Q	All right. And what the authors report	14:54:40
2		is that after 12 weeks of treatment, HbA1c was	14:54:42
3		decreased in all groups except the lowest	14:54:45
4		liraglutide dosage group. Treatment with the two	14:54:48
5		highest dosages reduced HbA1c significantly more	14:54:50
6		than placebo, correct?	14:54:55
7	A	Yep.	14:54:56
8	Q	All right. And there were five doses of	14:54:56
9		liraglutide tested in the trial that's reported in	14:54:58
10		Madsbad 2004, correct?	14:55:00
11	A	Yes, sir.	14:55:04
12	Q	And all of them decreased HbA1c except	14:55:05
13		for the lowest dose tested.	14:55:08
14		Is that right?	14:55:10
15	A	Very modest, very small A1c reductions.	14:55:11
16	Q	And the two highest doses tested resulted	14:55:13
17		in the greatest reductions in HbA1c, correct?	14:55:17
18	A	Similar to glimepiride.	14:55:20
19	Q	And you say in paragraph 146 of your	14:55:22
20		expert report that, In your opinion, the fact that	14:55:25
21		Madsbad 2004 did not show weight loss would have	14:55:30
22		been considered a failure, correct?	14:55:33

1	A	Correct.	14:55:35
2	Q	And the authors of Madsbad 2004 don't	14:55:36
3		characterize the study as a failure, correct?	14:55:39
4	A	In 2004?	14:55:41
5	Q	Well, in the article. The authors of the	14:55:43
6		Madsbad 2004 article don't characterize this study	14:55:46
7		as a failure, right?	14:55:49
8	A	The landscape in 2004, probably not. But	14:55:50
9		that was a failure; when it compared to glimepiride,	14:55:54
10		they having the same effect as glimepiride.	14:55:59
11	Q	Well, they compared it to -- pronounce it	14:56:01
12		for me again.	14:56:01
13	A	"Glimepiride."	14:56:06
14	Q	-- glimepiride, they don't characterize	14:56:06
15		this study as a failure, right?	14:56:08
16	A	They did not. But this study for a	14:56:11
17		person of skill in the art, when you get a new drug,	14:56:14
18		that for an injectable new drug, a GLP-1, that is	14:56:18
19		compared to a drug that is given once a day, an	14:56:23
20		oral, very expensive, they have the same A1c with no	14:56:26
21		changes in weight, any person of skill in the art	14:56:30
22		will characterize this as a failure.	14:56:33

1	Q	Well, the authors are persons of skill in	14:56:35
2		the art, right?	14:56:37
3	A	Yeah.	14:56:38
4	Q	And the authors state, at page 6, In	14:56:39
5		conclusion, the long-acting GLP-1 analog liraglutide	14:56:44
6		shows considerable promise as a once-daily therapy	14:56:48
7		in type 2 diabetes for lowering blood glucose	14:56:51
8		without weight gain or substantial risk of	14:56:54
9		hypoglycemia.	14:56:57
10		Correct?	14:56:58
11	A	Where does it say that?	14:56:59
12	Q	On page 6.	14:57:00
13	A	Where does it say that? Oh, yeah. Well,	14:57:05
14		with all due respect, the authors are entitled to	14:57:12
15		their opinion. But a person of skill in the art	14:57:15
16		will have looked at this data, and I would say 90	14:57:18
17		percent of the people will consider that as a	14:57:21
18		failure. I mean, they reduced a little bit of the	14:57:23
19		A1c similar to a tablet that cost very little, and	14:57:27
20		without the benefit of weight loss, it's considered	14:57:32
21		a failure.	14:57:36
22		But the point that I tried to make is	14:57:36

1 that those dose-response study of phase 2 was not 14:57:38
2 predictive of having a dose response where the 14:57:49
3 maximum there is going to have the maximum effect on 14:57:52
4 A1c and weight. 14:57:55
5 Q But it did have the maximum effect on 14:57:57
6 A1c. 14:58:00
7 A Not -- but not the previous dose. The 14:58:00
8 maximum dose was not greater than the other, 14:58:04
9 compared to the others, and compared to the placebo. 14:58:06
10 But again, the effect was very modest, and the last 14:58:09
11 two doses is 0.6 and 0.7 did not show any 14:58:12
12 difference. 14:58:16
13 Q But they were the two highest doses, 14:58:16
14 right? 14:58:18
15 A 0.6 to 0.75, there is a significant 14:58:18
16 difference in dose. 0.6 to 0.75 is a significant -- 14:58:24
17 Q Of the five doses tested, those were the 14:58:24
18 two highest, right? 14:58:27
19 A That means they level off at 0.6. No 14:58:28
20 further effect. 14:58:31
21 Q Okay. And the lowest dose tested showed 14:58:32
22 no effect on HbA1c, right? 14:58:34

1	A	That is correct. The effect was very	14:58:38
2		small, very modest. And considered by a person of	14:58:43
3		skill in the art as a negative effect.	14:58:48
4	Q	Well, says you, not the authors, right?	14:58:48
5		And as you noted, of the five doses that	14:58:53
6		were tested of liraglutide in the trial, the highest	14:59:01
7		dose was 0.75 milligrams, right?	14:59:04
8	A	Similar to the 0.60.	14:59:06
9	Q	Okay. And the five liraglutide doses in	14:59:08
10		Madsbad 2004 were chosen based on observations from	14:59:13
11		previous trials, right?	14:59:16
12		MR. BAUGHMAN: Object to the form.	14:59:19
13	A	I don't know what it's based on.	14:59:20
14	Q	Okay. Well, if you look at page 2, you	14:59:22
15		see there's a section there that says, Research	14:59:28
16		Design and Methods?	14:59:31
17	A	Page 2, yeah.	14:59:37
18	Q	Okay.	14:59:39
19	A	Where is the --	14:59:39
20	Q	And then if you look at the top of	14:59:41
21		column 3, it identifies the five doses that are	14:59:42
22		tested in the trial.	14:59:49

1	Do you see that, top of column 3?	14:59:51
2	A Yes.	14:59:53
3	Q And then it says, These dosages were	14:59:54
4	chosen based on observations from previous trials.	14:59:56
5	Correct?	14:59:58
6	A Okay, they reference 16 to 18.	14:59:58
7	So they are based on a single ascending	15:00:10
8	dose, healthy individuals, in healthy men, which I	15:00:18
9	appreciate your bringing this to my attention	15:00:24
10	because that, again, strengthens the point that	15:00:26
11	dose-response studies, just because they were done,	15:00:31
12	are going to be effective and infallible.	15:00:32
13	Q And then the authors go on to say, yet in	15:00:34
14	one of those previous trials, upon which -- or that	15:00:37
15	were used as a basis for dose selection in this	15:00:41
16	trial, one of those previous trials involved a	15:00:45
17	single dose of approximately 0.8 milligrams, right?	15:00:51
18	A 0.75, well, micrograms per kilo, I	15:00:54
19	believe.	15:01:01
20	Q Do you see where it says --	15:01:01
21	A Where it says?	15:01:02
22	Q -- at the top of column 3, just where we	15:01:03

1	were reading, it says, These dosages were chosen	15:01:06
2	based on observations from previous trials. In one	15:01:08
3	of those trials, a single dose of 10 micrograms per	15:01:10
4	kilogram, corresponding to approximately 0.80	15:01:14
5	milligrams, showed significant effects on glycemia,	15:01:18
6	but 2 of 11 patients reported nausea.	15:01:22
7	Correct?	15:01:24
8	A Yeah. Again, this is a dose of ten	15:01:26
9	micrograms per kilo.	15:01:29
10	Q Right.	15:01:31
11	A Which brings up the point about the	15:01:31
12	difference of the dosages there. You can see that	15:01:34
13	the precision is very small, the micrograms, to get	15:01:35
14	to a maximum of 0.8. Significant but two reported	15:01:39
15	nausea.	15:01:44
16	So there was very preliminary data, and	15:01:44
17	they chose probably the wrong dosages there.	15:01:47
18	Q Well, what the authors say is that they	15:01:50
19	looked at a previous trial that used approximately	15:01:53
20	0.8 milligrams, and that trial showed that that dose	15:01:55
21	had significant effects on glycemia, but 2 of the 11	15:01:59
22	patients reported nausea. Correct?	15:02:04

1 A That's what it says. 15:02:08

2 Q Okay. And then it says, so the highest 15:02:09

3 0.75 milligram dosage used in the Madsbad 2004 trial 15:02:10

4 was chosen to avoid causing unwanted side effects, 15:02:14

5 correct? 15:02:19

6 A That's what they probably wanted, but 15:02:19

7 they still had side effects. 15:02:22

8 Q Okay. And the lowest dosage, the article 15:02:23

9 goes on to explain, of 0.045 milligrams, was 15:02:26

10 considered too low to have any significant effect on 15:02:33

11 glycemic control, correct? 15:02:37

12 A That's what it says. 15:02:38

13 Q So the doses chosen for testing in 15:02:39

14 Madsbad 2004 included a high dose selected to 15:02:43

15 achieve significant glycemic control, while trying 15:02:47

16 to minimize GI side effects, and a low dose that was 15:02:51

17 likely to be suboptimal for glycemic control, 15:02:54

18 correct? 15:02:58

19 MR. BAUGHMAN: Object to the form. 15:02:58

20 A That was the dose response in 2004. That 15:02:59

21 those dosages probably were chosen wrongly because 15:03:04

22 they did not show the efficacy that they wanted, and 15:03:08

1 prompted Novo to what caused the delay on 15:03:11
2 development and had to do another dose response, 15:03:16
3 because as you know, those are not the dosages that 15:03:19
4 eventually liraglutide was approved for. 15:03:23

5 Q That's right. That's right. The dosages 15:03:25
6 that liraglutide was eventually approved at are 1.2 15:03:27
7 and 1.8 milligrams, right? 15:03:30

8 A Correct. 15:03:33

9 Q And none of the liraglutide dosing 15:03:33
10 regimens in Madsbad 2004 involve dose titration to 15:03:35
11 mitigate side effects, correct? 15:03:41

12 A It was not just about dose titration. It 15:03:43
13 was about the dose there, the dose ranges in terms 15:03:46
14 of potency reduction. The A1c reduction and the 15:03:50
15 weight reduction was considered very small or very 15:03:53
16 modest basically because the maximum dose that they 15:03:56
17 assumed that was 0.75, it was going to be the 15:03:59
18 maximum effect. That was not the maximum effect. 15:04:02

19 Q They picked that dose because they saw 15:04:05
20 side effects with the 0.8 milligram dose, right? 15:04:07
21 That's what the author said, right? 15:04:10

22 A They picked that dose -- 15:04:12

1	Q	0.75.	15:04:12
2	A	-- as a single ascending dose and	15:04:14
3		multiple ascending dose, but that was probably the	15:04:16
4		wrong dose.	15:04:19
5	Q	And the doses that are tested in this	15:04:19
6		weren't titrated, right? There's no titration	15:04:23
7		scheme in the trial that's reported in Madsbad 2004,	15:04:26
8		right? Right or wrong?	15:04:28
9	A	Let me read that there were no titration.	15:04:29
10		Because I mean, I don't know if they were doing the	15:04:34
11		titration.	15:04:36
12	Q	Okay.	15:04:36
13	A	Let me remind.	15:04:37
14		It doesn't talk about -- there was	15:05:48
15		probably a parallel study where they gave each dose	15:05:50
16		in parallel.	15:05:53
17	Q	Well, that's not in the article, right?	15:05:53
18		And there's nothing in the article about titrating	15:05:55
19		doses?	15:05:57
20	A	It doesn't say about titration.	15:05:58
21	Q	Okay. All right. And as we've already	15:06:00
22		discussed and you note this in paragraph 361 of your	15:06:04

1	declaration, subsequent studies of liraglutide	15:06:07
2	showed that it causes weight loss at the higher	15:06:10
3	doses of 1.2 and 1.8 milligrams, correct?	15:06:13
4	A Correct.	15:06:17
5	Q All right. And you cite the Victoza	15:06:18
6	label as evidence of that, correct?	15:06:21
7	A Correct.	15:06:22
8	Q Okay.	15:06:22
9	A And cite it as evidence that a	15:06:24
10	dose-response phase 2 study can fail.	15:06:26
11	Q Okay. Well, we've talked about whether	15:06:28
12	or not this is a failure or not.	15:06:30
13	But the Victoza label that you cite from	15:06:33
14	January 2010, it's prior art to the '462 patent,	15:06:36
15	right?	15:06:40
16	A 2010?	15:06:42
17	Q January 2010, Victoza label, that's prior	15:06:43
18	art to the '462 patent, right?	15:06:47
19	A Yeah.	15:06:48
20	Q Okay. And that label instructs patients	15:06:48
21	to titrate up to the 1.2 and 1.8 milligram doses,	15:06:55
22	correct?	15:07:00

1	A	They start with 0.6, 0.8.	15:07:01
2	Q	Yeah. According to the Victoza label,	15:07:05
3		you start with a 0.6 milligram dose to --	15:07:07
4	A	1.2.	15:07:11
5	Q	And then go to 1.2. And then if that	15:07:13
6		gives you good glycemic control, you can stay there	15:07:16
7		or then you can go up to 1.8, right? Correct?	15:07:19
8	A	Correct.	15:07:21
9	Q	All right. And the titration scheme is	15:07:21
10		intended to minimize GI side effects, right?	15:07:24
11	A	Yes, but the titration is on a weekly	15:07:26
12		basis. So not necessarily minimize. But I -- I	15:07:29
13		don't think that the results of Madsbad were	15:07:34
14		compromised by the lack of titration.	15:07:37
15	Q	Okay. And when it comes to semaglutide,	15:07:39
16		the two highest doses in the prior art NCT657	15:07:45
17		clinical trial protocol were 0.8 and 1.6 milligrams,	15:07:50
18		right?	15:07:55
19	A	Yes, sir.	15:07:55
20	Q	And in that protocol, NCT657, it	15:07:55
21		disclosed that the 0.8 milligram semaglutide dose	15:08:00
22		would be tested both with and without titration,	15:08:04

1	right?	15:08:06
2	A Correct.	15:08:07
3	Q And the 1.6 milligram dose would be	15:08:07
4	tested only with titration, right?	15:08:09
5	A Correct.	15:08:11
6	Q Okay. And that would suggest to a POSA	15:08:11
7	that the study designers had tolerability concerns	15:08:14
8	with the 1.6 milligram dose, and they possibly had	15:08:17
9	concerns, tolerability concerns, with the 0.8	15:08:21
10	milligram dose, correct?	15:08:27
11	MR. BAUGHMAN: Object to the form.	15:08:27
12	A I mean, they were testing two titration	15:08:28
13	regimens.	15:08:31
14	Q With two doses, right?	15:08:31
15	A With 0.8 and the 1.6.	15:08:33
16	Q And with 0.8, one of the experimental	15:08:34
17	arms had no titration --	15:08:37
18	A Correct.	15:08:38
19	Q -- and one of them had titration, right?	15:08:38
20	A Correct.	15:08:40
21	Q But the experimental arm with 1.6, it was	15:08:41
22	titrated?	15:08:43

1	A	Yes, sir.	15:08:44
2	Q	And that indicates to a skilled artisan	15:08:44
3		looking at that protocol that there was a concern	15:08:46
4		about side effects with the 1.6 milligram dose,	15:08:48
5		right?	15:08:52
6		MR. BAUGHMAN: Object to the form.	15:08:52
7	A	It will not indicate a concern. It will	15:08:53
8		indicate a strategy to mitigate potential side	15:08:56
9		effects.	15:08:58
10	Q	Okay. And with the 0.8 milligram dose	15:08:59
11		where there was one arm with no titration and one	15:09:02
12		arm with titration, that would indicate that there	15:09:04
13		was interest in learning if titration was required	15:09:08
14		for that dose or not with respect to side effects,	15:09:11
15		right?	15:09:14
16	A	That is the right interpretation.	15:09:14
17	Q	Okay. All right. Okay. I think we're	15:09:16
18		about done. You can set that aside. I just have a	15:09:20
19		few more questions for you, and then your counsel	15:09:23
20		may have some for you.	15:09:26
21		But have you received research grants	15:09:27
22		from Novo Nordisk?	15:09:35

1	A	Yes, sir.	15:09:36
2	Q	Can you give me an approximation of how	15:09:37
3		much in research funding used you've received from	15:09:40
4		Novo Nordisk over the years?	15:09:43
5	A	Well, the research comes to my clinic. I	15:09:44
6		mean, I have been involved in the development of	15:09:46
7		liraglutide. I've been involved in the development	15:09:50
8		of semaglutide, both for type 2 diabetes, for	15:09:52
9		obesity. I've been involved in the development of	15:09:54
10		degludec, and so on.	15:09:58
11		So I've probably done 30, 40 studies for	15:10:00
12		Novo Nordisk. I've done the same for Eli Lilly.	15:10:04
13		I've done the same for Sanofi, Sanofi-Aventis. I've	15:10:07
14		done the same for BI, and so on and so forth.	15:10:11
15		That goes to pay overhead for people, my	15:10:14
16		personnel and so on.	15:10:18
17	Q	I mean, can you ballpark for me at all	15:10:19
18		how much research funding you've received over the	15:10:21
19		years from Novo Nordisk?	15:10:24
20		MR. BAUGHMAN: Objection to the form.	15:10:25
21	A	I think that each study, as you know,	15:10:26
22		clinical trials are very expensive. I mean, I	15:10:29

1 probably have received the same from Novo Nordisk, 15:10:32
2 from Eli Lilly, could be hundreds of thousands, it 15:10:34
3 could be millions. I mean, over ten -- I've done 15:10:37
4 research for 35 years. 15:10:40

5 And so I mean, I can go through the 15:10:42
6 exercise and so on. Any information that you want 15:10:44
7 is pretty much open at CMS. You can see that it's 15:10:47
8 open. 15:10:51

9 Q Okay. Have you served as a consultant -- 15:10:51
10 obviously, setting aside this work, have you served 15:10:54
11 as a consultant to Novo Nordisk? 15:10:58

12 A I have served as a consultant for Novo 15:10:59
13 Nordisk, as a scientific advisor. I have served as 15:11:01
14 a scientific advisor for Sanofi. I have served as a 15:11:04
15 scientific advisor for Eli Lilly. I have served as 15:11:08
16 a scientific advisor for Boehringer Ingelheim. 15:11:11

17 So I've done this. I mean, my statements 15:11:15
18 here have nothing to go with my -- 15:11:17

19 Q I understand. I'm just asking the 15:11:19
20 questions. 15:11:20

21 How are you compensated for your work as 15:11:21
22 a scientific advisor or consultant for Novo Nordisk? 15:11:24

1	A	They have what is called fair value, fair	15:11:28
2		market value. And I'm a consultant by the hour, and	15:11:34
3		I also consulted -- paid by the hour and also they	15:11:41
4		give a travel allowance. I've been paid for	15:11:43
5		whenever I give a lecture for Eli Lilly or Novo	15:11:45
6		Nordisk or Sanofi, I get compensated. Not as much	15:11:50
7		as you, Counsel, but I do get compensated.	15:11:52
8	Q	Do you have any estimation of how much	15:11:54
9		you've been compensated for consulting work or	15:11:58
10		speaking work for Novo Nordisk over the years?	15:12:01
11	A	I mean, could be 20, 40, 50,000, 60,000.	15:12:03
12		I mean, I don't know. Everything, I'm an open book.	15:12:08
13		And the CMS, I mean you can actually get into there	15:12:12
14		and you can see that.	15:12:14
15	Q	Okay.	15:12:18
16	MR. ANSTAETT:	Why don't we just take a	15:12:18
17		very quick break. I'll make sure I don't have any	15:12:20
18		more questions, but I think we're done.	15:12:22
19		(Recess from 3:12 p.m. until 3:27 p.m.)	15:27:57
20	MR. ANSTAETT:	Dr. Rosenstock, thank you.	15:27:57
21		I don't have any further questions for you.	15:28:00
22	THE WITNESS:	Thank you.	15:28:02

1	EXAMINATION	15:28:03
2	BY MR. BAUGHMAN:	15:28:03
3	Q Dr. Rosenstock, I know it's been a long	15:28:04
4	time. There's been a lot of questions, you've seen	15:28:06
5	a lot of documents, and I know -- although you have	15:28:08
6	very good facility with it, I know English isn't	15:28:10
7	your first language, so I'll try to just ask a	15:28:13
8	couple things to clear up a few points.	15:28:15
9	You were asked some questions earlier	15:28:18
10	about claim construction. I'd ask you to turn to	15:28:20
11	paragraph 203, 2-0-3, of your declaration. It's on	15:28:22
12	page 64.	15:28:26
13	A Yeah.	15:29:05
14	Q And you see in your paragraph 203, you've	15:29:05
15	been instructed to assume the meaning for a phrase	15:29:09
16	from the claim, "a method for treating type 2	15:29:12
17	diabetes," correct?	15:29:16
18	A Yes, sir.	15:29:16
19	Q In your opinion, something isn't a	15:29:17
20	treatment if it's not safe, is it?	15:29:21
21	MR. ANSTAETT: Objection, leading.	15:29:23
22	A It has to be safe. It has to be safe and	15:29:25

1	tolerable.	15:29:29
2	Q And is it a treatment if it's not	15:29:31
3	effective?	15:29:33
4	A You mean if a treatment is not effective?	15:29:37
5	Q Yes.	15:29:40
6	A If it's not effective, it's not a	15:29:41
7	treatment.	15:29:43
8	Q You were also asked some questions about	15:29:45
9	whether the claim language 1.0 milligrams covered a	15:29:48
10	number of other amounts like 0.99 milligrams or 1.01	15:29:54
11	milligrams.	15:29:58
12	Do you remember those questions?	15:29:58
13	A Yes, sir.	15:29:59
14	Q Did you actually form an opinion in your	15:30:00
15	report about how broadly the claim term 1.0	15:30:03
16	milligrams would be interpreted in this case?	15:30:06
17	A No. I just specifically asked for the	15:30:08
18	1.0 milligram, that that was in the claim 1.	15:30:11
19	Q I'd like you to look at paragraph 281 of	15:30:14
20	your report, please.	15:30:17
21	A I did -- if I recall, I mean, I did say	15:30:21
22	that from 0.7 to 0.8 milligrams and above it behaved	15:30:24

1	differently.	15:30:30
2	Which paragraph again?	15:30:30
3	Q Paragraph 281 on page 88.	15:30:33
4	A Yeah.	15:30:39
5	Q And I believe counsel asked you some	15:30:41
6	questions about your basis for the red statement	15:30:43
7	here about criticality where you refer to 462's	15:30:47
8	multiple statements showing that the claimed	15:30:56
9	once-weekly 1.0 milligram dose operates differently	15:30:58
10	than other doses within the 0.1 to 1.6 milligram	15:31:01
11	range endpoints as to both efficacy -- skipping	15:31:06
12	ahead -- and tolerability, which supports the	15:31:09
13	criticality of that dose.	15:31:11
14	Do you remember those questions?	15:31:12
15	A Yes, sir.	15:31:14
16	Q Are there citations at the end of that	15:31:15
17	red sentence that actually show statements on which	15:31:17
18	you're relying?	15:31:21
19	MR. ANSTAETT: Objection, leading.	15:31:22
20	A Yeah. It says 240 and 59, and then it's	15:31:23
21	all the exhibits, Table 3A and 3B.	15:31:29
22	Q Okay. And that Exhibit 1001, that's the	15:31:34

1	'462 patent, correct?	15:31:37
2	A Yes.	15:31:38
3	Q So you're pointing to information from	15:31:39
4	the patent in support of that red statement,	15:31:42
5	correct?	15:31:45
6	MR. ANSTAETT: Objection, leading.	15:31:45
7	A Yes, because I mean, I can see that the	15:31:47
8	dosages above 0.8 milligrams, 0.8 milligrams were	15:31:50
9	different and more efficacious in terms of A1c and	15:31:57
10	weight loss.	15:32:02
11	Q And you continue discussing that at	15:32:02
12	paragraphs 282, 283, 284, and 285 of your	15:32:05
13	declaration.	15:32:11
14	Isn't that right?	15:32:12
15	MR. ANSTAETT: Objection, leading.	15:32:12
16	A Yeah. I mean, I'm emphasizing that that	15:32:14
17	dose is different in terms of the efficacy of how	15:32:19
18	different dosages behave in terms of the weekly	15:32:24
19	doses of 0.8 offer greater significant improvements	15:32:29
20	there than once-daily liraglutide.	15:32:35
21	Q And you speak about -- do you speak about	15:32:38
22	tolerability in those paragraphs?	15:32:42

1	A	I said as to tolerability, '462 patent	15:32:51
2		explained that nausea and vomiting increases with	15:32:58
3		dose.	15:33:01
4	Q	And then you refer to some testimony from	15:33:01
5		Dr. Bantle; is that right, and Dr. Jusko?	15:33:05
6	A	Yeah, which is some contradictory	15:33:06
7		statement with Dr. Bantle confirming that, higher	15:33:09
8		dose, some patients experience greater nausea and	15:33:12
9		greater instances of vomiting, and this would have	15:33:17
10		been expected.	15:33:18
11		But on the other hand, at different	15:33:19
12		points from my declaration, I said that they also	15:33:20
13		expected to have the maximum efficacy.	15:33:22
14	MR. BAUGHMAN:	I pass the witness.	15:33:28
15	MR. ANSTAETT:	Any other questions?	15:33:36
16	MR. BAUGHMAN:	I'm passing you back to	15:33:36
17		other, Counsel.	15:33:36
18	MR. ANSTAETT:	I think I just have one	15:33:36
19		question for you.	15:33:37
20		EXAMINATION	15:33:38
21	BY MR. ANSTAETT:		15:33:38
22	Q	Since counsel asked you about it, he was	15:33:39

1	asking you about -- you were reading I think from	15:33:41
2	paragraph 284, where you said, As Dr. Bantle	15:33:42
3	confirmed -- or excuse me, And Dr. Bantle confirmed	15:33:45
4	that at higher doses of semaglutide, some patients	15:33:49
5	experienced greater nausea and greater instances of	15:33:52
6	vomiting, and this would have been expected.	15:33:55
7	Do you see that?	15:33:57
8	A Yes, sir.	15:33:57
9	Q Do you agree with Dr. Bantle in that	15:33:58
10	regard, that at higher doses of semaglutide, it	15:34:00
11	would have been expected that some patients would	15:34:04
12	experience greater nausea and vomiting?	15:34:07
13	A First of all, there is dose responses in	15:34:15
14	terms of the higher the dose, the greater the	15:34:20
15	chances of having more nausea and vomiting. And at	15:34:23
16	higher dosages, you can -- in terms of dose	15:34:36
17	responses, you see more side effects.	15:34:38
18	But again, you need to look at that	15:34:41
19	because I don't know how much nausea and vomiting	15:34:44
20	they're going to have at 1.6. But you probably	15:34:48
21	would expect to have more nausea and vomiting, yes.	15:34:50
22	Q Okay.	15:34:54

1 MR. ANSTAETT: No further questions. 15:34:54

2 MR. BAUGHMAN: We're done. Thank you, 15:34:56

3 Dr. Rosenstock. Thanks, Counsel. 15:34:57

4 MR. ANSTAETT: That's it. Thank you. 15:34:59

5 (Transcript orders discussed.) 15:34:59

6 COURT REPORTER: Thank you. That's all I 15:36:36

7 need. 15:37:25

8 (Off the record at 3:37 p.m.)

9

10

11

12

13

14

15

16

17

18

19

20

21

22

1 CERTIFICATE OF SHORTHAND REPORTER - NOTARY PUBLIC

2
3 I, Lisa V. Feissner, RDR, CRR and Notary
4 Public in and for the District of Columbia, do
5 hereby certify:
6

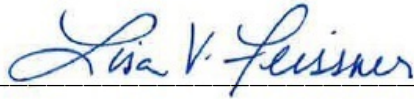
7 That JULIO ROSENSTOCK, M.D., the witness
8 whose deposition is hereinbefore set forth, was duly
9 sworn by me before the commencement of such
10 deposition, and that such deposition was taken
11 before me and is a true record of the testimony
12 given by such witness.
13

14 I further certify that the adverse party,
15 NOVO NORDISK A/S, was represented by counsel at the
16 deposition.
17

18 I further certify that the deposition of
19 JULIO ROSENSTOCK, M.D., occurred at the offices of
20 PERKINS COIE LLP on WEDNESDAY, MAY 15, 2024,
21 commencing at 9:08 and concluding at 3:37.
22

1 I further certify that I am not related
2 to any of the parties to this action by blood or
3 marriage, I am not employed by or an attorney to any
4 of the parties to this action, and that I am in no
5 way interested, financially or otherwise, in the
6 outcome of this matter.

7
8 IN WITNESS WHEREOF, I have hereunto set
9 my hand this 16TH day of MAY, 2024.

10
11
12 

13 NOTARY PUBLIC IN AND FOR
14 THE DISTRICT OF COLUMBIA
15 MY COMMISSION EXPIRES JUNE 15, 2028
16
17
18
19
20
21
22