1 UNITED STATES PATENT AND TRADEMARK OFFICE
2 BEFORE THE PATENT TRIAL AND APPEAL BOARD
3
4 XENCOR, INC.,
5 Petitioner,
6 vs.
7 MERUS N.V.,
8 Patent Owner.
_____/
9
In Re:
10 Patent Nos. 9,358,286 and 11,926,859
11 _____/
12
13
14
15
16 DEPOSITION OF
17 LEONARD G. PRESTA, Ph.D.
18 Friday, December 5, 2025
19
20
21
22 Reported by:
CARLA SOARES
23 CSR No. 5908
24
25

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15 DEPOSITION OF LEONARD G. PRESTA, Ph.D.,
16 Volume I, taken on behalf of Patent Holder, beginning at
17 8:34 a.m., and ending at 6:50 p.m., on Friday, December
18 5, 2025, before CARLA SOARES, Certified Shorthand
19 Reporter No. 5908.
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Yung Jin Choi, Xencor, Inc.

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(REPORTER'S NOTE: All quotations from exhibits are reflected in the manner in which they were read into the record and do not necessarily denote an exact quote from the document.)

EXHIBITS

NUMBER	DESCRIPTION	PAGE
Exhibit 4001	Document entitled "Studies on Protein Stability with T4 Lysozyme" (No Bates numbers)	83
Exhibit 4002	Document entitled "Chapter 9, The Design and Engineering of IgG-Like Bispecific Antibodies" (No Bates numbers)	103

1 EXHIBITS

2 NUMBER DESCRIPTION PAGE

3 Exhibit 4003 127

4 United States Patent No. US 10,351,631 B2

5 (No Bates numbers)

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--o0o--

1 San Francisco, California
2 Friday, December 5, 2025
3 8:34 a.m.
4
5 P R O C E E D I N G S
6 THE REPORTER: Good morning. My name is Carla
7 Soares. I am a California Certified Shorthand Reporter.
8 My CSR number is 5908.
9 At this time, will all counsel please
10 introduce themselves and state who they represent. Then
11 I will swear in the witness.
12 MS. MAYS-WILLIAMS: Ashley Mays-Williams, of
13 Paul Hastings, on behalf of Xencor and the witness. I'm
14 also joined by Michael Wolfe of Paul Hastings. Also
15 with us today is Robin Silva and Yung Jin Choi, both of
16 Xencor.
17 MR. ARMENIO: Peter Armenio, from Cahill
18 Gordon & Reindel, for patent owner, Merus.
19 LEONARD G. PRESTA, Ph.D.,
20 having been administered an oath, was examined and
21 testified as follows:
22 EXAMINATION
23 BY MR. ARMENIO:
24 Q Good morning, Doctor. Nice to meet you.
25 As you heard, my name is Peter Armenio. I'm

a lawyer for Merus, the patent owner in this proceeding.

Are you ready to have some cross-examination today?

A Yes.

Q Okay. Do you understand that that is the purpose of today's proceeding?

We have some written testimony from you, and today we'll be doing some cross-examination of that testimony.

Do you understand that?

A Yes.

Q And do you understand that you're now under oath to answer my questions truthfully and to the best of your ability?

A Yes.

Q And do you agree to do that?

A Yes.

Q If you do not understand one of my questions today, do you agree to ask me to either repeat the question or rephrase it so you do understand it?

A Yes.

Q And is there any reason, medicines or otherwise, why you would not be able to tell the truth today in response to the questions?

A Repeat that, please.

Q Sure.

Is there any reason today, whether it be medicines, jet lag, or some other condition, where you might not be able to answer questions truthfully and accurately today?

A No.

Q Great.

Let me show you your declaration in the proceeding regarding U.S. Patent 9,385,286, and this was marked as Xencor Exhibit 1002.

MS. MAYS-WILLIAMS: Peter, he's got a copy here, too, just in a binder. It has no notes. But I just wanted to make a note of that on the record.

And, Dr. Presta, you can use whatever version you're comfortable using.

BY MR. ARMENIO:

Q Dr. Presta, when were you first contacted by anyone regarding preparing what turned out to be Xencor Exhibit 1002?

MS. MAYS-WILLIAMS: Dr. Presta, I just want to caution you not to reveal the substance of any communications that you had with any attorney in your response. If you can answer the question without revealing the substance of any communications that

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Page 000009

you've had with any attorney in your response, you may do so.

THE WITNESS: It was October 2024.

BY MR. ARMENIO:

Q Okay. And we see that you have a date on the last page of Exhibit 1002 of February 11th, 2025; is that right?

A Yes.

Q And is that your signature on page 175 of the document?

A Yes, it is.

Q Okay. Between October 2024 when you were first contacted and February 11th, 2025, when you signed Exhibit 1002, approximately how many hours did you spend on this matter?

MS. MAYS-WILLIAMS: I just want to provide the same caution, Dr. Presta. You can answer the question just so long as you don't reveal the substance of any communications that you've had in your response.

THE WITNESS: I do not remember the total number of hours.

BY MR. ARMENIO:

Q What's your best recollection?

MS. MAYS-WILLIAMS: Objection. Asked and

answered.

THE WITNESS: Probably 16.

BY MR. ARMENIO:

Q 16, 1-6?

A 1-6.

Q In connection with the various documents cited in Exhibit 1002 -- as we go through the day, we'll note a number of exhibits are pointed out and cited -- how were those selected? Was it something you selected or did someone else select it for you?

MS. MAYS-WILLIAMS: Dr. Presta, I'll allow you to answer that question, but I just want to give you the same caution about not revealing the substance of any communications that you had with any attorney in your response. But if you remember, you can answer.

THE WITNESS: As far as I remember, they were -- the list was given to me.

BY MR. ARMENIO:

Q And was that list given to you by lawyers for Xencor?

MS. MAYS-WILLIAMS: Same caution, Dr. Presta, about your response. You can answer the question if you recall, but I want to give you the caution not to reveal any substance of any communications that you had with any attorney in your response.

1 THE WITNESS: They were given to me by Paul
2 Hastings.
3 BY MR. ARMENIO:
4 Q And you understand Paul Hastings is the law
5 firm representing Xencor in this proceeding; is that
6 right?
7 A Correct.
8 Q Other than the exhibit list given to you by
9 Paul Hastings, did you add any exhibits to the
10 declaration, Xencor Exhibit 1002, yourself?
11 MS. MAYS-WILLIAMS: I'll give you the same
12 caution, Dr. Presta, not to reveal the substance of any
13 attorney-client communications in your response.
14 THE WITNESS: No.
15 BY MR. ARMENIO:
16 Q With respect to the actual writing of
17 Exhibit 1002, is this something you wrote yourself in
18 the first instance, sitting at your computer and typing
19 it up in the first instance from a blank piece of
20 paper?
21 A No.
22 Q Did you receive an already-typed-up document
23 from lawyers for Xencor in the first instance?
24 MS. MAYS-WILLIAMS: I'll give you the same
25 caution, Dr. Presta, not to reveal the substance of any

1 communications that we had in your response.
2 THE WITNESS: After all of our meetings, I did
3 get a first draft.
4 BY MR. ARMENIO:
5 Q And that first draft was typed up in the first
6 instance by lawyers for -- well, lawyers at Paul
7 Hastings; is that right?
8 MS. MAYS-WILLIAMS: Same caution, Dr. Presta.
9 THE WITNESS: I received it from Paul
10 Hastings. I don't know who typed it up.
11 BY MR. ARMENIO:
12 Q And when did you receive that first draft,
13 typed up by someone, that you received from Paul
14 Hastings?
15 A If I remember correctly, January of 2025.
16 Q And do you remember when during the month of
17 January you received that first draft, typed up by
18 someone else, delivered to you by Paul Hastings?
19 A I do not remember an exact date. It was
20 earlier in the month rather than later.
21 Q And how many revisions did the document go
22 through between receiving the first draft and you
23 signing your name on February 11th, 2025?
24 MS. MAYS-WILLIAMS: Objection. Vague.
25 THE WITNESS: I didn't hear.

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Oh.

BY MR. ARMENIO:

Q So I'll reask the question.

Did you sign the first draft that came to you that was delivered by Paul Hastings after you read it?

A No.

Q Did you make any changes to that first draft?

A Yes.

Q How many drafts did the document go through between receiving the first draft from Paul Hastings earlier in the month of January 2025 and you having a final version that you signed as Exhibit 1002 on February 11th, 2025?

A If I remember correctly, three. First, second, and then final.

Q So the first draft, you made some changes. There was a second draft, you made some changes. The third draft, you signed; is that right?

A Yes.

Q Focusing in on just that time in early January 2025 when you got the first draft until February 11th, 2025, when you signed the document, how much time did you spend on the declaration?

1 MS. MAYS-WILLIAMS: I'm just going to provide
2 the same caution to you, Dr. Presta, about not revealing
3 the substance of any communications with any attorney in
4 your response.
5 But if you can answer the question without
6 revealing the substance of any communications, and if
7 you remember, you may do so.
8 THE WITNESS: In total, probably about 40
9 hours.
10 BY MR. ARMENIO:
11 Q I'm a little confused.
12 Earlier when I asked you how many hours you
13 spent between first being retained in October 2024 and
14 signing Exhibit 1002 on February 11th, 2025, you told me
15 you had spent 16 hours, 1-6.
16 And now I'm trying to understand what portion
17 of that 16 hours you spent between receiving the first
18 draft of the document typed up by somebody else in early
19 January 2025 and you signing a revised version of the
20 document on February 11th, 2025.
21 A I'm not understanding the timeline.
22 Q Between receiving the first draft in early
23 2025, what turned out to be Exhibit 1002, and signing
24 the document on February 11th, 2025, how much time did
25 you actually spend editing the document?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Pardon?

MS. MAYS-WILLIAMS: Objection. Vague, asked and answered.

THE WITNESS: Okay. So we have from first talking --

MS. MAYS-WILLIAMS: I just want to caution you not to reveal the substance of any communications that you've had with an attorney.

MR. ARMENIO: Counsel, the question doesn't ask for that. I think you're interfering with the deposition at this point.

MS. MAYS-WILLIAMS: I don't agree.

MR. ARMENIO: We're asking number of hours. There's nothing privileged about number of hours.

MS. MAYS-WILLIAMS: He just said, "I was talking to attorneys." So I was giving him caution, which I'm entitled to do.

Maybe you want to ask your question again. We got kind of far away from it.

MR. ARMENIO: Can you reread the question, please?

(Record read as follows:

"Question: Between receiving the first draft in early 2025, what turned out to be Exhibit 1002,

and signing the document on February 11th, 2025, how much time did you actually spend editing the document?")

THE WITNESS: That is -- second and third, probably the total of the 16. That's the 16.

BY MR. ARMENIO:

Q So you get the first draft of the document from someone. You receive it from Paul Hastings earlier in the month of January 2025. It goes through a first round of edit, a second round of edit. You sign the third round on February 11th, 2025.

And between receiving the first draft and signing your name, you spent about 16 -- 1-6 -- hours editing the document.

Is this a fair statement?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: I can't hear.

MS. MAYS-WILLIAMS: Sorry. I said, "Objection. Compound."

THE WITNESS: Yes.

BY MR. ARMENIO:

Q So now let's take a look at that document, please.

In the document, we've got a number of exhibits cited; for example, on page 7.

1 And you can -- in answering questions, you can
2 look wherever you want in your declaration, but I'm just
3 pointing things -- sometimes it's easier to have a home
4 base from which to ask a question. So home base for
5 this question is page 7, paragraph 21, please.
6 Do you see at the end of that paragraph you
7 cite an Exhibit 1013?
8 A Yes.
9 Q And that's not the only exhibit you cite in
10 your declaration. You cite a number of exhibits,
11 right?
12 A Yes.
13 Q Did you read the entirety of Exhibit 1013?
14 A Yes.
15 Q And it tells us in Exhibit 1013, you say in
16 your declaration, "20 monoclonal antibodies had been
17 approved by the U.S. Food and Drug Administration for
18 therapy" by 2012.
19 Is that right?
20 THE WITNESS: "More than 20 monoclonal
21 antibodies had been approved."
22 BY MR. ARMENIO:
23 Q And none of those were bispecific at that
24 point; right?
25 A That, I'm uncertain of.

1 Q In preparing your declaration, did you go back
2 and look and see when the FDA first approved any
3 bispecific antibody of any kind?
4 MS. MAYS-WILLIAMS: Dr. Presta, I'll just
5 caution you not to reveal the substance of any
6 communication with any attorney in your response.
7 THE WITNESS: Could you repeat the question?
8 BY MR. ARMENIO:
9 Q Sure.
10 In preparing Exhibit 1002, specifically -- it
11 could have been in connection with paragraph 21 or some
12 other paragraph -- did you go back and look and see when
13 was the first time the U.S. FDA ever approved a
14 bispecific antibody made by any bispecific antibody
15 technology?
16 MS. MAYS-WILLIAMS: I'll give you the same
17 caution about protecting communications in your
18 response.
19 THE WITNESS: Yes.
20 BY MR. ARMENIO:
21 Q And what did you find out when you went back
22 and looked?
23 A If I remember correctly, the first bispecific
24 was blinatumomab, but I do not remember the year.
25 Q And do you remember the technology used with

1 blinatumomab to associate different binding entities,
2 one to the other?
3 MS. MAYS-WILLIAMS: Objection. Vague, scope.
4 THE WITNESS: That was from Amgen using tandem
5 single-chain Fv.
6 BY MR. ARMENIO:
7 Q And Amgen had a group working in bispecific
8 antibodies for a number of years at around the same time
9 you were working in bispecific antibodies at Genentech
10 and Merck, right?
11 A That, I do not know.
12 Q Do you know the name Gunasekaran Kannan?
13 A Yes.
14 Q Have you ever met Dr. Kannan?
15 A No.
16 Q In your declaration, I see you cite a
17 Kannan -- excuse me.
18 In this declaration, you cite a Gunasekaran
19 paper, and in the declaration about the other patent --
20 the '859 Merus patent we'll talk about later -- you
21 cite a Kannan published patent application; is that
22 right?
23 A Yes.
24 Q That's the same human being, right?
25 Gunasekaran Kannan?

A It is.

Q And sometimes in some of the documents -- it's not your fault. But in some of the documents, people have flipped his first name and last name. But whether we say "Gunasekaran Kannan" or "Kannan Gunasekaran," that is the same human being, scientist, at Amgen, right?

A As far as I'm aware, yes.

Q Okay. Great.

So let's take a look, if we can, at page 83 of your declaration. And specifically, I'm looking at paragraph 168 that spans page 83 and 84. Please take your time to get there and take a peek. Starting on 83 and then going over to 84 is where my questions will be.

You write that "By 2012, 'more than 45 different [bispecific antibody] formats had been established.'"

Is that right?

A More than 45.

Q And you believe that to be a true statement when you signed Exhibit 1002 on February 11th of this year, right?

A Yes.

Q And you give us a citation to Exhibit 1013; is

that right?

A Citation 1013.

Q On the continuation of this paragraph 168 on page 84, you actually reproduced for us Figure 2 from Exhibit 1013, correct?

A Yes.

Q And this has got the 45 different bispecific antibody formats that were established by 2012, right?

A That's the figure from the -- from 1013.

Q And you say in your declaration that "A prior art scientific publication from that year" -- 2012 -- "depicted these various bispecific antibody formats that had been developed," and you say they're shown below.

You give us the figure, and then you cite to Exhibit 1013, Figure 2, correct?

A Figure -- 1013, Figure 2.

Q Right.

So now if we look on page 84 of your declaration where you reproduced that figure, can you see that there are seven rows of different formats?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: There are -- there are seven rows of formats.

///

BY MR. ARMENIO:

Q And only one of those rows relates to asymmetric bispecific IgG and IgG-like molecules, right?

A There is only one row that's labeled "asymmetric bispecific."

Q And that "asymmetric," that's the row where we potentially can have differences between the heavy chains, right? That's what makes them asymmetric bispecific IgGs, right?

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: Can you repeat the question?

BY MR. ARMENIO:

Q Sure.

So let's take a look at asymmetric bispecific IgG and IgG-like molecules.

If we look at that row, do you see the first entry is "KIH IgG"?

A Right.

Q What does the "KIH" stand for?

A Knob-in-hole.

Q And then we've got a "KIH IgG common LC."

What does the "common LC" stand for?

A Common light chain.

Q The next one is "CrossMab."

1 Now, in the CrossMab, you can see, the bottom
2 blocks, it has the same shape as the KIH IgG and the
3 KIH IgG common LC.
4 Do you see that?
5 A The same shape. Agree.
6 Q And so "CrossMab," that's got a KIH aspect to
7 it?
8 A In the original. This was a design from
9 Roche, and they did use the KIH.
10 Q And then the next one, you've got
11 "KIH IgG-scFab," F-A-B; is that right?
12 A Yes.
13 Q And we can see again from the shapes that are
14 in the depiction, KIH, and also in the title, KIH is
15 again used with this format, right?
16 A That's how it's labeled.
17 Q Next we have "mAb-fv." And again, we see the
18 shapes depicted in this format as also including a KIH
19 technology, right?
20 A According to the picture, yes.
21 Q On the far right of this row, we see
22 SEED-body," S-E-E-D, "body." That's got a different
23 shape on the bottom part of the antibody, right?
24 It doesn't have a KIH shape like the other
25 ones, does it?

A Correct.

Q So what's going on with the SEED-body technology?

A It's been a long time since I looked at that.

If I remember correctly, I think they incorporated parts of a human IgA into the IgG.

Q So in a SEED-body, you've got a mixed stack of IgA and IgG heavy chain components?

A If I remember the SEED technology correctly.

Q So in the row regarding asymmetric bispecific IgG and IgG-like molecules, six of the seven depicted formats don't have anything to do with charges on the heavy chain, right?

A Say that again, please.

Q Sure.

When we're looking at this row from Exhibit 1013, Figure 2 that you repeated in your declaration at page 84, in that asymmetric bispecific row, of the seven formats depicted, six of them are either KIH or SEED formats, right?

A The only one that I -- so the fifth one over, the "mAb-fv," they're using a certain design to represent KIH, but that particular format doesn't say "KIH." So I don't know that it is KIH.

Q Okay. You do know that mAb-fv is not a charge

engineering format, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: For this application, I do not know that.

BY MR. ARMENIO:

Q In Exhibit 1013, Figure 2, out of all 45 different bispecific antibody formats depicted, only one of them involves changing charges on the heavy chain, right?

A With the proviso that I do not remember what the SEED -- the particulars, the one that says, "charge pairs."

Q And in the "charge pairs," do you see that there are four dots: two blue dots and two red dots?

A It's a little too small for that. Sorry.

Q Did you take note of that when you were preparing your declaration, that in the Exhibit 1013, Figure 2 that you were citing, there were two charge pairs indicated in that antibody format?

A I do not remember that I looked at that detail.

Q In connection with this case, and specifically this declaration, Exhibit 1002, if we look at page 50, please, on that page, in paragraph 99, you say, "I have applied the ordinary and customary meaning to all claim

terms of the '286 patent in my analysis below."

Do you see that?

A That first sentence in paragraph 99.

Q And was that a true statement when you signed the declaration on February 11th, 2025?

A Yes.

Q And what claim construction analysis, if any, did you yourself do before including that sentence in your final declaration signed on February 11th, 2025?

MS. MAYS-WILLIAMS: I object to the form of the question.

I just want to caution the witness not to reveal the substance of any attorney-client communications in your response. If you can answer the question without revealing the substance of communications that you had with any attorney, then you may do so.

THE WITNESS: I applied the meaning that I understood from dealing with patents over the years. But I am not a lawyer.

BY MR. ARMENIO:

Q Did you yourself review the prosecution history for the '286 Merus patent that's the subject of this declaration in trying to figure out the meaning of any claim terms?

A For the '286, I do not remember.

Q You do not remember doing that?

A I do not remember doing that.

Q Did you yourself look at the different claims in the patent to see what impact the different claims may have on the meaning of claim terms in other claims in the '286 patent as part of claim construction for your declaration?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: I did look at the claims in the patent.

BY MR. ARMENIO:

Q So let's take a look -- and I'll put in front of you -- you probably already have it in your binder, but just for completeness of the record -- it's Merus's patent 9,385,286. It's the subject of your declaration and has previously been marked as Xencor Exhibit 1001.

So when you reviewed the claims, did you take any note of claim 8 when trying to construe the meaning of any claim term elsewhere in the claims?

A So that is claim 8 in column 73?

Q Yes. Did you specifically look at claim 8 and say, "Oh. Let me factor that into a claim construction analysis I'm doing in connection with my declaration,

Exhibit 1002"?

A I don't understand the question.

Q Okay. Let me ask it a different way and we'll see if we get there.

When we read claim 8, it first refers to "The method of claim 1."

Do you see that?

A Yes.

Q And then it says, "wherein each variable region of the first and second antibody heavy chains recognizes a different target epitope."

Do you see that?

A Yes.

Q Okay. So reading that, since it's talking about "each variable region of the first and second antibody heavy chains," doesn't that tell you that antibody heavy chains in claim 1 have to have variable regions?

Did you factor that into your claim construction analysis or not?

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: I do not remember.

BY MR. ARMENIO:

Q You don't remember factoring claim 8 into

your construction of antibody heavy chains in claim 1, right?

MS. MAYS-WILLIAMS: Asked and answered.

THE WITNESS: Correct.

BY MR. ARMENIO:

Q If we look at page 10 of your declaration, Exhibit 1002, you give us a demonstrative. I'm going to ask you a few questions about that once you have a chance to get there. Page 10, please.

A I'm on page 10.

Q And on page 10, you give us a demonstrative antibody structure; is that right?

A Correct.

Q When a person of ordinary skill in the art, as you have defined such a person, thinks about an antibody, what they visualize is what you have shown as a demonstrative on page 10 of your declaration, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: What a POSA would think would depend on the context of what they were discussing.

BY MR. ARMENIO:

Q So we're discussing right now your statement that you used the plain and ordinary meaning in the claim terms, right? We've already reviewed that. You say that very clearly in paragraph 99. You say, "I

apply the ordinary and customary meaning to all claim terms," right?

And now what I'm trying to understand is the ordinary and customary meaning for "antibody." What is the ordinary and customary meaning for "antibody" that you used in your analysis set forth in Exhibit 1002?

MS. MAYS-WILLIAMS: Objection. Vague and compound.

THE WITNESS: An antibody -- the term "antibody" can include many different constructs.

BY MR. ARMENIO:

Q In claim 1 of the '286 patent, the claim starts, "A method for producing a heterodimeric antibody."

Is that right?

A "A method for producing a heterodimeric antibody."

Q In paragraph 26, which is right below your demonstrative antibody on page 10, you talk about what it means to be a homodimeric antibody, right?

A Repeat the question again so I have it clear.

Q Sure.

In paragraph 26 of your declaration, Exhibit 1002, you discuss what it means to be a homodimeric antibody, correct?

A Correct.

Q And that's made from two of the same thing. It makes it homodimeric, right?

A That's what is explained in paragraph 26.

Q And in paragraph 32, you tell us for heterodimeric antibodies, there are two different things, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Please, the question again.

BY MR. ARMENIO:

Q Sure.

In paragraph 32 [sic], you talk to us and explain to us what "heterodimeric" or "heterodimers" means. And you say, quote, "Made up of two ('-dimer') different ('hetero-') components," right?

A "Made up of two ('-dimer') different ('hetero-') components, bispecific antibodies are often 'heterodimeric' or 'heterodimers.'"

Q Just focusing on the "heterodimeric" piece first, that means two different components, right?

A Somewhere in the structure, two different components.

Q Well, it's not just somewhere in the structure, right?

If I have an antibody that's got a light chain

1 and a heavy chain, those are differences in the
2 structure. And a monospecific antibody with a light
3 chain and a heavy chain isn't heterodimeric, right?
4 A Say that again, please.
5 Q Let's focus on the second half of your
6 sentence here in paragraph 32 under your
7 Demonstrative 4.
8 You say, "bispecific antibodies are often
9 'heterodimeric' or 'heterodimers,'" right?
10 A "Bispecific antibodies are often
11 'heterodimeric' or 'heterodimers.'"
12 Q But not all bispecifics are heterodimeric or
13 heterodimers, right?
14 A Correct.
15 Q And you gave us -- and we walked through the
16 chart of 45 bispecific formats from 2012, right?
17 A That was Figure 2.
18 Q And we can -- if we wanted to, we could go
19 through one by one and see which format would be
20 heterodimeric and which format would not be, right? If
21 we wanted to do that exercise, we could?
22 A Through Figure 2.
23 Q Yes, sir.
24 A Yes.
25 Q And a person of ordinary skill in the art

could do that exercise. They could look through Figure 2 and say, "All right. These are all bispecific formats. This one is a heterodimeric format. This one is not, this one is."

A person of ordinary skill in the art, as you have defined such a person, would be able to readily distinguish those things within Figure 2 of Exhibit 1013, correct?

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: Where is Figure 2 again?

I got it. Page 17.

A POSA would have been able to look through this and look at the different formats, perhaps not understand the details of each format.

BY MR. ARMENIO:

Q From this figure, a POSA could, at a minimum, see differences and investigate further if they needed to with papers and available literature, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: In addition, a POSA would hopefully have read some of these papers.

BY MR. ARMENIO:

Q In fact, they might have read a whole bunch of them, right?

A I did.

Q Understood. Understood.

Now, when we're talking about your ordinary and customary meaning, what ordinary and customary meaning did you use for "antibody heavy chain" in the claims of the '286 patent?

A So again, "antibody" is context-dependent.

Q "Context-dependent" is different than "ordinary and customary meaning." You said you used ordinary and customary meanings for a person.

So what's the ordinary and customary meaning of "antibody heavy chain" to a person of ordinary skill in the art in 2012?

MS. MAYS-WILLIAMS: Objection. Vague and compound.

THE WITNESS: Defining "antibody" by a POSA would be context-dependent. What are we talking about?

BY MR. ARMENIO:

Q So if we look at your paragraph 99 statement, it really -- to make it accurate, it should say, "I have applied context-dependent ordinary and customary meanings to all the claim terms of the '286 patent in my analysis below."

A Where are we? Paragraph 99?

Q Yes, sir. On page 50.

A Okay. "I have been informed that claims are typically given their ordinary and customary meaning in the technological field of the patent."

Q When you say -- 99, shouldn't we revise it to say that you have applied the context-dependent ordinary and customary meaning to all the claim terms of the '286 patent in your analysis below if we're going to make it accurate?

MS. MAYS-WILLIAMS: Objection. Misleading.

THE WITNESS: In 99, "I have applied the ordinary and customary meaning to all the claim terms of the '286 patent in my analysis below."

I stand by that statement.

BY MR. ARMENIO:

Q Okay. We can agree you don't say anything about context-dependent in that sentence in paragraph 99 of your declaration, right?

A I did not and still do not think I have to include "context-dependent."

Q For determining ordinary and customary meaning, since you say in your view it's context-dependent, what's the relevant context?

A A POSA would understand there are full-length antibodies; there are antibody fragments --

Q That's not my question, sir.

1 What context do you have to look at -- what's
2 the context? What do you have to review? If something
3 is context-dependent, what's the context you have to
4 look at? That's what I'm asking you.
5 MS. MAYS-WILLIAMS: So I didn't interrupt you
6 out of respect for the court reporter. But I'd also ask
7 that you give the witness the respect and allow him to
8 finish his response.
9 So, Dr. Presta, you may finish your response
10 before you tackle this new question. Go ahead, please.
11 Go ahead, please.
12 MR. ARMENIO: So, Counsel, we can disagree.
13 This is not a regular deposition, as you know well and
14 fully. It's a cross-examination.
15 And so if you really want the doctor to answer
16 a question I have not asked, I'm just going to move to
17 strike it because it's nonresponsive. I'm asking the
18 context. Okay?
19 MS. MAYS-WILLIAMS: And he can provide a full
20 answer. He's entitled --
21 MR. ARMENIO: No. He can answer the question.
22 MS. MAYS-WILLIAMS: He's doing his best to
23 answer the question. He's sitting here under oath, and
24 he's doing his best to answer the questions fully and
25 completely. Now, you must let him do that.

1 MR. ARMENIO: I disagree with your
2 characterization.
3 Q So, Doctor, for context-dependent, when you're
4 saying claim construction is context-dependent, what is
5 the context you are saying a person has to -- a person
6 of ordinary skill has to review? Is it textbooks? Is
7 it scientific papers? Is it patents? What is the
8 context they have to review to understand
9 context-dependent ordinary and customary meaning?
10 MS. MAYS-WILLIAMS: There are about seven
11 questions pending. Which one would you like him to
12 answer?
13 THE WITNESS: The context will depend on
14 the -- on what kind of antibody we are discussing.
15 BY MR. ARMENIO:
16 Q In connection with paragraph 99 in your
17 determining ordinary and customary meaning, did you look
18 at any textbook definitions of "antibody heavy chain"?
19 A No.
20 Q In connection with your ordinary and customary
21 meaning that you say is context-dependent, did you look
22 and do a literature search for what "antibody heavy
23 chain" means to the majority of practitioners as of 2012
24 in this area?
25 A No.

Q In connection with your ordinary and customary meaning, did you look through the entire specification of the '286 patent to see what information was provided about antibody heavy chains and what that might mean?

A Yes.

Q Okay. What did you look at?

A In the claims of the '286.

Q Other than the claims, did you look at anything else in the '286 patent to determine what you believed was the context-dependent meaning of "antibody heavy chain"?

A I read the specification, but I paid most attention to the wording in the claims.

Q In your understanding of "antibody heavy chain" in the claims of the '286 patent, does each antibody heavy chain have to have a variable region?

A When I read claim 1 of the '286, it does not mention variable domains.

Q So in your construction of "antibody heavy chain" that you applied to your entire analysis of the '286 patent set forth in Exhibit 1002, antibody heavy chain does not require the presence of a variable region; is that correct?

A Could you repeat, please?

MR. ARMENIO: Sure.

1 Could you read it back?
2 (Record read as follows:
3 "Question: So in your construction of
4 'antibody heavy chain' that you applied to your
5 entire analysis of the '286 patent set forth in
6 Exhibit 1002, antibody heavy chain does not
7 require the presence of a variable region; is that
8 correct?")
9 THE WITNESS: That is correct.
10 BY MR. ARMENIO:
11 Q If we look at Demonstrative 2, that
12 demonstrative antibody structure you gave on page 10 --
13 A I'm at page 10.
14 Q -- do we see -- it mostly looks like the
15 letter Y, right? Generally if we looked on the page, it
16 looks like the letter Y, right?
17 MS. MAYS-WILLIAMS: Objection. Vague.
18 BY MR. ARMENIO:
19 Q It's not a trick question.
20 A No, no. That's often how it is explained to
21 people who don't know anything about antibodies.
22 Q That's fine.
23 If we look at the bottom of the Y, that
24 actually has a job biologically, right?
25 MS. MAYS-WILLIAMS: Objection. Vague.

1 THE WITNESS: The base of the Y is referred to
2 as the "Fc region" and has several functions.
3 BY MR. ARMENIO:
4 Q Okay. So let's talk about the functions of
5 the Fc region.
6 What are the functions of the Fc region that a
7 POSA would have been aware of in 2012 biologically?
8 And when I say "biologically," I'm not trying
9 to be tricky. When an antibody like this goes into the
10 human body, the Fc region is actually, in wild-type
11 antibodies, going to do something, right?
12 MS. MAYS-WILLIAMS: Objection. Vague,
13 compound, and there are multiple questions in there.
14 I just want to make sure you have the question
15 in mind when you're responding.
16 THE WITNESS: With the proviso that we're
17 talking about IgG formats --
18 BY MR. ARMENIO:
19 Q We can certainly start there.
20 MS. MAYS-WILLIAMS: Please don't interrupt the
21 witness.
22 Were you finished? I just want to make sure
23 that the record is clear and that you have an
24 opportunity to give your testimony.
25 Were you done? And if not, please continue.

THE WITNESS: So for IgG formats, the Fc can perform primarily three functions.

There is a receptor called the FcRN that is involved in homeostasis of antibodies.

The Fc also binds to the complement system.

And the Fc region also binds to a set of receptors called "Fc gamma receptors," each of those having a slightly different function.

BY MR. ARMENIO:

Q Making changes in the Fc region has the potential to disrupt any one or more of the three functions for the Fc region that you just listed, correct?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: That is actually a very big research area in antibodies.

BY MR. ARMENIO:

Q Would you agree with me this far: In 2012, a person of ordinary skill in the art would know that making changes to the Fc region could potentially impact any of the three known functions for the Fc region?

THE WITNESS: Can you repeat that, please?

(Record read as follows:

"Question: Would you agree with me this far: In 2012, a person of ordinary skill in the art

would know that making changes to the Fc region could potentially impact any of the three known functions for the Fc region?")

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Pardon?

MS. MAYS-WILLIAMS: Objection. Vague. I apologize.

THE WITNESS: A POSA would have known that.

BY MR. ARMENIO:

Q And a POSA would know that the more changes you make to an Fc region, the greater the chance you could disrupt any of the Fc's three known functions, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Again, can you repeat? Sorry.

(Record read as follows:

"Question: And a POSA would know that the more changes you make to an Fc region, the greater the chance you could disrupt any of the Fc's three known functions, right?")

THE WITNESS: Again, this is an area where we have to narrow what we were talking about because that question is -- covers a lot of science.

BY MR. ARMENIO:

Q Would you agree with me this far: If I change

a dozen amino acids in the Fc region, I'm going to potentially be more concerned about disrupting Fc function than if I change two, in general?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Again, context. I could change 12 residues and not affect anything.

BY MR. ARMENIO:

Q So for you, you're saying which 12?

A I would have to know what was being changed in order to use my knowledge to say that would or would not affect potentially.

Q And in 2012, were there papers and publications that warned against touching, changing, certain portions of the Fc region?

A There were papers dealing with mapping residues in the Fc to all the different receptors. Shields 2001 JBC.

MS. MAYS-WILLIAMS: We've been going for about an hour. Would you like to take a break, get your coffee?

THE WITNESS: Get more coffee.

MS. MAYS-WILLIAMS: We'll keep it short, Peter.

MR. ARMENIO: That's fine with me.

(Recess, 9:34 a.m. - 9:44 a.m.)

MR. ARMENIO: We'll go back on the record, please.

Q Doctor, in an IgG antibody, each heavy chain has three constant regions, right? CH1, CH2, and CH3; is that correct?

A It depends on how you define "antibody."

Q Why don't we start with in nature.

A In nature.

Q An IgG antibody that we find in nature will have three constant regions in each heavy chain: a CH1 region, a CH2 region, and a CH3 region, correct?

A Not necessarily.

Q For the other IgG subtype antibodies found in nature, they all have either three or four constant regions, right?

THE WITNESS: Repeat that, please.

(Record read as follows:

"Question: For the other IgG subtype antibodies --")

MR. ARMENIO: I'll restate the question.

Q For the other Ig antibodies -- so we've got IgG, we've got IgA, we've got IgM, and I'm sure you know of even more Ig subtypes that occur in nature -- isn't it true that they all have at least three constant region domains: CH1, CH2, and CH3?

A If we attach the proviso that we are speaking of human antibodies, that statement is correct.

Q And you would agree with me in looking at the '286 patent that you discuss in your declaration, they weren't trying to find solutions to help cure mice or other animals; they were looking for potential human therapeutics, right?

MS. MAYS-WILLIAMS: Objection. Mischaracterizes the document.

THE WITNESS: As far as I remember, this patent covers humans.

BY MR. ARMENIO:

Q And there's even a claim that you remember to pharmaceutical compositions, right?

A Yes, one of the claims does cover.

Q And when a person of ordinary skill in the art reads about something being for a pharmaceutical composition, they understand that we're thinking about something that might be given to a human being as a treatment, right?

A Again, context-dependent.

Q In the context of the '286 patent, that's what we're talking about for pharmaceutical compositions, administration to a human being, right?

A In the context of the '286, the pharmaceutical

1 composition, I would assume, is for a human.
2 Q So let's look at page 12 of your declaration,
3 Exhibit 1002, please.
4 A I'm at 12.
5 Q Sure.
6 And you've got, at the top of the page, the
7 second half of a paragraph 29 started on the prior page.
8 You're free to read from the beginning of paragraph 29
9 if you want to orient yourself. I'm going to have
10 questions about your last sentence in that paragraph.
11 Just let me know when you're ready.
12 A Okay.
13 Q And this last sentence of paragraph 29, you
14 explain how the Fc region, more specifically the CH3
15 domain of the Fc region, plays a critical role in
16 dimerization, right?
17 A The Fc region does play a critical role.
18 Q And then you say that "Interactions occurring
19 between amino acid residues at the CH3-CH3 interface
20 contribute to the formation and stability of the heavy
21 chain linking."
22 Is that right?
23 A That is correct.
24 Q And you believed that to be a true statement
25 when you signed your declaration, right?

A And I still believe that.

Q That was my next question.

And you have no reason to doubt that any POSA would disagree [sic] with that. In your view, a person of ordinary skill in the art would believe that statement to be true, the "interactions occurring between amino acid residues at the CH3-CH3 interface contribute to the formation and stability of the heavy chain linking."

A person of ordinary skill in the art in 2012 would believe that statement to be true, right?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: A POSA would understand that to be true in 2012.

BY MR. ARMENIO:

Q And these interactions at the CH3-CH3 interface, they actually create part of the structure of the antibody, right? Bringing the monomers together to form a dimer, right?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: I'm a little bit confused there.

BY MR. ARMENIO:

Q Sure. So let me ask you a different question. And I appreciate what you're doing. It's exactly what I asked you at the beginning. When you don't understand a

1 question I ask you, please ask me to repeat it and
2 rephrase it. I'm happy to do that.
3 So these interactions that you're talking
4 about between two residues at the CH3-CH3 interface, you
5 say they contribute to the formation and stability of
6 the heavy chain linking.
7 Is their contribution by creating structure
8 like salt bridges between the CH3-CH3 regions? These
9 interactions become structural, right?
10 MS. MAYS-WILLIAMS: Objection. Compound.
11 THE WITNESS: There are different kinds of
12 interaction at the CH3-CH3. They can contribute to
13 structure, but they may also have additional modes of
14 stabilizing the antibody.
15 BY MR. ARMENIO:
16 Q One interaction that can occur at the CH3-CH3
17 interface is a salt bridge; is that right?
18 A Now, in order to answer that, I need to give
19 the proviso that CH3/CH3 interface can have two
20 components: an interior and a peripheral. And as far as
21 natural antibodies, the salt bridge could only be at the
22 periphery.
23 Q And that salt bridge is between oppositely
24 charged amino acids that exist at the periphery of the
25 CH3 interface in a natural antibody, right?

A When we have a charge-charge interaction that stabilizes the entire CH3 domain.

Q And that charge-charge interaction actually becomes part of the structure of the joined antibody and can be called a salt bridge, correct?

A So we -- one has to distinguish between two terms: "salt bridge" and "hydrogen-bonded salt bridge." Both can occur.

Q And are both structural features holding together an antibody?

A These are structural features, but they may not necessarily be involved in holding it together.

Q They are structural features that could be involved in holding together one CH3 domain with its opposite CH3 domain to hold together an antibody, right?

A That is a possibility.

Q When we look at claim 1 of the '286 patent, it tells us that we're going to have "a first nucleic acid molecule encoding a first antibody heavy chain."

Do you see that in 1a(i)?

A Right.

Q And in that first antibody heavy chain, we're going to have "at least one substitution of a neutral amino acid residue in the CH3 domain by a positively

charged amino acid residue."

Do you see that?

A 1a(i).

Q And so in 1a(i), in the CH3 domain of an antibody heavy chain, we're going to change a neutral amino acid residue to a positively charged amino acid residue, right?

A At least one substitution of a neutral for a positively charged.

Q Now if we look at 1a(ii), now we're going to look at a second antibody heavy chain, and that's going to have at least one substitution of a neutral amino acid residue in the CH3 domain by a negatively charged amino acid residue; is that right?

A Second molecule with a change neutral to negative.

Q And when we look further in the claim in 1b, starting at the fourth line of 1b, it says, "wherein the at least one positively charged amino acid residue substituted in the CH3 domain of the first antibody heavy chain interacts with the at least one negatively charged amino acid residue substituted in the CH3 domain of the second antibody heavy chain in the interface between said first and second antibody heavy chains to produce a heterodimeric antibody."

Do you see that?

A In 1b, yes.

Q And is it your understanding that this positive charge/negative charge interaction of the CH3 domain of the first antibody heavy chain and the second antibody heavy chain, according to the patent, that produces a heterodimeric antibody?

A I'm still a bit unclear with exact -- exactly what you're asking.

Q As you read the claim, the substituted positively charged amino acid residue from the first antibody heavy chain interacts with the negatively charged amino acid residue in the second heavy chain, and that interaction, according to the claim, produces a heterodimeric antibody, right?

A "Produces a heterodimeric antibody." The problem I have is just because the two interact, that might not necessarily give you the heterodimeric antibody.

Q And to satisfy the claim, there has to be an interaction that does give you the heterodimeric antibody, right?

A Yes.

Q So if there's just an interaction between the positively charged amino acid substitution on the first

antibody heavy chain and the negative amino acid substitution on the second antibody heavy chain, and those don't interact to produce a heterodimeric antibody, then that does not satisfy claim 1, correct?

A Correct.

Q And when I've got an interaction as required by the claim that actually produces a heterodimeric antibody, that is a structural feature, that interaction of the resulting antibody, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: We'd have to define "structural." I mean, a lot of these terms could be very general.

BY MR. ARMENIO:

Q Would you agree with me this far: The interaction discussed in claim 1, section (b), isn't a potential or theoretical interaction, it's an interaction that must produce a heterodimeric antibody to satisfy the claim?

A I agree.

Q In your declaration, you give us, as part of a background, right -- the background starts -- you call it a "Technological Overview." It starts on page 6, Roman numeral V.

I'm going to go forward into the part of the

technological overview that's on page 22. I want to always give you context. And you're free to look for yourself if you would like further context in your declaration. But my next questions are going to be on page 22.

On page 22, you discuss the knob-in-hole approach, KIH; is that right?

A In the section starting on page 22 labeled "Knob-into-Hole Approach," we do go through that, yes.

Q And you give us Demonstrative 6 on page 22; is that right?

A I don't understand. Oh, demonstrative.

Q On top of the picture it just says, "Demonstrative 6 - 'Knob-into-Hole Approach,'" right?

A I see it.

Q And that's actually a particular knob-in-hole approach depicted there, right?

MS. WILLIAMS: Objection. Vague.

THE WITNESS: It's a schematic of knob-into-hole. I couldn't tell particulars from that.

BY MR. ARMENIO:

Q Okay. A person of ordinary skill in the art looking at Demonstrative 6 would see there's a knob-in-hole feature, but there also appears to be a

disulfide bridge feature, and there also appears to be a common light chain feature from the schematic, right?

A In the schematic, what is highlighted is the knob-into-hole section.

Q Okay. Under the red box that says "Knob-in-Hole," that little line going from the CH3 region that's colored in black and the CH3 region that's colored in white, a POSA would know that that line is meant to represent a disulfide bridge, right?

A Assuming the POSA had read my papers, yes.

Q Okay. And when we look at the light chain, that's kind of got the hash-marked, zebra-striped coloring in the depiction, right?

A Those are the light chains.

Q And with this striping being the same, a POSA would understand that to be schematically representing a common light chain, right?

A A POSA might be a little less certain about that part. Again, these are schematics.

Q Fair enough.

So knob-in-hole as a technology, that was disclosed in the '286 patent, right? We can look, for example, column 4 around line 29 going to around line 37.

A What were the line numbers, please?

Q Sure.

Column 4, line 29 to line 37.

This knob-in-hole approach that you're mentioning in your declaration, Exhibit 1002, is also mentioned and discussed in the '286 patent, correct?

A Yes.

Q And on line 37, we see "Merchant et al. 1998." And I'll give you a copy of the paper as we get to that point in the deposition.

But that could also be called "Presta et al. 1998," right?

A It is "Merchant et al. 1998," with respect to Maggie Merchant.

Q And you were a co-author on that paper, right?

A I was. Yes.

Q So Merus in the '286 patent cites knob-into-hole and cites a number of things including one of your co-authored papers with Maggie Merchant, right?

A At lines 35 to 37.

Q And now a little farther down in column 4, starting -- it looks about at line 53 and going to about line 59, they discuss the work in your paper with Maggie Merchant in a little more detail, to talk about how

knob-in-hole was combined with a disulfide -- an additional disulfide bond between the two CH3 domains, right?

A Right. That's in lines 53 to about 57.

Q And Merus tells us that with knob-in-hole just by itself, those of skill in the art were seeing perhaps up to 87 percent heterodimeric purity; is that right?

A I think in the original knob-into-hole, we were better than 87 percent.

Q Okay. So Merus here is saying, in the '286 patent, 87; but then they cite your paper with Maggie Merchant and say that was increased to 95 percent with the addition of the disulfide bond; is that right?

A That's what we reported in the paper.

Q And that, to you, is an accurate statement, this Merus statement, that you and your colleague, Maggie Merchant, and other colleagues, were able to get a 95 percent heterodimeric purity by using knob-in-hole plus a disulfide bond strategy; is that right?

A That's what we reported in the paper.

Q And there was nothing to do with charge reversal, charge swap, no kind of charge engineering. You achieved that 95 percent by using knob-in-hole technique and an additional disulfide bond technique,

correct?

A Correct.

Q Now, if we look at page 24 of your paper --

A The paper or declaration?

Q I apologize.

If we look at page 24 of your declaration -- thank you for your clarification -- you see a Section 2, and it says, "Common Light Chain (CLC) Approach."

Do you see that?

A On page 24, yes.

Q Would you agree with me that the common light chain approach does not actually promote heterodimerization; it just reduces the number of possible contaminating species?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Repeat that again, please.

BY MR. ARMENIO:

Q Sure.

And I invite you -- you can read your own paragraphs 49 and 50, and then I'll ask you the question again. I'll give you a second, and then I'll ask you the question again.

A Okay.

Q Okay. Maybe I'll say it this way: As you have explained it, when a POSA uses a common light chain

1 approach in a bispecific antibody scenario, they go from
2 having ten possible results of the bispecific pairing,
3 which you show in paragraph 49, and they reduce it down
4 to three possible results, right?
5 A Agreed.
6 Q And so the common light chain approach
7 doesn't actually make the CH3 regions any more or less
8 likely to bond with each other. They just reduce the
9 number of possible outcomes from the two chains binding,
10 right?
11 A The common light chain solves the problem
12 that has nothing to do with the formation of the
13 heterodimer.
14 Q And if we look in the '286 patent, if we look
15 at column 3, there's a paragraph that goes -- column 3,
16 line 19 to about line 40.
17 Take all the time you need to take a look and
18 see if you agree with me that Merus's '286 patent
19 discloses the use of common light chain technology.
20 A Okay.
21 Q And do you agree that Merus's '286 patent
22 discloses common light chain technology in a way that's
23 consistent with how you discuss the common light chain
24 approach in your declaration, Exhibit 1002?
25 A The disclosure of the common light chain is as

in my declaration and in previous publications.

Q And page 26, that's the next place in your declaration, page 26, the next thing I'm going to ask you about.

Take a moment. Take a look at the figure and the accompanying text, page 26.

And the figure, it's called "Demonstrative 7," that's what you and Maggie Merchant, in your 1998 paper, did with combining a disulfide linkage with knob-in-hole, KIH, right?

A That was the Merchant, et al., paper.

Q And in paragraph 52, when you say, "We demonstrated that amino acids modified," you were part of the "we," right?

A Correct.

Q And this is the Merchant, et al., paper, and we've already discussed that that was noted, mentioned, in Merus's '286 patent, correct?

A That the Merchant paper was referenced, yes.

Q Including that the Merchant paper, you got 95 percent heterodimeric purity, right?

A That was in the paper.

Q And heterodimeric purity that approaches or equals 95 percent, you would call that efficient production of the heterodimer, right?

A That would be a good number to get.

Q 95 percent heterodimeric purity is a good number to get?

A Yes.

Q A POSA in 2012 would believe that 95 percent heterodimeric purity is a good number to get, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: If you could get 95 percent, you were doing good.

BY MR. ARMENIO:

Q And I believe in one of your papers -- and we can look at it as we go along if you want more specificity -- I believe you referred to it as near quantitative yield at 95 percent. And if you don't remember that, that's fine. I'll show you the exhibit --

A Yeah, I don't remember.

Q -- later in the day.

A So I don't know about that.

Q Quite all right. We'll get to that exhibit a little later in the day.

My next set of questions are going to be about paragraph 55. That's on page 28 of your declaration, please.

A Okay.

Q Now, in this paragraph, you're talking about a paper that is, in paragraph 55, referred to as Gunasekaran, right?

A That's the JBC paper, Journal of Biological Chemists.

Q And this is Gunasekaran Kannan as the author of this paper, is that right, as we discussed earlier?

A That is his name.

Q Let me give you a copy so we all have it in front of us. And this was previously marked by Xencor as Exhibit 1012.

In your declaration, you mention the Gunasekaran paper, and this paper dealt with changing existing charged amino acids at the periphery of the CH3 domain to the opposite charge; is that a fair description?

A That's what the Exhibit 1012 covered.

Q And one of the things Dr. Kannan and the co-authors are pointing to is, they pointed to earlier work. And this is on the first page, right-hand column, first full paragraph.

They say, "A strategy was proposed earlier by Carter and co-workers to produce an Fc heterodimer using a set of 'knob-into-hole' mutations in the CH3 domain of Fc."

Do you see that?

A First sentence in the second paragraph.

Q And are you aware of the Carter that's being referred to in that statement? Carter and co-workers with the knob-into-hole?

A Does that refer to Carter or to the publications? I mean, you asked me, and I don't know whether you're asking me did I know Carter, or did I know the publications.

Q Sure. Let's -- absolutely. Let's break it up.

Did you know Carter, the person?

A Yes.

Q Okay. And was Carter involved in antibody engineering work?

A The way for me to explain that, I was the architect; he was the contractor.

Q So in an unfortunate choice of words by Dr. Kannan, you would be in the "co-workers" section of that sentence; is that right?

A Unfortunately.

Q So you and Carter and others are mentioned as producing knob-into-hole mutations in the CH3 domain of the Fc, right?

A Yes.

Q And then the paper continues to talk about how this may lead to alteration of residue packing complementarity between the CH3 domain interface within the structurally conserved hydrophobic core.

Do you see that?

A Second sentence. Yes.

Q And you would agree with that; where you put the knob-into-hole mutations was in the hydrophobic core of the CH3 domain of the antibody heavy chain, right?

A Agreed.

Q And now in Dr. Kannan's view, he wanted to explore making changes that retained the integrity of the hydrophobic core and drive Fc heterodimer formation in a different way, right?

A That's what the paper states.

Q One of the things he mentions a few lines down in this same column, "In contrast to the knob-into-hole design, the homodimers were evenly suppressed due to the nature of the electrostatic repulsive mechanism."

Would a POSA have understood that in your knob-in-hole design, you're going to get even less homodimer formation between the two knobs versus the two holes?

There will be some difference in amount of

homodimer formation. They're still going to be lower than your heterodimer formation, but the amount of homodimers type 1 and type 2, if you will, will be different?

MS. MAYS-WILLIAMS: Objection. Vague, compound.

BY MR. ARMENIO:

Q I'm just asking, that's what Dr. Kannan is saying here, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: And that's what we found in the original paper.

BY MR. ARMENIO:

Q And so would you agree with this statement that Dr. Kannan makes here, "In contrast to knob-into-hole design, the homodimers were evenly suppressed due to the nature of the electrostatic repulsive mechanism"? And that's a contrast to knob-in-hole?

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: I'd have to refresh myself with the paper to see what they -- what numbers they got.

BY MR. ARMENIO:

Q And we'll get to that as either second next or

third next that we're getting to. So it won't be long.

So let's dig into the -- what's called in your declaration the "Gunasekaran paper," but it's Exhibit Xencor 1012.

The modifications that are evaluated here are all at the periphery of the CH3 domain; is that right?

A As far as I remember, that's true.

Q And if we look on page -- it says 5 of 22 in the Xencor number, or 19641 in the original journal numbering, you see there's a Figure B on the upper right of that page?

A I see it.

Q And in Figure B, we're seeing a depiction of the CH3 domain interface, right?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: Where is the description of B in the figure?

BY MR. ARMENIO:

Q Sure. It's in the small type under all the figures. On the second line it starts, "B, the figure shows."

A There it is.

Q "The figure shows the backbone trace of the CH3 domain interface structure."

1 Do you see that?
2 A This is one CH3 that we're looking into.
3 Q And we can see at the periphery, we've got
4 charged amino acid residues, and those are indicated
5 with the blue and red coloring, right?
6 A Agreed.
7 Q And then in the middle of that Figure B,
8 that's the hydrophobic core. That's the interior,
9 right?
10 A In Figure B, yes.
11 Q And in Figure B, S364 is shown to be present
12 in the hydrophobic core of the CH3 domain, correct?
13 A I cannot tell that from this figure.
14 Q Okay. If we read a little bit more about the
15 Figure B, it says, "Structurally conserved and buried
16 (solvent accessible surface area is less than or equal
17 to 10 percent) residues are shown in the ball-and-stick
18 model," okay?
19 S364 is shown with a ball-and-stick model,
20 right?
21 MS. MAYS-WILLIAMS: Objection. Compound,
22 scope.
23 THE WITNESS: Repeat the question, please.
24 BY MR. ARMENIO:
25 Q Sure.

Why don't I ask you -- why don't you go ahead and read, in the description of the figures, the second, third, fourth, and fifth lines, and any more of it if you'd like. But I think -- that's where I got my information to serve as the basis for the question. So I think it will help for you to take a look at that first.

A Okay.

Q So the paper is telling us that "Structurally conserved and buried residues have the ball-and-stick model, and solvent-exposed or structurally not conserved residues are shown in a stick representation."

Did I read that correctly from the paper?

MS. WILLIAMS: Objection. Scope.

THE WITNESS: So it would -- I would have to look on my own, three dimensions, which is what I'm used to.

What I don't -- what I can't figure out is "structurally conserved." Does the side chain have to be both structurally conserved and buried, or are they -- is the "and" linking two different kinds of residues?

BY MR. ARMENIO:

Q Understood.

For the S364 residue, a person of ordinary

skill in the art in 2012 knew that that was part of the CH3 domain, right?

A S364 is in the CH3 domain.

Q And further, in 2012, a person of ordinary skill in the art would know that S364 is present in the hydrophobic core of the CH3 domain, right?

A If the POSA didn't know that, they could look at the structure and determine that.

Q So in 2012, a person of ordinary skill in the art would either know right off the top of their head or easily determine from reference material that S364 was in the hydrophobic core of the CH3 domain, correct?

A Correct.

Q Same question for L368.

In 2012, a person of ordinary skill in the art would know that the L368 residue was in the hydrophobic core of the CH3 domain, and they would know that either right off the top of their head or would easily determine it from looking at an available reference material, right?

A Agreed.

Q Now, the paper we've been talking about, Exhibit 1012, tells the reader not to touch the hydrophobic core, right?

A Where is that?

Q So let's take a look at page 4 of 22 by the Xencor exhibit number, and it's page 19640 of the journal numbering. And we can look at the top of the right-hand column, but you're free to look at other portions of the paper if you would like.

Why don't I give you a moment to look at the top carryover paragraph and perhaps the next few lines. Let me know when you've had a chance to orient yourself in the document.

A Okay.

Q And this paper -- and you cited this paper in your declaration, right? Paragraph 55 and other places, right?

A Yes.

Q Okay. And so this paper that you cited tells us that in addition, exploiting charged residues as opposed to hydrophobic residues at the CH3 domain interface may have benefits in terms of retaining the generally favorable biophysical properties of the Fc; is that right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: May have.

BY MR. ARMENIO:

Q And benefits in terms of retaining favorable biophysical properties, those biophysical properties of

the Fc would include, for example, the three types of interactions the Fc region is involved in that you mentioned for us earlier today, right?

A State that again, please.

Q Sure.

The favorable biophysical properties of the Fc referred to on this page of the Gunasekaran paper, Exhibit 1012, would include the three potential functions of the Fc region in a human antibody that you mentioned to us earlier today, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: And, yeah, I don't think they discuss that.

BY MR. ARMENIO:

Q Then the paper continues, and it says, quote, "It has long been established that the hydrophobic core of protein domains plays an important role in protein folding and stability," right?

A That is true.

Q And the paper goes on to then explain how it created charge-pair mutations of specific residues that were not in the hydrophobic core of the CH3 domain.

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: That's the basis of this paper.

///

BY MR. ARMENIO:

Q And in your declaration, you cite and quote parts of the Gunasekaran paper, Exhibit 1012, right?

A Yes.

Q You did not cite or quote any of the two sentences we just read about maintaining, retaining favorable biophysical properties or the important role of the hydrophobic core of the protein domain, right?

A I did not include those two sentences in my analysis.

Q In preparing your declaration, did you reread the Gunasekaran paper, Exhibit 1012, front to back, or did you remember it because you had seen it previously in your work and for other reasons?

MS. WILLIAMS: I just want to caution the witness not to reveal the substance of any attorney-client communications in your response. But if you can answer the question without doing so, you may.

THE WITNESS: I reread all of the papers.

BY MR. ARMENIO:

Q Gunasekaran, if we look on the same page, lower down on the right-hand column, the last column, last paragraph starts, "When additional charge-pair mutations were combined."

Do you see that?

A Yes.

Q And he reports, "The combination of K409D:K392D in the Fc fragment with D399'K:E356'K in the scFv-Fc resulted in heterodimer formation almost exclusively."

Do you see that?

A I see that sentence.

Q So a POSA reading this paper would say, "They got almost pure heterodimer by using their charge reversal strategy at the periphery of the CH3 domain and leaving the hydrophobic core intact, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: That's the data they reported.

BY MR. ARMENIO:

Q And you, in connection with this case, have seen further data regarding charge swap technology at the periphery of the CH3 domain that led to 100 percent heterodimer formation, right?

A That is what is in reference 1012.

Q In addition to reference 1012 that you can get 100 percent by using charge swap at the periphery of the CH3 domain and leaving intact the hydrophobic core, that's also reported in the Lazar patent, Exhibit 1004, that you discuss in your declaration, right?

A Sorry. I need a copy of that one.

Q Sure. Let's see where we've got that hiding.

MS. MAYS-WILLIAMS: Actually, if we're going to go into Lazar, it's been about an hour. Let's take a break.

THE WITNESS: Hmm?

MS. MAYS-WILLIAMS: It's been about an hour and we're going to go into a new exhibit, so let's take a break. Off the record?

MR. ARMENIO: Yes.

MS. MAYS-WILLIAMS: Off the record.

(Recess, 10:43 a.m. - 10:57 a.m.)

MR. ARMENIO: Back on the record.

Q Doctor, we were talking about the paper by Gunasekaran Kannan, Exhibit 1012, and he was telling us that his charge swap strategy at the periphery of the CH3 domain could result in heterodimer formation almost exclusively.

Do you remember that discussion?

A Yes.

Q And if we look at Xencor Exhibit 1004, you refer to this in your declaration. There should be a copy in front of you there.

MS. MAYS-WILLIAMS: I think he's just orienting himself.

It's right here.

1 THE WITNESS: Oh, okay.
2 BY MR. ARMENIO:
3 Q And you cite and rely upon Xencor Exhibit 1014
4 in your declaration, right?
5 A I do rely on 1014 in the declaration.
6 Q And in 1014, if we look at, for example,
7 page 10 of 137 using the Xencor exhibit numbering at the
8 bottom, that's sheet 9 of 36, the figures, we can see
9 that there is a report of 100 percent heterodimerization
10 for a set of charge swapped amino acid residues, right?
11 A That's in Figure 6, continued on page 9 of 36
12 near the bottom.
13 Q And if we look 12 and 13 lines up, there are
14 two reports, and both 100 percent heterodimer formation,
15 right?
16 A There are two sets that seem to be exactly the
17 same.
18 Q And they both report 100 percent
19 heterodimerization; is that correct?
20 A That's what they have listed.
21 Q And for each of the residues, we see a letter,
22 a number, and a letter, right?
23 So, for example, reading left to right, the
24 first one is K370D, right?
25 A For the empty Fc, yes.

Q And a POSA would read that as -- naturally at residue number 370 there's a K, but in this instance it's been changed to a D, right?

A That's the standard format we use.

Q And if I read all the way across, I see there are three residues in the empty Fc, and there are three residues in the scFv-Fc, right?

A For this particular construct, yes.

Q And each of those is changing from a charge to the opposite charge for each residue, right? The Ks change to Ds, and the Es change to Ks, right?

A As well as the D399 to K.

Q So if I read from left to right, K370 goes to a D, K392 goes to a D, K409 goes to a D, E356 goes to a K, E357 goes to a K, D399 goes to a K, right?

A You said D399, right?

Q Yes, sir.

A Okay. I agree.

Q And that, Lazar tells us, gives you 100 percent heterodimer formation, right?

A That's the data they have in the table.

Q A POSA knows that's the maximum. There is no 101 percent with heterodimerization, right? 100 percent is the max, right?

A The POSA would understand that, yes.

Q And we see that's reported twice, right, in two lines?

A For that mutation set, yes.

Q All right. And then we see that if we look at page 12 of 137 by the Xencor exhibit numbering, sheet 11 of 36 of the figures, we see another report of 100 percent heterodimerization, right?

A In Figure 7, page 12 of 137, about the middle.

Q And in that one, we also see six residues identified by number. Three Ks are turned into Ds, right? K370 is turned into a D, K392 is turned into a D, K409 is turned into a D; is that right?

A In the empty Fc, yes.

Q And then for the scFv-Fc, E356 goes to a K, E357 goes to a K, and D, like "David," 399 goes to a K, right?

A In the scFv-Fc, yes.

Q So that's another charge swap construct, right?

A That is a charge swap.

Q And 100 percent heterodimerization reported, right?

A That's what the data says.

Q And for the empty Fc, we see what that looks like in Figure 1 of Lazar on page 2 of 137, correct?

MS. MAYS-WILLIAMS: Objection. Vague.
BY MR. ARMENIO:
Q So if we look at the right-hand -- there are figures on the bottom row. There are three. On the right hand, it says, "Fc Homodimer 2 [empty Fc] times 2."
Do you see that?
A On the right-most figure?
Q Yes, sir.
And so the right-most figure, bottom right of Figure 1 of the Lazar patent, we see two empty Fc constructs homodimerized, right?
A Figure 1, right side.
Q And in the empty Fc construct, we can agree there is no variable heavy chain region, right?
A As appearing from the picture.
Q So a POSA looking at empty Fc as illustrated in Figure 1 would know empty Fc does not have a variable region, correct?
A A POSA would discern that.
Q In this Lazar reference that you cite, when you were preparing your declaration, did you note whether the Lazar reference mentioned the Gunasekaran paper, Xencor Exhibit 1012?
Is that something you took note of mentally

while you were doing your review in connection with your declaration?

A I do not remember if I looked in Lazar for the Gunasekaran.

Q Sitting here today, you don't remember one way or another whether Lazar mentions Gunasekaran, right?

A I would have to go through the Lazar again to determine that.

Q Okay. So let's take a look in Lazar. It's page 12, specifically paragraph 125. Take a moment and take a look at that paragraph. Again, it's paragraph 125 on page 12 of the text.

So after the figures, then it will start with pages of text in the published application. And specifically it will be page 12 of the text, paragraph 125.

A We're going by numbers up at the top?

Q We can, or Xencor numbers, it's page 49 of 137 in the Xencor exhibit numbers.

A Okay. I have that.

Q So why don't you take a moment and review paragraph 125.

A Okay.

Q Do you see that the Lazar reference in paragraph 125 cites to the Gunasekaran Journal of

1 Biological Chemistry article, Volume 285, No. 25,
2 pages -- it says 1937, but through 19646 -- do you
3 understand that to be referring to the Xencor
4 Exhibit 1012 you and I have reviewed today in this
5 deposition?
6 A Yes.
7 Q And it says the words "all entirely
8 incorporated herein by reference."
9 Do you see those words?
10 A The last part of 125.
11 Q When you were doing your review and analysis
12 that went into your declaration about the Merus '286
13 patent, did you take that statement that Gunasekaran was
14 entirely incorporated herein by reference into account
15 in your analysis in some way?
16 A That was -- the 1012 was in my analysis
17 because it was in the list of exhibits that I needed to
18 consider.
19 Q Understood.
20 Do you, sitting here -- let me ask it this
21 way: In preparing your declaration for submission to
22 the board in this case, did you know what it meant for a
23 reference to be, quote, "entirely incorporated herein by
24 reference"?
25 A That it's all part of the specification.

Q Okay. And is it your understanding, then, that a person of ordinary skill in the art reading Lazar, paragraph 125, would know that the Gunasekaran reference, Exhibit 1012, is entirely incorporated -- the whole paper, Exhibit 1012, is incorporated into Lazar by reference? Right?

A The context would have to be, why was the POSA reading this patent, and to what level are they going to be reading it?

Q When the patent -- Lazar patent publication says it incorporates Gunasekaran entirely by reference, that includes the statements in Gunasekaran about the importance of the hydrophobic core, right?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: That would be my understanding.

BY MR. ARMENIO:

Q And now Gunasekaran, when it talks about it being long-established that the hydrophobic core of protein domains plays an important role in protein folding and stability, Dr. Kannan actually has end note 17 for that, right?

A That is reference 17 in the paper.

Q And so this isn't something that Dr. Kannan is just saying without attribution. He's citing the reader to reference 17, right?

A Brian Matthews. Yes.

Q And in your review of the Gunasekaran paper in connection with this case, did you pull and review reference 17?

A No.

Q Did anybody give you reference 17?

A Not that I remember.

Q Did you ask anybody for reference 17?

MS. MAYS-WILLIAMS: Objection. I'm going to instruct you not to answer that.

THE WITNESS: Pardon?

MS. MAYS-WILLIAMS: I'm going to instruct you not to answer that one.

THE WITNESS: I will follow counsel.

BY MR. ARMENIO:

Q I don't know that I agree with counsel, but I don't know that I have to make an issue of it, either.

We can agree that you didn't read reference 17 in connection with your preparation of your declaration, Exhibit 1002, in this case, right?

A I did not reread it.

Q And in your answer, you said you did not reread it. Do you recall reading it at some point in your career?

A I do recall reading Brian Matthews' paper.

MR. ARMENIO: Let's show you that paper that's 17 and see if this is the one you read at some point prior or not. And we'll mark this as Merus Exhibit 4001.

(Exhibit 4001 was marked for identification and is attached hereto.)

MS. MAYS-WILLIAMS: Before we get started, I'm just going to go ahead and object on the basis of hearsay and lack of authentication.

BY MR. ARMENIO:

Q So, Doctor, why don't you take a moment and compare reference 17 in the Gunasekaran paper to Merus Exhibit 4001, the Matthews paper that I just put in front of you.

MS. MAYS-WILLIAMS: Objection. Scope.

BY MR. ARMENIO:

Q So if you look at Gunasekaran, the endnotes references are on page 10 of 22 using the Xencor numbering, or page 19646 of the journal numbering.

And you can see reference 17 is to "Matthews, B.W. (1995) Advanced Protein Chemistry 46, 249 to 278."

Is that right?

A That's the reference 17.

Q Okay. And the paper I've put in front of you as Merus Exhibit 4001 by Brian Matthews, Advances in

1 Protein Chemistry, Volume 46, pages 249 to 278, does
2 that match up with reference 17 in the Gunasekaran
3 paper, Exhibit 1012?
4 MS. MAYS-WILLIAMS: Objection. Scope.
5 THE WITNESS: Reference 17 is this paper.
6 BY MR. ARMENIO:
7 Q So we can agree that reference 17 in
8 Exhibit Xencor 1012, which you cited and discussed in
9 your declaration, is Merus Exhibit 4001?
10 MS. MAYS-WILLIAMS: Objection. Scope.
11 THE WITNESS: Is this --
12 MR. ARMENIO: If we could put an exhibit
13 sticker on this.
14 MS. MAYS-WILLIAMS: I'm not going to object to
15 placing the sticker on the document, but I do want to
16 make note for the record, again, that I object to this
17 document on the basis of hearsay and lack of
18 authenticity.
19 BY MR. ARMENIO:
20 Q So, Doctor, what you've had placed in front of
21 you is Merus Exhibit 4001. That correlates and is
22 reference 17 from the Gunasekaran paper discussed in
23 your declaration, correct?
24 MS. MAYS-WILLIAMS: Objection. Scope.
25 Sorry. Did you say Exhibit 4001? I'm just

lost. I'm sorry.

THE WITNESS: Exhibit 4001 corresponds to reference 17 in the Gunasekaran paper.

BY MR. ARMENIO:

Q Perfect.

And you did not reread Exhibit 4001 in connection with preparing your declaration in this case, correct?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: I did not.

BY MR. ARMENIO:

Q Do you remember reading Merus Exhibit 4001 at any time?

MS. MAYS-WILLIAMS: Asked and answered.

THE WITNESS: I remember reading it. That was a long time ago.

BY MR. ARMENIO:

Q Fair enough.

If we look at page 277 of Matthews, Matthews tells us that, quote, "Taken together, substitutions of core residues confirm the overall importance of the hydrophobic effect as the dominant factor in stabilizing the folded structures of proteins," closed quote, correct?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: "Taken together, substitutions of core residues confirm the overall importance of the hydrophobic effect as the dominant factor in stabilizing the folded structure of proteins."

BY MR. ARMENIO:

Q And that is consistent with what Dr. Kannan is citing it for as citation 17 in the Gunasekaran paper, correct?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: I have to go through this entire reference to make sure that that's what Kannan was -- was quoting from this paper.

BY MR. ARMENIO:

Q Both Gunasekaran, which is Xencor Exhibit 1012, and Matthews, which it cites, Merus Exhibit 4001, tell the reader that the residues in the hydrophobic core are important to protein folding and stability, correct?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: These statements were known even before these.

BY MR. ARMENIO:

Q So a person of ordinary skill in the art in 2012 would know that the residues in the hydrophobic core of the CH3 domain were very important to protein

folding and stability, correct?

MS. MAYS-WILLIAMS: Objection. Scope, vague.

THE WITNESS: Again, that would be true, but there are other factors involved.

BY MR. ARMENIO:

Q When we look at the order of operations, for lack of a better term, does each chain fold first and then dimerize, or do they dimerize and then fold?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: You're referring to the Fc of an antibody?

BY MR. ARMENIO:

Q Sure.

A That's very complicated. It's -- I don't know that it is either one of those.

Q From general knowledge from a person of ordinary skill in the art and/or from their review of Exhibit Xencor 1012 and Merus 4001, a person of ordinary skill in the art would know that the hydrophobic core of the CH3 region in a heavy chain is very important to protein folding and stability, right?

MS. MAYS-WILLIAMS: Objection. Vague, scope.

THE WITNESS: A POSA, in 2012, would know that the hydrophobic core was one of the factors contributing to stability. I'm not sure a POSA would understand the

1 intricacies of what controlled protein folding.
2 BY MR. ARMENIO:
3 Q When we look in the Merus '286 patent, it
4 mentions the Gunasekaran paper and its charge reversal
5 strategy, right? And I can point you to column 5 if it
6 helps.
7 So if you look in the Merus '286 patent,
8 that's the subject of your declaration.
9 A That's the declaration.
10 Column 5, you said?
11 Q Right.
12 And where we started in this line of
13 questioning, we started in your declaration where you
14 discussed the Gunasekaran paper. Then we took a look at
15 the Gunasekaran paper itself and its citations.
16 And now my question to you is whether the '286
17 Merus patent actually cites and discusses the
18 Gunasekaran paper.
19 A Column 5, second full paragraph, they
20 reference the Gunasekaran, et al., 2010.
21 Q And they -- further, Merus discusses the
22 Gunasekaran 2010 paper and calls it a "charge reversal
23 strategy," right?
24 A Id est, a charge reversal strategy.
25 Q And that's a fair characterization of the

1 Gunasekaran paper, right? That it reflects a charge
2 reversal strategy?
3 A That was the point of the Gunasekaran paper.
4 Q And earlier today, we mentioned the SEED,
5 S-E-E-D, technology. If we look a little higher in
6 column 5, lines 5 to 16, we see that Merus also
7 discusses the SEED technology and approach for making
8 bispecific antibodies, right?
9 A That's in the '286, column 5, first full
10 paragraph.
11 Q So when we look at the prior methods for --
12 and approaches for bispecific antibodies mentioned in
13 your declaration, the knob-in-hole, the knob-in-hole
14 with a disulfide bond, charge reversal, the SEED
15 approach shown in the figure, the Merus '286 patent
16 discusses each and every one of those, correct?
17 A Column 5, yes.
18 Q It also discusses the common light chain
19 approach which, as we discussed, doesn't affect
20 heterodimerization but reduces the number of possible
21 products, right?
22 A So where is the discussion of common light
23 chain again?
24 Q Column 3 --
25 A Column 3. Okay.

Q -- lines 19 to 40.
A Okay.
Q So the Merus '286 patent mentions all of these approaches, right?
A It does.
Q And a last question or two, and then we can put the Gunasekaran and Matthews papers aside for now.
You did not cite the Matthews paper, Merus Exhibit 4001, anywhere in your declaration, correct?
A As far as I remember, no.
Q Let's look at Lazar, page 66 of 137 in the exhibit numbering, please. I'm going to be asking you a few questions about Example 2 that also goes over to the next page.
So why don't you just take a moment, orient yourself. Take a look at it if you'd like. And then we'll ask questions.
A So we're looking at the examples? Okay.
Q And as before, you're free to look at whatever you want. But where my questions are springing from, they're springing from the examples.
A Okay.
Q Great.
In your declaration, you talk about Example 2 of Lazar, right?

A Where is --

Q For example, it's on page 68, paragraph 131; and then it's also page 86, paragraph 171. You can look at either one first. We will get to both of them.

A What was the second one, the reference?

Q Page 86, paragraph 171.

So let's take a look at Example 2. Example 2 talks about a screen for Fc variants, right? It's in the first sentence.

A Yes.

Q And they were screening using an empty-Fc/scFv-Fc system that is illustrated in Figure 1, right?

A That's the system they use to screen their mutations.

Q And we already looked at Figure 1; is that correct?

A In Figure 1, the middle bottom is the system they used.

Q And so what they're looking at is, they're looking at the scFv Fc, and they're looking at the empty Fc, and they're looking at rates of heterodimerization and homodimerization between those monomers, right?

A For each of their tested variants one and two, they analyzed how much heterodimer and how much each of

the homodimers.

Q As shown in Figure 1, none of the variants are an IgG antibody, right?

A Again, that depends on how we define it. But --

Q Well, we know -- sorry. Go ahead.

MS. MAYS-WILLIAMS: Go ahead. Finish your answer.

THE WITNESS: -- this is the system they use to test.

BY MR. ARMENIO:

Q The system they use to test, the scFv component on one of the monomers, that actually comes from a mouse, right?

A Say that again, please.

Q The scFv portion the one of the monomers, right -- because only one of the monomers has the scFv, right? Is that correct so far?

A That is correct.

Q And that scFv that exists on only one of the monomers, it's the only scFv, that is derived from a murine anti-CD3 antibody, OKT3, correct?

A That's what it states in paragraph 239.

Q So as a first instance, I know a human IgG antibody is not part mouse, right?

A They are describing a test system.

Q And right now, I'm trying to understand what they tested. And what they tested, neither of the monomers that they tested is a human IgG heavy chain, right?

A The system they used was designed to be easily --

Q Not my question.

MS. MAYS-WILLIAMS: Let him finish. Let him finish.

Go ahead, Dr. Presta.

THE WITNESS: The system they used was designed to make analysis of their variants as easy as possible.

MR. ARMENIO: I apologize. For the record, I have to object and move to strike.

Q It's no offense to you. It's just part of the proceeding we're in.

Can we agree that a human IgG heavy chain does not have a murine component?

A With the proviso that we're talking about native IgG, I agree.

Q Can you agree with me that a native human IgG heavy chain has a CH1 domain in addition to a CH2 and CH3 domain?

A Agreed.

Q And a person of ordinary skill in the art would agree with the statements just made that a native human IgG heavy chain does not have a murine component and does have a CH1 domain, right?

A Agreed.

Q And so all of the test results we see -- and they're reported in Figure 5 and Figure 6 and Figure 7 -- these are all made with the Figure 1 constructs; is that right?

A That's in the Figures 5, 6, and 7.

Q And can we agree that everything discussed in Example 2 of Lazar, Exhibit 1004, was made using the Figure 1 constructs?

A That was their test system.

Q Can we agree that there is nothing in Example 2 that discloses combining a human IgG heavy chain with another human IgG heavy chain in Example 2?

That's not what they were looking at in that example, right?

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: Example 2 covers their test system. Further examples they transfer to other formats.

BY MR. ARMENIO:

Q And Example 2, you will agree with me, discusses only their test system, and their test system is depicted in Figure 1 of Xencor Exhibit 1004, correct?

A Correct.

Q Let's take a look at -- I think this is sometimes referred to as Arathoon. We need to get you a better publicist because this is another Presta publication.

A You will notice Genentech always goes alphabetic. So I have no control.

Q This one is previously marked as Xencor Exhibit 1006.

So Xencor Exhibit 1006, this is a document you discuss in your declaration regarding the '286 patent; is that right?

A Correct.

Q And in this publication, you are one of the named co-inventors along with Arathoon and Merchant and Carter, some of the names we've seen and discussed earlier today, right?

A We were co-inventors.

Q And what all of you were working on was a knob-in-hole approach, KIH approach, in some instances with an added disulfide bond, in some instances with

common light chain, right?

A That's the gist of what we did.

Q Nothing in Xencor Exhibit 1006 about charge reversal or charge swap; that wasn't what you were looking at in this published patent application, right?

A We did not consider charges, reversal or otherwise, in this particular study.

Q And so a person of ordinary skill in the art reading 1006, Exhibit 1006, they would say, "I see what Dr. Presta and his colleagues are doing there. They're working on KIH. They're working on perhaps disulfide bonding. They may have common light chain. But they're not working on charge reversal, charge swap. They're not working on anything to do with charge to do with heterodimer formation," right?

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: For this patent application, we did common light chain, we did knobs-into-holes, we did disulfide bonds.

BY MR. ARMENIO:

Q In this application, Exhibit 1006, you didn't do any kind of charge reversal, charge swap, or charge engineering, correct?

A Correct.

Q And a person of ordinary skill in the art reading Exhibit 1006 would understand that having read the document, right?

A They should have.

Q Let's take a look.

This is marked already as Xencor Exhibit 1015. You're a co-author on this paper with Ridgeway and Carter; is that right?

A Protein Engineering, 1996, John Ridgeway, me, and Paul Carter.

Q And you cite this paper in your declaration, correct?

A Yes.

Q And in this paper, we had a discussion about what level of yields you may or may not have reported. We can see there's a reported yield in the abstract at the beginning of the paper and maybe other places as well.

But even in the abstract, we can see a yield; is that right?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: In the abstract, we do state a yield in our system.

BY MR. ARMENIO:

Q And in that statement, what you're presenting

there is the yield of heterodimeric formation for an actual IgG hybrid antibody, right?

A The test system was -- one arm was an anti-CD3 fab. The other arm was a CD4Fc fusion to make analysis doable.

Q So not a complete IgG antibody, but a test system with two variable regions?

A Again, as in the other reference, we used a test system that made analysis much easier than if we had used a full IgG.

Q In your test system in Exhibit 1015, there were two variable regions; is that right?

A No.

Q Just one?

A The anti-CD3 had a variable region. The other arm had a human CD4 protein fused to the Fc. So there was no variable region.

Q Understood.

So just one variable region in what you reported?

A Correct.

Q In this paper, you use the knob-in-hole approach to bispecific formation; is that right?

A This was the original knob-into-hole paper.

Q This one did not have a disulfide bond added

to the knob-in-hole mutation, right?

A In this paper, we did not investigate additional disulfides.

Q And even without the disulfide bonding, you're reporting 92 percent heterodimer formation; is that right?

A That's what was reported in this paper.

Q And similar to our discussion before, if we look in the discussion on page 619 of the paper, 3 of 5 of the exhibit, you call that "efficient heterodimerization," right?

A Compared to not knobs-in-holes, which theoretically would be 50 percent, 92 percent was great. First time this has ever been done.

Q And when we see reference to Carter, et al., knob-in-hole papers, this is the paper, right? This is the one? This is the first report of knob-in-hole?

A This is the first report of knob-in-hole, or of any Fc-Fc CH3 engineering.

Q Let's take a look at another one of the papers we discussed earlier today. This is Xencor Exhibit 1017. And you're a co-author with Maggie Merchant, Paul Carter, and others; is that right?

A Exhibit 1017, I was a member of the group of authors.

Q And you cited this exhibit in connection with your declaration, correct?

A I think it's on there. Yes.

Q And if we look on the second page of the exhibit, page 678 of the paper, there's a Figure 1 presented; is that right?

A Left side of page 2 of 5.

Q And we see in that figure depicted a knob-in-hole set of mutations, correct?

A Correct.

Q And we also see an additional disulfide bond between the CH3 domains, correct?

A That's what that lower part of the figure represents.

Q And we don't see any charge reversal, charge swap, charge engineering of any kind reflected, correct?

A That was not the purpose of this study.

Q And in Table 1, you reported yields up to and including -- I see a 95 plus/minus 2, I see a 95.5 plus/minus .5.

So yields at least approximating 95 percent are reported, correct?

A In Table 1.

Q And in 2012, that was, as you report in the abstract on the first page of the paper, near

1 quantitative heterodimerization, correct?
2 A That's what's in the -- in the abstract.
3 Q And by "near quantitative," you and your
4 authors meant it's almost completely heterodimers using
5 this approach, right?
6 A Again, compared to no engineering at
7 50 percent.
8 The point of this paper was, if you add the
9 disulfide onto the knob-in-the-hole, we increase the
10 heterodimerization.
11 Q And so, for example, if a person of ordinary
12 skill were following the art, they would see your prior
13 paper with Ridgeway and Carter, Xencor Exhibit 1015, and
14 see that you improved the heterodimerization yield by
15 adding the disulfide bond in Exhibit 1017, right?
16 A That was the point of the paper.
17 Q And with that added disulfide bond, you were
18 at near quantitative heterodimerization without touching
19 anything to do with charge, right?
20 MS. MAYS-WILLIAMS: Objection. Vague.
21 THE WITNESS: As stated in the paper, we could
22 get 95 percent with combination.
23 BY MR. ARMENIO:
24 Q Now, there's a discussion at some point in
25 your declaration about Arathoon and Lazar.

Now, Arathoon, as seen from that example, that's knob-in-hole with disulfide bond, right? And you've got the Arathoon patent in your pile if you want to look at it.

A No, that's -- I know that patent.

Q I mean, that's you, right?

And then Lazar, Lazar is charge. It's looking at charge issues.

MS. MAYS-WILLIAMS: I object to the form of the question. Vague, mischaracterizes evidence.

THE WITNESS: Could you say it again, please?

BY MR. ARMENIO:

Q Sure.

Lazar and Arathoon take two different approaches to bispecific antibody formation, right?

MS. MAYS-WILLIAMS: Objection. Form.

THE WITNESS: Yes.

BY MR. ARMENIO:

Q In connection with this case, did you investigate what was known in the literature and available to persons of ordinary skill in the art about whether you should or should not try to combine knob-in-hole approaches with charge approaches?

A Please state that again so I can get it straight.

Q Sure.

In connection with preparing your declaration, did you investigate whether there was any literature available to a person of ordinary skill in the art in 2012 that would inform them whether they should or should not try to combine a knob-in-hole bispecific formation approach with a charge engineering bispecific antibody formation approach?

A That was discussed in the Cabrera patent.

MR. ARMENIO: Let's take a look.

Please mark it as Exhibit 4002.

(Exhibit 4002 as marked for identification and is attached hereto.)

MS. MAYS-WILLIAMS: I'm going to object to this exhibit on the basis of hearsay and lack of authenticity. It's also outside the scope of Dr. Presta's declaration.

BY MR. ARMENIO:

Q Once you've had a chance to review Merus Exhibit 4002, Dr. Presta, can you tell me whether you reviewed this document in connection with preparing your declaration in this case?

A I did not.

Q Have you had occasion to review Merus 4002 previously in your work?

A I have read this paper when it first came out.

Q And you personally don't have any doubts that Merus 4002 was an actual paper available to be read by those of ordinary skill in the art in 2012, do you?

MS. MAYS-WILLIAMS: I'm still going to object on the basis of hearsay and lack of authenticity and scope.

THE WITNESS: I don't remember -- so this was in -- this publication was a chapter in a book by Roland Kontermann called "Bispecific Antibodies." And I don't know how available that book was to everybody.

I do remember that Zhenping sent me a copy.

BY MR. ARMENIO:

Q So you certainly had a copy of the book that contained Merus Exhibit 4002?

A No, I had a copy of the reprint from that book.

Q Understood.

So during your work -- ordinary course of your work as a scientist, you reviewed Merus 4002, right?

A I read --

MS. MAYS-WILLIAMS: Objection. Hearsay, lack of authenticity, and scope.

THE WITNESS: I read 4002 many, many years ago.

BY MR. ARMENIO:

Q And 4002, we can agree you did not include this in your declaration to the board regarding Merus's '286 patent; is that right?

A I did not include it.

Q And if we look at page 156, you see there's a Section 9.3.1.4, "Other Novel Fc-Heterodimer Formats"?

A I see that section.

Q Do you see the statement seven lines down, quote, "If the knobs-into-holes technology is combined with the charge polarity engineering, a higher ratio of heterodimer formation may be achieved. However, a drawback of these methods is the inclusion of multiple mutations in the CH3 domains, which may pose an immunogenic risk in therapeutic settings."

Do you see that?

MS. MAYS-WILLIAMS: Objection. Vague, scope.

THE WITNESS: I see that sentence.

BY MR. ARMENIO:

Q And do you agree, as a general principle, that the more mutations you make in a CH3 domain, the greater immunogenic risk in a human therapeutic setting?

MS. MAYS-WILLIAMS: Objection. Vague, scope.

THE WITNESS: We would have to narrow what we're thinking about in the CH3 domain.

BY MR. ARMENIO:

Q As a general principle, with antibodies that are going to be administered to a human being, the farther a person or scientist gets away from the native human antibody format, the more likely there can be an immunogenic or other problem, right?

MS. MAYS-WILLIAMS: Objection. Scope, vague.

THE WITNESS: We have to put -- to focus this. It's a very broad subject.

BY MR. ARMENIO:

Q Understood.

So let's take a look at the '286 patent and see if it helps us. If we look at column 11, lines 20 to 30 --

A Which line numbers again, please?

Q Sure. 20 to 30 in column 11, please. I want you to take a moment, orient yourself. I have a few questions.

A And we're looking at "Antibodies for therapeutic use are preferably as close to natural antibodies of the subject to be treated as possible (for instance human antibodies for human subjects)."

Q You would agree with that statement, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: No.

BY MR. ARMENIO:

Q We can see that Merus, in the '286 patent, is saying, "If you are going to have a therapeutic antibody, you should preferably stay as close to natural antibodies as possible."

That's what they're saying, right?

A That's what they said. I do not agree.

Q And they have claims to pharmaceutical compositions that are going to be administered to human beings, right?

A They do have a claim for pharmaceutical compositions.

Q And in Merus 4002, Pei Jin and co-author are telling us to be careful about multiple mutations in the CH3 domains because they may pose an immunogenic risk in therapeutic settings.

That's what they're saying, right?

MS. MAYS-WILLIAMS: I'm going to object again to this exhibit and every question relating to this exhibit on the basis of hearsay and lack of authenticity.

I'm also going to object on the basis of this exhibit being outside the scope of the declaration of Dr. Presta.

MR. ARMENIO: Can you reread the question,

please?

(Record read as follows:

Question: And in Merus 4002, Pei Jin and co-author are telling us to be careful about multiple mutations in the CH3 domains because they may pose an immunogenic risk in therapeutic settings. That's what they're saying, right?")

MS. MAYS-WILLIAMS: Objection. Hearsay, lack of authenticity, scope.

MR. ARMENIO: So, counsel, you now objected to the same question three times. I had the question reread so the witness could actually hear it and respond. Your objections are on the record. If you make it again, you're just being disruptive.

So can you please reread the question?

Counsel's objections are noted, right? The record doesn't disappear, Doctor. But I want you to be able to hear the question, and then I would ask you to respond, please.

MS. MAYS-WILLIAMS: And I'll make the same objections.

Go ahead.

MR. ARMENIO: If you do, it's just being disruptive purposefully, and it's improper.

///

(Record read as follows:

"Question: And in Merus 4002, Pei Jin and co-author are telling us to be careful about multiple mutations in the CH3 domains because they may pose an immunogenic risk in therapeutic settings. That's what they're saying, right?")

MS. MAYS-WILLIAMS: Same objection.

THE WITNESS: That's what they said. I don't necessarily agree with it.

BY MR. ARMENIO:

Q In connection with this case, did you review the entire prosecution history for the '286 patent that Merus obtained?

MS. MAYS-WILLIAMS: I think that's asked and answered. We can take it before we take a break.

I just do want to say, if we're going to move on to another exhibit, it might be a good time for lunch.

But go ahead and answer the question if you understand it.

THE WITNESS: Can you give me the question again?

MR. ARMENIO: I think it's clear that since counsel would like us to take our lunch break, I don't think anyone needs to have one more question before

1 lunch.
2 So why don't we all go, enjoy our lunch, and
3 we'll have plenty of time when we come back. I
4 appreciate your patience all morning.
5 (Recess, 12:06 p.m. - 12:44 p.m.)
6 MR. ARMENIO: Back on the record.
7 Q Welcome back from lunch, Doctor. Are you
8 ready to proceed?
9 A Um-hum.
10 Q And do you recognize you're still under oath
11 from this morning?
12 A Yes.
13 Q Great.
14 So before we took our lunch break, we were
15 just about to talk about the prosecution history for the
16 '286 patent.
17 In connection with your own patents, have you
18 been involved in the actual back-and-forth interactions
19 with the patent office, so-called patent prosecution?
20 A Luckily, no.
21 Q So as a result of that, are you somewhat
22 unfamiliar with the documents that make up a patent
23 prosecution history file?
24 MS. MAYS-WILLIAMS: Objection. Vague.
25 THE WITNESS: I've looked at some, but I've

not been intimately involved in the whole process.
BY MR. ARMENIO:
Q Okay. Let me show you one for the '286 patent, and let's see how we do. Xencor has already marked this for us as Exhibit 1008.
We can see that this exhibit, Xencor 1008, is a 346-page document. Did you review this document in connection with preparing your declaration in this case, Exhibit 1002?
A No.
Q And given that you did not review the document in connection with preparing your declaration in this case, Exhibit 1002, it's fair to say you didn't take any particular statements made in connection with this prosecution file into account in your declaration, right?
A Statements from this?
Q From inside this document. Since you didn't review it --
A No.
Q -- we can safely say you didn't rely on any statement one way or the other that might be contained in this document in preparing your declaration, Exhibit 1002, correct?
A I did not.

Q And you can put that aside then.

When we look at the '286 patent, in particular, I want to ask you a few questions about column 18. So I'm going to give you a moment to get to column 18, and I'm going to ask questions especially around line 7 to around line 21.

Take a moment and orient yourself to that part of the document, and when you're ready, I'll ask you some questions.

A Down to about what line?

Q 7 to about 20 is, I think, enough context. But, of course, you're always free to look at more if you want. But I think it's a good start for the questions that I'll have for you.

A Okay.

Q So in the patent, column 18 in Exhibit Xencor 1001, around line 7, it says, quote, "The present invention in this embodiment does not exchange charged contact amino acids by amino acids of opposite charge but substitutes non-charged CH3 amino acids for charged ones."

Do you see that?

A Between 7 and 10. Yes.

Q And so the inventors of the '286 patent are making a statement that differentiates between charge

swapping, taking one charged amino acid and flipping it to an opposite charge, versus what they're doing in the '286 patent of substituting non-charged CH3 amino acids for charged ones.

Do you see that?

A I agree with that.

Q And charge swapping, we saw an example of charge swapping in the Gunasekaran 2010 paper that we talked about earlier today, right?

A In the 1011. No, 1012.

Q Exactly right. Exhibit 1012.

The paper by Gunasekaran, we saw in that paper an example of charge swapping, right?

A That was the main point of that paper.

Q And the inventors of the Merus '286 patent are differentiating themselves in this statement from the charge swapping by saying what they're doing is different. They're saying they're substituting non-charged CH3 amino acids for charged ones.

That's what they're saying, right?

A That's what that statement says.

Q And they say, if we continue on, "The approach of the present invention provides not only a method for efficiently steering the dimerization of CH3 domains but also has the advantage that at least one additional

charge-charge interaction in the CH3 interface is created."

Do you see that?

A Yes.

Q And then it explains that "in view of this additional charge-charge interaction on top of the existing charge pairs in the CH3-CH3 interface, the dimers according to the invention are generally more stable as compared to the wild-type dimers," right?

A For that last part, I need to see -- check the data.

Q For purposes of my question, it's more -- do you see the statement I'm pointing to? And then I'll ask you a question about it.

Do you see the statement I'm pointing to --

A Yes.

Q -- about an additional charge-charge interaction?

A I see that statement.

Q Now, if a person of ordinary skill in the art practices the '286 patent, leaves the existing charged amino acids alone, and changes a neutral to a positive in one heavy chain and a neutral to a negative in another heavy chain, you create, according to the inventors, an additional charge pair, right, as compared

to the native antibody format?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Pardon?

MS. MAYS-WILLIAMS: I said, "Objection. Vague." It's also compound.

THE WITNESS: Assuming that those two interact, the two substitutions interact at the interface.

BY MR. ARMENIO:

Q And that's not a given. You have to know whether they interact to produce a heterodimer, right?

A Because the two wild-type amino acid side chains interact does not necessarily mean when you substitute, the substitutions will interact.

Q Understood.

If we make the substitutions of neutral to charge as set forth in the '286 patent and they interact to produce a heterodimer, you will have an additional charge-charge interaction over and above the wild-type charge-charge interactions, correct?

A You will have that additional interaction.

Q In the papers we've discussed today, we have not seen anyone suggest to add an additional charge-charge interaction over and above the wild-type charge-charge interactions, correct?

A In the papers we have discussed thus far, no.

Q So nobody has suggested an additional charge-charge pair over and above the wild-type charge-charge pairs in the paper we've discussed -- papers we've discussed and references we've discussed today, correct?

A We may have to look more closely at that.

I can't quite find it, but I remember -- I think I remember in the Kannan Gunasekaran, they did make a statement about, we've done charge-charge, but you could also think about neutral to charge. It would take a while to find it.

MS. MAYS-WILLIAMS: Take the time you need.

THE WITNESS: I know it's in here.

BY MR. ARMENIO:

Q So what I think you're referring to is a reference in your other declaration, which is part of the peril of doing two IPR depositions on the same day.

So for my question, on the references we've discussed so far today that are in your declaration regarding the '286 patent, none of those references suggest adding an additional charge pair over and above the existing charge pairs as far as you remember, right?

MS. MAYS-WILLIAMS: You said "references." Including those in the declaration, right?

1 MR. ARMENIO: For this patent. Yes, please.
2 THE WITNESS: I don't remember if it's in
3 the -- in 1012, the statement that you can additionally
4 go from neutral to charge.
5 BY MR. ARMENIO:
6 Q So that's where, if we had the time, we'd go
7 through and read, front to back, Exhibit 1012. And if
8 the statement is in there, it's there, and if it's not,
9 then nothing we've reviewed regarding the '286 patent is
10 telling us to add an additional charge, as far as you
11 recall?
12 MS. MAYS-WILLIAMS: Objection. Form.
13 Take your time. Take the time you need.
14 THE WITNESS: Have we looked at 1007?
15 MS. MAYS-WILLIAMS: Do you want 1007?
16 THE WITNESS: I remember it either being in
17 1012 or 1007. I don't think we've done 1007 yet.
18 BY MR. ARMENIO:
19 Q Okay. So Exhibit 1012 or Exhibit 1007 would
20 be the places you would want to look if we had the time
21 and would read those front to back.
22 If there's a statement about additional --
23 adding an additional charge pair over and above the
24 wild-type charge pairs, that's where you would look --
25 MS. MAYS-WILLIAMS: Objection.

1 BY MR. ARMENIO:
2 Q -- from the documents we've discussed so far
3 today; is that fair?
4 MS. MAYS-WILLIAMS: I don't think that is
5 fair. Objection. It's not a memory test.
6 You can take the time to look. If you can't
7 remember --
8 MR. ARMENIO: And I'm not trying to make it a
9 memory test.
10 Q I'm asking, as far as you recall, if there is
11 such a statement, it's in Exhibit 1012 or Exhibit 1007,
12 as far as you remember?
13 MS. MAYS-WILLIAMS: But you're asking him off
14 the top of his head, and we have hundreds of pages in
15 front of us. I don't think that that's a fair question.
16 MR. ARMENIO: It's perfectly fair to ask
17 somebody what they remember. Whether they remember it
18 or not, they can testify to their memory, always.
19 THE WITNESS: I remember the statement. I
20 think it is in 1012 or 1007.
21 BY MR. ARMENIO:
22 Q In connection with this declaration, you cited
23 Xencor Exhibit 1036; is that right?
24 A So in the list of documents, it says that one
25 is reserved.

Q So you looked at 1036 for the other declaration, the '859 patent, not for the '286 patent? Is that what that means?

A As far as I remember -- and I'm not a lawyer -- I don't know what "reserved" means -- I looked at that -- at this for the '859.

Q Okay. Let's look at it now in connection with the '286 patent for a minute.

This is the Desjarlais U.S. Patent 10,472,427.

Do you see that?

A That's the patent number.

Q And you see on the first page, top left, the applicant is Xencor, Inc., the petitioner in this case; is that right?

A The petitioner being the applicant?

Q In this proceeding where we have an inter partes review before the board, Xencor, Inc., is petitioning to invalidate one or more claims in Merus's '286 patent, and they're also the assignee, the applicant, of Exhibit 1036, right?

A So they're the applicant, the assignee, and the petitioner? Okay. Now I understand.

Q Okay. So they're all those things, Xencor, Inc., right?

Now, if we look on the list of references,

page 2 of Xencor's '427 patent, Exhibit 1036, if we count up in the right-hand column from the bottom -- I counted 13 -- we see a reference to Lazar, et al.; is that right?

A That's 2011/0054151.

Q And that's the same Lazar as we've been talking about during the day today, Xencor Exhibit 1004, correct?

A I can't tell that from this.

Q Okay. If you look at Exhibit 1004 in your stack, please, and then let's compare the publication in the top right of Exhibit 1004 with the number on Xencor Exhibit 1036.

A The numbers agree.

Q So the Xencor '427 patent had, at a reference cited, the same Lazar published patent application that we have discussed today as Exhibit 1004, correct?

A Say that again, please.

MR. ARMENIO: Sure.

Could you read the question back, please?

(Record read as follows:

"Question: So the Xencor '427 patent had, at a reference cited, the same Lazar published patent application that we have discussed today as Exhibit 1004, correct?")

THE WITNESS: The 1004 is on page 2 of the '427.

BY MR. ARMENIO:

Q Great.

Can you turn to the back of the '427 patent? Specifically, claim 1. It might be the second-to-last page.

What's claimed there in claim 1 of the Xencor '427 patent that was granted over the Lazar reference, Exhibit 1004?

MS. MAYS-WILLIAMS: Objection to scope.

THE WITNESS: Did you ask what the claim is?

BY MR. ARMENIO:

Q What does the claim state?

A Number 1, "A heterodimeric protein comprising: a first monomer comprising a first variant Fc domain, and a second monomer comprising a second variant Fc domain, wherein said first and second variant Fc domains comprise amino acid variant set L368D and S364K, according to the EU index as in Kabat," K-A-B-A-T.

Q And L368D, that's a neutral to charge substitution; is that right?

A It is.

Q And S364K, that's a neutral to charge substitution; is that right?

A It is neutral to charge.

Q And those are both in the CH3 domain, those substitutions?

A At 368, 364, yes.

Q And the United States Patent Office granted that claim in Xencor's '427 patent, right?

A Again, I'm not a lawyer. But if it was patented, I'm assuming that they went with the claim.

Q And the fact that that claim was patented over the Lazar reference, Exhibit 1004, was not part of your analysis in your declaration that was Exhibit 1002, correct?

A Yeah, I did not do '427 for the '286 declaration.

Q Let's take a look at previously marked Xencor Exhibit 1005.

MS. MAYS-WILLIAMS: Actually, before we get into the next exhibit, let's get you a coffee. You said you wanted a coffee after lunch.

We'll be right back.

THE REPORTER: Off the record, Counsel?

MS. MAYS-WILLIAMS: Yeah, off the record. We'll be right back.

THE REPORTER: Are we off, Counsel?

MR. ARMENIO: Yeah, if this is what is

1 happening. I just want to make sure this is a true
2 coffee break and there's not a conference.
3 MS. MAYS-WILLIAMS: There's not a conference.
4 He said he wanted a coffee earlier; so I'm getting that.
5 THE WITNESS: It can't be a conference if I
6 don't go.
7 MR. ARMENIO: Fair enough.
8 Off the record.
9 (Recess, 1:13 p.m. - 1:21 p.m.)
10 MR. ARMENIO: Back on the record, please.
11 Q Doctor, we've got in front of you
12 Exhibit 1005. You were discussing in your declaration
13 what's called the Cabrera reference; is that right?
14 A 1005 is the Cabrera WO 2012/058768.
15 Q And Exhibit 1005 is one of the references you
16 discuss in your declaration, Exhibit 1002, correct?
17 A It was part of my analysis.
18 Q And in particular, in your analysis in your
19 declaration, you discuss constructs AZ33 and AZ34; is
20 that right?
21 A Okay. Question again, please?
22 Q Sure.
23 In your declaration regarding the '286 patent,
24 Exhibit 1002, you discuss, in connection with Cabrera,
25 Exhibit 1005, constructs AZ33 and AZ34, correct?

A Correct.

Q And if we look on the Xencor exhibit numbering, page 41 of 239, we can see the amino acid substitutions in AZ33 and AZ34, right?

A Which one are we looking at again?

Q It's in Exhibit 1005, Cabrera, page 41 of 239, using the Xencor exhibit numbering.

A Okay.

Q Now, on that page, we can see the amino acid substitutions that are made in AZ33 and AZ34; is that right?

A AZ33 and AZ34, trends A and B.

Q And now AZ33 and AZ34 have three amino acid substitutions on each of A and B in common; is that correct?

A Those being in A, L351Y, F405A, and Y407V.

And on the B chain, T366I, K392M, and T394W are common to both AZ33 and AZ34.

Q The one difference between AZ33 and AZ34, as depicted on page 41, Exhibit Xencor 1005, is the S400E on the A component and N390R on the B component; is that correct?

A That's on page -- oh, 41 of 239. Okay.

In the A chain, S400E, and in the B chain, N390R are the addition in AZ34 compared to AZ33.

Q Now, if we look on page 172 of 239, there's a Figure 26B. And please take your time and locate that figure, please.

And Figure 26, the figure overall has a title, "Heterodimer Purity Determination after Protein A purification using non-reducing SDS-PAGE," correct?

A Wait. We're on what page?

Q Page 172 of 239, Figure 26.

A Okay. I'm there.

Q Great.

And on page 172 of 239 of Exhibit 1005, Figure 26 is titled "Heterodimer Purity Determination after Protein A purification using non-reducing SDS-PAGE," correct?

A That's the title of Figure 26.

Q And if we look at Figure 26B, we see estimated heterodimer purity numbers reported, correct?

A Estimated heterodimer purity is listed in the figure.

Q And there are estimated heterodimer purities reported for AZ33 and AZ34, correct?

A Correct.

Q And the estimated heterodimer purity reported for both AZ33 and AZ34 is, greater than symbol, 95 percent, correct?

A That's what the figure shows.

Q So AZ33, that heterodimer, it forms without the additional amino acid substitutions present in AZ34, correct?

A Yes.

Q And it forms at a greater-than-95-percent level of heterodimeric purity for AZ33, correct?

A That's within the figure.

Q And AZ34, with the extra amino acid substitutions, is reported to have the same heterodimeric purity, greater than 95 percent, right?

A Both say greater than 95 percent.

Q And below in what's figure -- this is a staining, right? How would a person of ordinary skill in the art refer to the picture under the numbers?

A It's -- as stated in the title, it's an SDS-PAGE gel that's stained, and then you take a picture.

Q And so we see, both visually and with numbers, that AZ33 forms heterodimers at a very high rate; in fact, it's listed at greater than 95 percent, right?

A Both 33 and 34 are listed as greater than 95 percent.

Q And as we discussed earlier, to a person of ordinary skill in the art in the year 2012, 95 percent

1 or higher for heterodimeric purity is very good, right?
2 A It is still very good.
3 Q And I think you called it, in your paper with
4 Maggie Merchant, near quantitative heterodimeric
5 production with 95 percent, right?
6 A We used that term back then. I don't know
7 that I would use it now. But that's what we had.
8 MR. ARMENIO: Let's put that aside.
9 Let's take a look at Merus -- and we'll mark
10 this as Merus Exhibit 4003.
11 (Exhibit 4003 was marked for identification
12 and is attached hereto.)
13 MS. MAYS-WILLIAMS: Before we start, I will
14 object on the basis of hearsay and lack of authenticity
15 as well as scope.
16 BY MR. ARMENIO:
17 Q Do you see Merus Exhibit 4003, Doctor, is
18 United States Patent 10,351,631?
19 A Yes.
20 Q And are you a listed co-inventor on this
21 patent?
22 A Yes.
23 Q And if we look at related U.S. application
24 data on the first page, left-hand column, two-thirds of
25 the way down, there's a number 60 in parentheses, and

there's some related U.S. application data.

Do you see that?

A Next to the 60 in parentheses?

Q Yes, sir.

Do you see that?

A Yes.

Q And it tells us that there were two provisional applications, and they give the numbers, and they were both filed on September 5, 2013, right?

A Both were filed on September 5, 2013.

Q And that date is after the date you have used for your analysis with respect to the '286 patent in your declaration, right?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: Say that again, please.

BY MR. ARMENIO:

Q Sure.

In connection with your '286 patent declaration, I understood you to do your analysis from the perspective of a person of ordinary skill in the art in 2012; is that right?

A For '286, 2012 April-something was the date I considered.

Q And we can agree that September 5, 2013, is after any day in April 2012, right?

A Agreed.

Q Now, in this patent in which you are a co-inventor, you explain a little bit about the background of bispecific antibodies in column 2, and specifically I'm looking at about line 33 to about line 48.

Please take a moment and orient yourself. I'll have a few questions for you.

A What lines again, please?

Q Probably starting around 33 and going to around 38 in column 2.

A Okay.

Q And at line 33, you and your co-inventors state, quote, "There remain significant technical difficulties in construction, expression and production of bispecific antibodies," closed quote.

Was that a true statement when you and your co-inventors made it in September of 2013?

A That's a general statement that could be considered generally true.

Q And you reviewed this patent before it issued, right? The application, at least, before it issued, as one of the co-inventors, I assume.

A Yeah.

Q And you wouldn't let a false statement go in

one of your patent applications, right?

A There are statements that are very general and very true. But one also has to consider the context when you're trying to come up with specific examples.

Q Okay. Let's look just a little bit farther. Line 39, column 2 of your '631 patent, quote, "Various forms of protein engineering have been used to match heterologous heavy chains, plus appropriate pairwise matching of heavy and light chains to efficiently yield a bispecific IgG," closed quote.

Is that another true statement when you and your co-inventors made it in September of 2013?

A True.

Q Continuing on, we see line 47, quote, "However, all of these efforts have been fraught with difficulty," closed quote.

Was that also a true statement when you and your co-inventors made it?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: Again, it's true. It's still true. But that depends on the context.

BY MR. ARMENIO:

Q Continuing on, line 49, you and your co-inventors state, quote, "Thus, despite efforts directed toward the development of bispecific

1 therapeutic antibodies, there remains a great need for
2 developing more efficient platforms that can lead to
3 more efficient and flexible production of bi- and
4 multispecific antibodies," closed quote.
5 True statement when you wrote it?
6 MS. MAYS-WILLIAMS: Objection. Scope.
7 THE WITNESS: That statement will always be
8 true.
9 BY MR. ARMENIO:
10 Q So certainly it was true in September of 2013,
11 right?
12 MS. MAYS-WILLIAMS: Objection. Scope.
13 THE WITNESS: And it is still true.
14 BY MR. ARMENIO:
15 Q The prior art references didn't make
16 everything in bispecific antibody production simple and
17 easy as of September of 2013 when you and your
18 co-inventors made these statements, right?
19 MS. MAYS-WILLIAMS: Objection. Scope, vague.
20 THE WITNESS: Can you say that again, please?
21 MR. ARMENIO: Sure.
22 Can you read it back, please?
23 (Record read as follows:
24 "Question: The prior art references didn't
25 make everything in bispecific antibody production

simple and easy as of September of 2013 when you and your co-inventors made these statements, right?")

THE WITNESS: Again, true then; true now.

MR. ARMENIO: So what I'd like to do, and suggest to you, Doctor, and all in attendance, is that we take a break for about ten minutes, and we can change all of the paperwork. Because now we're going to go and start talking about your other declaration which mostly has different exhibits. There might be a couple, and I can work with your counsel to pick out the couple that we might use for both.

Does that make sense to everyone?

MS. MAYS-WILLIAMS: Sure.

MR. ARMENIO: We're off the record.

(Recess, 1:40 p.m. - 1:55 p.m.)

MR. ARMENIO: Let's go back on the record.

Q Dr. Presta, are you ready to continue?

A Yes.

Q Great.

Let me show you your declaration regarding U.S. Patent 11,926,859, and this one also says "Xencor Exhibit 1002," but it's in a separate proceeding regarding the '859 patent.

And you can look at the one I've handed you.

If you brought one yourself, you can look at that one. As long as we're looking at the one regarding the patent ending in the last three digits '859.

In connection with your '859 patent declaration, were you contacted for the first time about being involved in the '859 patent proceeding at the same time as you were contacted regarding the '286 patent proceeding?

A Yes, I was.

Q Was your process for preparing the '859 declaration the same as it was for your '286 patent declaration?

MS. MAYS-WILLIAMS: I know we did this before. I'm just going to caution you not to reveal the substance of any attorney-client communications in your response. If you can answer the question without revealing the substance of any attorney-client communications, you may do so.

THE WITNESS: Again?

MR. ARMENIO: Sure.

Could you reread the question, please?

(Record read as follows:

"Question: Was your process for preparing the '859 declaration the same as it was for your '286 patent declaration?")

THE WITNESS: The process was, I went through the same general method of looking at all the references, et cetera.

BY MR. ARMENIO:

Q And someone typed up a first draft for you and sent it to you; is that right?

MS. MAYS-WILLIAMS: I just want to caution you not to reveal the substance of any attorney-client communications in your response. If you can respond without revealing the substance of any attorney-client communications, you may do so.

THE WITNESS: The same process as with the '286. Lots of discussions, first drafts, edits.

BY MR. ARMENIO:

Q How many rounds of edits did your '859 declaration go through before it was finalized?

MS. MAYS-WILLIAMS: Same caution as before.

THE WITNESS: If I remember correctly, still three.

BY MR. ARMENIO:

Q And do you recall, was your receipt of the first draft of the '859 declaration around the same time in January of 2025 that you received the first draft of the '286 declaration?

MS. MAYS-WILLIAMS: Same caution.

1 THE WITNESS: I think I received the '859 a
2 week or two after the '286.
3 BY MR. ARMENIO:
4 Q And when did you sign the final version of
5 your '859 declaration?
6 A Where is the --
7 MS. MAYS-WILLIAMS: The last page.
8 THE WITNESS: Last page of this?
9 MS. MAYS-WILLIAMS: Yeah.
10 THE WITNESS: Okay. Exhibit 286 [sic], on
11 February 11th as well, I think.
12 BY MR. ARMENIO:
13 Q So signed them on the same day?
14 A February 11th, 2025.
15 Q From the time you received the first draft of
16 the '859 declaration, which was, sounds like, maybe a
17 week or so after the first draft of the '286
18 declaration, how many hours did you spend working on the
19 '859 declaration edits and the like until you signed it
20 on February 11?
21 A So from the time I received the first draft to
22 the time I signed? Somewhere between 30 and 36 hours.
23 Q And similar to your '286 declaration, did you
24 bring with you a list of all the exhibits cited in your
25 '859 declaration?

A Yeah. I have the -- you mean this list of -- yes.

Q And do you have an understanding of about how many pages worth of documents those exhibits are?

A I would not hazard to take a guess. It was a lot.

Q In connection with the documents cited in your '859 declaration, similar to your '286 declaration, were those documents selected for you by someone else?

MS. MAYS-WILLIAMS: I just want to caution you not to reveal the substance of any communications you've had with an attorney in your response. But if you can answer the question without revealing the substance of any communications that you've had with any attorney, you may do so.

THE WITNESS: I was provided with a list of exhibits to consider.

BY MR. ARMENIO:

Q And for the '859 patent, did you yourself do any research to find other documents or add more documents to the list you were provided?

A I did not.

Q You've got on page 5 of your '859 declaration a section, "Person of Ordinary Skill in the Art."

Do you see that?

A Page 5?
Q Yes, sir.
A Yes.
Q And is that the same person of ordinary skill in the art for the '859 patent that you used for the '286 patent?
A Can we --
MS. MAYS-WILLIAMS: Yeah.
THE WITNESS: The wording is exactly the same. Paragraph 16 is the same.
BY MR. ARMENIO:
Q And you mention two or more years of experience in the production of bispecific antibodies; is that right? That being part of the qualification you proposed for a person of ordinary skill in the art?
A Where is that?
Q In the last line of paragraph 16.
A To be a POSA, to look at this, yes.
Q For production of bispecific antibodies in the '859 declaration, you include the same Figure 2 from Exhibit 1013 on page 17 of this declaration, correct?
A The figure on page 17 is from the Kontermann publication.
Q And that's the same figure you had in your '286 patent declaration, correct?

A It's the same figure from the Kontermann in both.

Q And so this figure gives us 45 different bispecific antibody formats that were available for consideration in March 2012, right?

A More than 45 different formats.

Q And only seven of those formats have any changes in the Fc region, right?

A Only seven, you said?

Q Yes, sir.

A Those are all in the fourth row down.

Q So you and I can agree, out of the 45 ways of making a bispecific antibody that a person of ordinary skill in the art was aware of in March of 2012, only seven of those 45 ways involved changes in the Fc region, right?

A There are seven listed in this figure. There could have been others Kontermann did not include.

Q So if we're going by Exhibit 1013, Figure 2, the 45 bispecific antibody formats depicted there, only seven of the depicted bispecific antibody formats involved changes in the Fc region, right?

A Only seven of the 45.

Q And out of those seven, only one shows any adjustment of charge pairs in the Fc region, right?

A Line 4, six over, is labeled "Charge Pairs."

Q So if I'm reading Exhibit 1013 in March of 2012, and I'm a person of ordinary skill in the art who wants to make a bispecific antibody, I've got 45 different ways to go, and only one of them involves making a charge pair change in the Fc region, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: According to this figure, yes.

BY MR. ARMENIO:

Q In your '859 declaration, you include a section similar to your '286 declaration, "Technological Overview"; is that right?

A What page?

Q Starting on page 6, Roman numeral V.

A The sections are similar in the two.

Q And in your '859 declaration, like your '286 patent declaration, you discuss the KIH -- knob-in-hole -- approach? We see that on page 22, for example, right?

A The KIH starts on page 22.

Q And you also discuss combining the KIH approach with a disulfide linkage, and we see a depiction of that on page 25; is that right?

A In Demonstrative 7.

Q And then you talk about electrostatic steering

1 approach, and you discuss the Gunasekaran paper,
2 Exhibit 1012, that we discussed earlier today; is that
3 right?
4 A 1012 is the Gunasekaran reference.
5 Q And all of those approaches were discussed in
6 the '859 patent. I'll give you an extra copy. I know
7 you have one in your binder, but it can't hurt to have
8 another. That's Exhibit 1001 in this proceeding.
9 MS. MAYS-WILLIAMS: Take a look.
10 THE WITNESS: I just want to make sure. Yeah.
11 BY MR. ARMENIO:
12 Q So each of -- and maybe to sum it up, there's
13 a paragraph 45 on page 21 of your '859 patent
14 declaration where you list four techniques that you say
15 were known by 2012 for more efficient bispecific
16 antibody production.
17 A What page was that again?
18 Q Paragraph 45 on page 21.
19 A Paragraph 45, page 21. Yes.
20 Q And each of those four techniques was
21 disclosed and discussed in the Merus '859 patent,
22 right?
23 For example, knob-into-hole, we can see that
24 column 40 [sic], lines 46 to 54, right?
25 A What were the line numbers again?

Q 46 to 54 of column 4 in the '859 patent.
A I'm not seeing that. Column 40?
Q 4. Just the number 4.
A Oh, 4. I thought --
Q I apologize if I wasn't clear.
So if we look at column 4 of the '859 patent, lines 46 to 54, that discusses the knob-in-hole approach for bispecific antibody production, right?
A 46 through 54, knob-into-hole.
Q Common light chain is discussed in the '859 patent in the paragraph in column 3 starting at 35 and continuing down probably until about 55, right?
A All right. 50 to 55?
Q About 35 to 55.
A No, 50.
Q In column 3, we see a discussion of how one can use common light chain technology to reduce the number of species that will be produced when you're trying to make a bispecific antibody, right?
A Well, the discussion of common light chain is really 50 to 56, 57.
Q Great.
So we can agree in column 3 of the '859 patent there is a discussion of a common light chain approach to bispecific antibody production, right?

A As background.

Q And then the third one you mentioned in your paragraph 45 is interchain disulfide pairing, and that's discussed in the '859 patent at column 5, line 3 to about line 9; is that right?

A Column 5, the Merchant reference.

Q And then No. 4 on your list in paragraph 45 in your declaration is electrostatic interactions, and that's discussed in the '859 patent in column 5, line 34 to line 49, where it discusses, among other things, the Gunasekaran 2010 paper, right?

A Paragraph 34 through 49.

Q So if we look at your paragraph 45 in your '859 declaration where you list four techniques for more efficient bispecific antibody production, Merus's '859 patent discloses and discusses all four of them, right?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: I can agree with "discusses." I don't know what "disclose" means.

BY MR. ARMENIO:

Q Fair enough.

In Merus's presentation to the United States Patent Office, it told the patent office a little bit about each of the four techniques you mention in your paragraph 45 as being bispecific antibody production

1 techniques: knob-in-hole, common light chain, interchain
2 disulfide pairing, and electrostatic interactions,
3 right?
4 MS. MAYS-WILLIAMS: Objection. Form.
5 THE WITNESS: In the patent, it does describe
6 these as previous technologies.
7 BY MR. ARMENIO:
8 Q On page 30, there's a paragraph 58 that comes
9 over from 29 into 30. And you provide a figure, a
10 supplementary table, in fact, from the Gunasekaran 2010
11 paper that we looked at earlier today, right?
12 A This is page 30?
13 Q Yes, sir.
14 And just so we're clear, it's 30 of your
15 declaration, 36 of 143 of the exhibit. And it's
16 paragraph 58.
17 A This is Supplementary Table No. 1 from the
18 Gunasekaran JBC, 1012.
19 Q And in the Gunasekaran paper, Exhibit 1012,
20 Gunasekaran is telling us what CH3 domain residues
21 contact other CH3 domain residues on a corresponding
22 chain, right?
23 A Supplementary Table 1 is a list of CH3 domain
24 interface residues in the first chain, A, and their side
25 chains -- and their side chain contacting residues in

the second chain, B.

Q And now, when something is in bold -- supplementary Table 1 tells us below that the positions involving interaction between oppositely charged residues are indicated in bold, right? So that's what the bolding means?

A That's the little "a."

Q So am I reading that right?

When I see a bolded residue, I look for another bolded residue to see its opposite charge interaction, right?

A That's what Footnote A says.

Q So, for example, if I'm looking at Lys A370 in bold, that's telling me it's going to interact with its opposite charge at Glu B 357', right?

A That's what the sub A tells us.

Q And a person of ordinary skill in the art would be able to read and understand the chart as presented in Supplementary Table 1 and understand contacting residues and interaction between oppositely charged residues on chain A and chain B, right?

MS. MAYS-WILLIAMS: Objection. Form.

THE WITNESS: That's some of the information in Supplementary Table 1.

///

BY MR. ARMENIO:

Q And a person of ordinary skill in the art, as you have defined that person, they'd be able to understand -- read and understand this chart and what it means, right?

A Correct.

Q If we look at page 56 of your declaration, 62 of 143 of the exhibit, you've got a statement regarding ordinary and customary meaning, and that you applied the ordinary and customary meaning to all of the claim terms of the '859 patent; is that right?

A In 103, "I have been informed that claims are typically given their ordinary and customary meaning in the technological field of the patent. However, when claim terms have no standard meaning in the art, I understand that the terms must be interpreted in light of the patent claims, disclosure, and the 'prosecution history.'"

Q Did you read the prosecution history of the '859 patent?

A I looked at the '935.

Q Other than looking at the '935 provisional, did you look at anything else in the prosecution history for the '859 patent?

A No.

Q What ordinary and customary meaning did you apply to the claim term "heterodimeric antibody" in the '859 patent?

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: Could you say that again, please?

BY MR. ARMENIO:

Q Sure.

In paragraph 104 of your declaration, you say that you have applied the ordinary and customary meaning to all the claim terms of the '859 patent in your analysis below, right?

A The first sentence of 104.

Q And if we look at claim 1 of the '859 patent, we can see the term "heterodimeric antibody" is a claim term of the '859 patent, right?

A That's in claim 1, "heterodimeric antibody."

Q And my question to you is, what is the ordinary and customary meaning for "heterodimeric antibody" that you used in your analysis in your '859 declaration?

A An antibody -- and again, for the POSA, that's a very general term -- can have several different definitions depending on what you're talking about. And heterodimeric, again, means that you have two different

chains.

Q Did any aspect of the specification of the '859 patent inform your definition of "heterodimeric antibody" for your analysis in your declaration?

A I don't understand the question.

Q Sure.

You just gave me a construction of "heterodimeric antibody." And I'm asking, in creating that construction, did you read anything in particular in the '859 specification to inform your definition?

MS. MAYS-WILLIAMS: Objection. Mischaracterizes his testimony, form.

THE WITNESS: Could you say that -- I can't hear you.

MS. MAYS-WILLIAMS: Sorry. I said, "Objection. Mischaracterizes his testimony, form."

THE WITNESS: Did I get my -- is the question did I get my definition of "heterodimeric antibody" from the patent?

BY MR. ARMENIO:

Q Let's start with that question.

A No.

Q What was the source of your definition of "heterodimeric antibody"?

A Many years of experience dealing with

1 different forms.
2 Q Did you go to any textbook or reference to get
3 a generally accepted definition of "heterodimeric
4 antibody" for use in your analysis?
5 A No.
6 Q And on page 59, you see there's a section --
7 subsection that starts "Provisional Application
8 No. 61/635,935," and the title continues.
9 Do you see that section?
10 A On page 59? Yes.
11 Q In connection with your analysis of whether
12 that '935 provisional application does or does not
13 describe the claimed antibody, were you provided any
14 legal standards to use in your analysis?
15 MS. MAYS-WILLIAMS: I just want to caution you
16 not to reveal the substance of any communications that
17 you've had with any attorneys in your response. But if
18 you can answer the question without revealing the
19 substance of communications with your attorneys, you may
20 do so.
21 THE WITNESS: The question again?
22 MR. ARMENIO: Could you read it back?
23 (Record read as follows:
24 "Question: In connection with your analysis
25 of whether that '935 provisional application does

or does not describe the claimed antibody, were you provided any legal standards to use in your analysis?")

MS. MAYS-WILLIAMS: So you can say "yes," "no," "I don't recall." But do not reveal the substance of any communications that you had with any attorneys in your response.

THE WITNESS: I still don't understand the question.

BY MR. ARMENIO:

Q Okay. In the section that starts on page 59, you're giving an analysis of what, in your view, the '935 provisional application does or does not describe; is that right?

A And while the '935 application is listed on the face of the '859 patent, it does not describe a heterodimeric antibody with the specific pair of amino acid insertions on a first and second CH3 domain at positions 364 and 368, respectively, recited in the claims of the issued '859 patent."

Q And I definitely understand that's what you wrote in paragraph 109.

What I'm trying to understand now is, in connection with reaching that statement and any other part of your analysis of whether or not the claimed

antibody is or is not described by the provisional application '935, were you given any legal standards to apply?

MS. MAYS-WILLIAMS: Again, you can say "yes," "no," or "I don't recall" or "I don't know."

THE WITNESS: I do not recall.

BY MR. ARMENIO:

Q So you do not recall being informed of the legal standard for when a provisional provides enough detail for a claim versus when it does not provide enough detail for a claim, correct?

MS. MAYS-WILLIAMS: Objection. Form, mischaracterizes the testimony.

THE WITNESS: Again, I'm -- I'm not getting the gist of the question.

BY MR. ARMENIO:

Q Do the words "ipsissimis verbis" mean anything to you?

A No.

Q Do the words "blaze marks" mean anything to you in this context?

A No.

Q Do the words "possession of the invention" mean anything to you in this context?

A Yes.

Q In connection with doing any of your analysis here, did anyone tell you the test for whether a document does or does not provide an adequate description of a claimed subject matter?

A I don't remember.

Q So that means you don't remember anyone ever conveying that test to you, correct?

A I don't remember discussing that kind of test.

Q When we look inside the '859 patent, that's Exhibit Xencor 1001 in this case, we see on column 13, there's a Table A.

Do you see that?

A Column 13a, Table A.

Q And column A, Table A, similar to the Gunasekaran supplementary table, tells us which CH3 interface residues in chain A contact which CH3 residues in chain B, correct?

A That's the title of Table A.

Q And when you look through it, you see very familiar pairings, right? Like for S364 -- I'm sure you know this in your sleep -- the contact residue in chain B is L368 and K370, right?

A I think this is the same table as the Kannan.

Q And do you have an understanding, whether through your own work with patents or because you were

told by someone else, that the '859 patent is a continuation in the same family as the '286 patent?

A I do not remember being told that.

Q And do you have an understanding that because it's a continuation, the specification of the '859 patent is the same as the specification in the '286 patent? Were you aware of that when you did your analysis?

A That the specifications were at least similar.

Q So you knew they were at least similar, but you didn't know they were the same?

A I didn't check that they were exactly the same.

Q And nobody told you that since they are continuations of each other, it's the same specification? Nobody told you that fact?

MS. MAYS-WILLIAMS: Objection. Asked and answered.

THE WITNESS: I do not remember being told or considering this.

BY MR. ARMENIO:

Q The reason I ask is, in column 18, there's a discussion about additional charge-charge interactions. And it's the same text as we already talked about for the '286 patent.

And if you understand that the text is the same, I would ask you whether, if I asked you the same questions about the text in the '859 patent, your answers would be the same as you already gave earlier today when the same text appeared in the '286 patent.

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: Column 18?

BY MR. ARMENIO:

Q Sure.

If we look at column 18, line 50, and look at 50 to 56, you will see identical text that we already talked about earlier today in the '286 patent. And if we want to talk about it all over again, we can, but I'd like to see if we can shortcut that.

MS. MAYS-WILLIAMS: Objection. Vague.

THE WITNESS: I remember the discussion.

BY MR. ARMENIO:

Q And if I asked you the same questions about creating an additional charge pair in the '859 patent, since the language is the same, would you give me the same answers you gave me for the '286 patent?

A Yes.

Q If we look in column 29, about line 63, there's a description of what we see in

1 Figures 7A, 7B, 7C, and 7D.
2 Do you see that?
3 A So this is column 29?
4 Q Yes, please. Around line 63 to line 65.
5 A This is Figure 7A, B, C, D?
6 Q Yes, sir. And it tells us those figures show
7 prevention of homodimerization by substitution of
8 neutral amino acids for charged amino acids, right?
9 A That's the title of the figure.
10 Q And if we turn to 7A, for example -- you can
11 look at any of the other 7B, C or D if you'd like --
12 it's on page 18 of 79 of the exhibit, sheet --
13 A 18?
14 Q 18 of 79 of the exhibit, sheet 13 of 39 of the
15 drawings.
16 A Here's the figure. Okay. Figures.
17 Q And is what we see in these figures staining
18 on gels and then taking a picture of it?
19 MS. MAYS-WILLIAMS: Objection. Vague.
20 THE WITNESS: I'm looking for where they
21 describe the figures.
22 BY MR. ARMENIO:
23 Q Well, that's where we were, in column 29,
24 where it says, "Figures A, B, C, and D are prevention of
25 homodimerization by substitution of neutral amino acids

for charged amino acids."

A That provides no experimental description. So...

Q So you see the qualitative description. And then look further in the patent, you see in column 41 there's a Table 7?

A Column 41, Table 7.

Q And in this table, we see the effect of certain amino acid substitutions on homodimer formation, right?

A That's what's in the table.

Q And, for example, it lists the S364K amino acid substitution as having a plus-plus effect on homodimer formation, right?

A Construct 17 -- no.

Q It's S364K, construct number 20.

A 20.

Q It has a plus-plus effect listed for homodimer formation, right?

A They are measuring homodimer formation.

Q To be more specific, inhibition of homodimer formation, right?

If we look at the top of the column, it says, "Effect on homodimer formation. Minus equals no effect, plus-plus-plus equals max inhibition," right?

MS. MAYS-WILLIAMS: Objection. Compound question.

THE WITNESS: Pardon?

MS. MAYS-WILLIAMS: Objection. Compound question.

THE WITNESS: In this table, they are measuring how well or how poorly each of these constructs is at forming a homodimer.

BY MR. ARMENIO:

Q At forming a homodimer or at inhibiting formation of a homodimer?

A So if it is a negative -- so if they have a negative, that means that construct can form a homodimer.

Q And if it's a double positive?

A The double positive is between -- the triple positive they define as maximum inhibition of forming the dimer. Double positive is in between.

Q If we look at column 40, and lines 5 to 10, it explains to us what they were looking for here and that they were looking for substitutions that would result in repulsion of identical heavy chains, i.e., reduced homodimer formation via electrostatic interactions, correct?

A That's what they state.

1 Q And the results of that first step are in
2 Table 7, correct?
3 A The results of that analysis is Table 7.
4 Q Now, in the '859 patent, if we look at
5 column 37, lines 65 and 66, carrying over to column 38,
6 it tells us that the "CH3 variants that fully prevent
7 homodimerization when expressed alone are preferred, to
8 prevent or minimize undesired byproducts (homodimers)
9 upon co-expression with a second CH3 variant for
10 heterodimerization."
11 A Where was this at?
12 Q Column 37, line 65 --
13 A Okay.
14 Q -- carrying over to the top two lines of
15 column 38.
16 So the patent is telling us what it prefers,
17 and it says, quote, "CH3 variants that fully prevent
18 homodimerization when expressed alone are preferred, to
19 prevent or minimize undesired byproducts (homodimers)
20 upon co-expression with a second CH3 variant for
21 heterodimerization," correct?
22 A That's what it states. I would not agree with
23 that.
24 Q That's what the inventors are saying, that
25 they prefer the variants that prevent homodimerization

when expressed alone, right?

A That's what they state and they prefer.

Q And if we look at Table 7, when you look at things, residues that are expressed alone, S364K, F405K, and Y407K inhibit homodimerization the most all by themselves, right, of every other variant in the whole table?

A Say that again.

Q Sure.

If I'm looking for a single change, one residue changed, the three single residue changes that have the greatest inhibition on homodimerization in Table 7 are S364K, F405K, and Y407K, correct?

MS. MAYS-WILLIAMS: Objection. Compound question.

THE WITNESS: What was the first one again?

BY MR. ARMENIO:

Q S364K.

A That's what the data says. Again --

Q And the patent tells us -- in column 42, it gives us information about F405 and Y407, correct?

MS. MAYS-WILLIAMS: Dr. Presta, you weren't finished with your earlier answer. You said, "That's what the data says. Again --"

Would you like to finish your response?

THE WITNESS: I personally find this analysis meaningless regarding formation of a heterodimer.

MR. ARMENIO: Objection. Sorry for the procedure, but objection. Motion to strike. Nonresponsive.

Q We can agree that the Table 7 data on homodimerization inhibition for single amino acid changes shows the greatest inhibition for S364K, F405K, and Y407K, correct?

MS. MAYS-WILLIAMS: Objection. Compound question, asked and answered.

THE WITNESS: That's what Table 7 shows.

BY MR. ARMENIO:

Q And in column 42, Merus discusses, at approximately line 19 through line 25, F405 and Y407.

Do you see that?

A "For example, it is known that residues F405 and Y407 have multiple interactions at the CH3-CH3 interface."

Q And if we go back to our chart, Table A, we can see that F405 in chain A has three contact residues in chain B, correct?

A F405. K393, T394 -- excuse me -- and K409.

Q And out of those three contact residues, two are already charged, right? K409 and K392?

A 392.
Q We agree on that, right?
A Yes.
Q Similarly, if I look at Y407, that one has multiple contact residues in chain B. This time it's four such contact residues, right?
A T366, T394, Y407 in the second chain, and K409.
Q And for Y407, one of the contact residues in chain B is already charged; K409, correct?
A According to Table A.
Q So of the three amino acid substitutions in Table 7 that, by themselves, have the greatest indicated inhibition on homodimer formation, the one with the fewest contact residues in chain B is S364, correct?
MS. MAYS-WILLIAMS: Objection. Vague, compound question.
THE WITNESS: The question again, please.
(Record read as follows:
"Question: So of the three amino acid substitutions in Table 7 that, by themselves, have the greatest indicated inhibition on homodimer formation, the one with the fewest contact residues in chain B is S364, correct?")
MS. MAYS-WILLIAMS: Same objection. Vague,

compound.

THE WITNESS: According to Table A.

BY MR. ARMENIO:

Q And now, in Table A, S364 is indicated as being in contact in chain B with L368 and K370, correct?

A That is what is in Table A.

Q And we know from Gunasekaran, for example, that K370 is already involved in a salt bridge with 357 Glu B357 in Gunasekaran Exhibit 1012, correct?

A The two residue numbers again, please?

Q Sure.

We know that K370 is already involved in a native format in a salt bridge in an electrostatic interaction with Glu B357 as indicated by Gunasekaran Supplementary Table 1, Exhibit 1012, right?

A As well as Table A in '859.

Q And so if I make S364 charged, if I want to have a complementary charge in chain B that can come in contact with it, it's going to be L368 that I've got to put the complementary charge on, because K370 is already involved in a salt bridge, correct?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: All we know is those two interact.

///

BY MR. ARMENIO:

Q We know S364 contacts L368 and K370. We know that, right?

A That's what the table tells us.

Q We know K370 is already charged and interacting in a salt bridge with E357, right?

A Those are contacting residues, according to A.

Q And so if I want to put a complementary charge to a charge I add to S364, my option is to put a complementary charge on the L368 residue, correct?

A So the question is, you put a charge on one, what would you put on the other?

Q If I wanted to -- let's look at Table 7. That tells me I get the good inhibition of homodimer formation with a substitution that changes S364 to K, right?

A Where is Table A again?

Q Table A is in column 13, and Table 7 is in column 41.

And so now if I'm looking at the S364K amino acid modification, if I want a complementary charge to that K that's now on 364, and I look in chain B, I'm either going to put a D or an E on 368 because that's the only thing that contacts 364 in chain A that is not already charged, right?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: We have a complicating factor with K370. So I would have to really think about putting charges at 364, 368, with a positive charge already at 370.

BY MR. ARMENIO:

Q We can agree that the complementary charge for K is either a D or an E, right?

A Agreed.

Q We can agree that for the 364 residue in chain A, the only residues that it contacts in chain B are at 368 and 370, right?

A Agreed.

Q We can agree that in chain B, the 370 residue in the native state is already a K and is involved in a salt bridge with the E at 357 on the opposite chain?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: That's what's shown in the table.

BY MR. ARMENIO:

Q So the only available contact residue for me to modify that is in contact with 364 in chain A that is not already charged is residue 368 in chain B, correct?

MS. MAYS-WILLIAMS: Objection. Asked and answered.

THE WITNESS: That's the only one that you could introduce a charge.

BY MR. ARMENIO:

Q We agree, right? That's the only one that doesn't already have a charge on chain B that's in contact with 364 on chain A, right?

MS. MAYS-WILLIAMS: Objection. Asked and answered, compound.

THE WITNESS: From a scientific standpoint, you have problems with these assumptions.

BY MR. ARMENIO:

Q Is it correct, if I'm reading Table A and Table 7, if I've got an S364 to K substitution, the only place where I can make a change in chain B that's actually going to be in contact with the 364 in chain A that is not already charged is at the 368 residue in chain B, right?

MS. MAYS-WILLIAMS: Objection. Asked and answered, compound.

THE WITNESS: You can make the change. Whether that will actually affect heterodimers is a completely different problem.

BY MR. ARMENIO:

Q That's the indicated change to a person of ordinary skill seeing that S364K is one of the top three

single changes to inhibit homodimer formation, and the only one that isn't dissuaded by column 42's discussion of F405 and Y407, right?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: You lost me there.

MR. ARMENIO: Why don't we read it back and we'll see how we do. And if I need to reask it, I will.

(Record read as follows:

"Question: That's the indicated change to a person of ordinary skill seeing that S364K is one of the top three single changes to inhibit homodimer formation, and the only one that isn't dissuaded by column 42's discussion of F405 and Y407, right?")

THE WITNESS: Okay. I still don't understand the question.

BY MR. ARMENIO:

Q Okay. Let's see if we can walk through it.

For single amino acid changes, Table 7 tells us the three single amino acid changes that have the biggest inhibition on homodimer formation are S364K, F405K, and Y407K, correct?

A The three that have the most effect on homodimer formation, yes.

Q And of those three in column 42, lines 19 to

25, Merus tells us F407 and -- strike that question.

In column 42, lines 19 to 25, Merus tells us for F405 and Y407, those residues are complicated; so you may not want to make changes there, right?

MS. MAYS-WILLIAMS: Objection. Mischaracterizes the document, vague and compound.

THE WITNESS: For example, it is known that residues 405 -- F405 and Y407 have multiple interactions at the CH3 interface, including interactions with residues that are already charged, which may be problematic after introduction of multiple charge mutations among these interacting residues.

The same applies at 354.

BY MR. ARMENIO:

Q In column 42, Merus specifically mentions, lines 19 to 25, F405 and Y407, correct?

A "It is known that residues F405, Y407," et cetera.

Q Merus, in column 42, lines 19 to 25, does not specifically mention S364K, correct?

A It does not mention it.

Q We know if I am trying to introduce an additional charge pair into the CH3 domain, and I add a K at 364 in chain A, I can look at column 13, Table A, and see what residues in chain B come in contact with

the 364K change residue in chain A, right?

MS. MAYS-WILLIAMS: Objection. Asked and answered, compound.

THE WITNESS: 360S -- Table A, S364, F405, Y407, all contact at least one neutral residue and one charged residue.

So when they make -- when they talk -- on 42, lines -- it starts on line 18, "For example, it is known that residues F405 and Y407 have multiple interactions at the CH3-CH3 interface, including interactions with residues that are already charged, which may be problematic after introduction of multiple charge mutations among these interacting residues."

Again, the same applies to S364.

MR. ARMENIO: Objection. Motion to strike. Not responsive.

Q My question, Doctor, is very specific: for a 364 residue in chain A, Table A in column 13 tells us the contacting residues in chain B, right?

MS. MAYS-WILLIAMS: Objection. Asked and answered.

THE WITNESS: Same answer. Yes.

BY MR. ARMENIO:

Q And there are two such contacting residues in chain B for 364 residue in chain A, correct?

A That's what it says in Table A.

Q And of those two contacting residues in chain B, only one of them, 368, is not already charged in the wild-type chain, right?

A True. Same for F405, Y407.

Q Well, for those, they have multiple other -- right? You've got a T --

A But --

Q -- 394, you've got two different Ts for 407. Those have even more interactions, right? I thought we already established that.

MS. MAYS-WILLIAMS: Objection. Vague, compound.

THE WITNESS: I maintain, when they talk in column 42 about F405 and Y407 having problems with substituting in new charges, the same would apply to S364.

BY MR. ARMENIO:

Q But we can agree it doesn't say that in column 42. It doesn't say anything about 364 in column 42, lines 19 to 25, correct?

A That does not mean my statement is not true.

Q But you can agree with my statement that column 42, lines 19 to 25, does not say anything about 364, S364?

MS. MAYS-WILLIAMS: Objection. Asked and answered, compound.

THE WITNESS: It does not say anything about S364.

BY MR. ARMENIO:

Q If we look in column 40, lines 45 to approximately 50, Merus tells us, "In a follow-up, the identified substitutions will be used to generate bispecific antibodies or mixtures of bispecific or monospecific antibodies by engineering matched pairs of CH3 residues in one or more IgG heavy chains - CH3 regions," right?

A That's the description in those lines.

Q And further on in the column, Merus tells us, starting in line 62, quote, "The rationale for this approach is that repulsive charges are engineered into available pair of contacting residues." And then "Samples are subsequently analyzed," right, "on SDS-PAGE to identify pairs in which dimer formation is reduced, as visualized by the presence of bands of approximately 72 kD."

And that, if we look back, is what we saw in Figure 7, right? The SDS-PAGE bands?

MS. MAYS-WILLIAMS: Objection. Compound, vague.

THE WITNESS: I'm not following the logic of the rationale onward. This is not making sense to me.

MS. MAYS-WILLIAMS: Maybe now is a good time for a break. I think it's been more than an hour.

MR. ARMENIO: We've got a couple questions, and then sure.

MS. MAYS-WILLIAMS: It's up to you, Len. What do you think?

THE WITNESS: That's fine.

BY MR. ARMENIO:

Q In paragraph -- same place, column 40, line 59, Merus tells us, "The residues to be tested in the present study are contact residues as previously identified," and they mention Gunasekaran as one of the citations for previous identification of contact residues, right?

A Correct.

Q And you confirmed already that Table A in column 13 of the '859 patent provides similar contact residue information as Gunasekaran in 2010, correct?

A That's not my confusion.

MR. ARMENIO: I'm sorry. Can you read back the question and the answer, please?

///

1 (Record read as follows:
2 "Question: And you confirmed already that
3 Table A in column 13 of the '859 patent provides
4 similar contact residue information as Gunasekaran
5 in 2010, correct?
6 Answer: That's not my confusion.")
7 BY MR. ARMENIO:
8 Q So maybe we didn't understand each other.
9 The Table A in column 13 of the '859 patent
10 provides similar information as Supplementary Table 1 in
11 Gunasekaran 2010, correct?
12 A Agreed, but that's not my point of confusion.
13 We discussed the sentence after that starting
14 at 62.
15 Q I didn't say you were confused about anything,
16 Doctor. I asked whether it confirmed. I didn't say
17 confused.
18 MS. MAYS-WILLIAMS: Let him finish.
19 Go ahead.
20 THE WITNESS: It -- the Gunasekaran and
21 that -- and the sentence 59 through 62 confirm each
22 other.
23 The next sentence says that "The rationale for
24 this approach is that repulsive charges are engineered
25 into each available pair of contacting residues."

1 That sentence makes no sense to me. In fact,
2 that is the opposite of what I would do.
3 BY MR. ARMENIO:
4 Q And is the opposite of having complementary
5 charges, right? That's having repulsive charges?
6 A If you went to make a heterodimeric, you do
7 not want to put in repulsive charges.
8 MR. ARMENIO: You asked for a break?
9 MS. MAYS-WILLIAMS: Let's take a break.
10 (Recess, 3:16 p.m. - 3:31 p.m.)
11 MR. ARMENIO: Let's go back on the record,
12 please.
13 BY MR. ARMENIO:
14 Q Doctor, I'd like to show you what's already
15 been marked as Xencor Exhibit 1030.
16 Do you understand Xencor Exhibit 1030 to be
17 the '935 provisional application you mentioned earlier
18 today?
19 A Yes.
20 Q And in your review and analysis, did you find
21 the same disclosure in the '935 provisional with respect
22 to the issues you discussed in your '859 patent
23 declaration as was found in the '859 patent itself?
24 A The Table 7 especially is identical.
25 Q Right.

And is there any difference between the '935 provisional, Exhibit 1030, and the '859 patent itself, Exhibit 1001, that you believe to be relevant to your '859 declaration, opinions, and analyses?

A Again, is there any difference between these two that would affect my -- not that I remember.

Q So if I went through -- and we can just touch base. We won't spend a lot of time, given your answers.

If I look in the '935 provisional at page 17 of 103, I'll see Table A listing the CH3 domain interface residues that we already discussed in connection with the '859 patent itself; is that right?

A The Table A in the '935 and the '859 are the same.

Q If we go forward a little bit, on page 37 of 103 in the '935 provisional, it describes Figure 7, "prevention of homodimerization by substitution of neutral amino acids for charged amino acids."

That's similar between the '935 provisional and the '859 patent, correct?

A Figure 7 are the gels?

Q Yes.

A Okay. Yeah.

Q Moving forward, on page 48 of 103 in the '935 provisional, we see, at line 10, the statement, quote,

"CH3 variants that fully prevent homodimerization when expressed alone are preferred, to prevent or minimize undesired byproducts (homodimers) upon co-expression with a second CH3 variant for heterodimerization," closed quote.

That's the same language we reviewed in the full-length '859 patent, correct?

A This was page 48, what lines?

Q 10, 11, and 12.

And that's the same language we saw at the bottom of column 37 and the top of 38 in the '859 patent, right?

A Let me check.

Where was it in '859?

Q Column 37, line 65 and 66, column 38, lines 1 and 2.

A It does correspond.

Q If we look further in the '935 provisional, it includes Example 13 with Table 7 on pages 51, 52, 53, and 54 of the '935 provisional that we've discussed in the '859 patent, right?

A Table 7 is in both.

Q And the discussion, page 51 of the '935 patent, about line 10, "The objective was to obtain a list of residues that, when substituted by a charge

1 residue, would result in repulsion of identical chains
2 such that these mutations may be used to drive homo-
3 and/or heterodimer formation upon mixed expression of
4 different IgG heavy chains."
5 Similar text as in the '859 patent that we
6 reviewed; is that right?
7 A I don't remember this sentence that we
8 covered. Is it '859?
9 Q Column 40, line 10.
10 A I see the sentence. I don't necessarily agree
11 with it.
12 Q But the sentence is the same --
13 A In both.
14 Q -- in the '935 provisional and the '859
15 patent, right?
16 A Yes, it is.
17 MS. MAYS-WILLIAMS: Slow down so the court
18 reporter --
19 THE WITNESS: Okay.
20 BY MR. ARMENIO:
21 Q And then in the '935, we see the next
22 sentence, quote, "In a follow-up, the identified
23 substitutions will be used to generate bispecific
24 antibodies or mixtures of bispecific or monospecific
25 antibodies by engineering matched pairs of CH3 residues

in one or more IgG heavy chain CH3 regions," closed quote.

A Where is this again?

Q In the '935 provisional, it's at line 14 through 17.

A Of what page?

Q Page 51 of 103.

A Right.

Q And that language is the same as we see in the '859 patent, column 40, lines 46 through 51 -- excuse me -- through 50.

A Agreed.

Q Lastly, the language on page 54 of the '935 provisional, starting at line 13, about F405 and Y407, that language is the same as the language in column 42, approximately lines 19 to 25, correct?

A The language is the same; my objection is the same.

Q In connection with your '859 declaration, you cite a Kannan published patent application; is that right?

A Cite what again?

Q A published patent application to Gunasekaran Kannan. And it's, to be specific, Xencor Exhibit 1007.

A Yes.

Q The Exhibit 1007 was published on 16 July 2009; is that right?

A I see that at the top of the first page.

Q The Gunasekaran paper that we discussed earlier today, Exhibit 1012, that was published in June of 2010; is that right?

A Where is the publication date?

Q There's one at the bottom left, right over page 1 of 22.

A Okay. Yes. Agreed.

Q So we can agree that the Gunasekaran paper was later in time than the publication of the Kannan patent modification, Exhibit 1007, correct?

A The paper was published after the W0 2009/089004, which is Xencor 1007.

Q And just to confirm, whether we say "Kannan Gunasekaran" or "Gunasekaran Kannan," it's the same scientist involved in both the paper, Exhibit 1012, and the published patent application, Exhibit 1007, right?

A Agreed.

Q Now, in your declaration, you talk about the Kannan paper -- excuse me -- the Kannan published application, and you talk about it in paragraph 180. It's at page 108 of 143.

I'll give you a second to get there. It's

1 paragraph 180 on page 108 of 143 in your declaration.
2 A Page 108 of 143.
3 Q You've got a discussion there about -- where
4 you say something about the charge engineering strategy,
5 whether it can be extended.
6 Do you see that?
7 A In paragraph 180?
8 MS. MAYS-WILLIAMS: Slow down.
9 BY MR. ARMENIO:
10 Q And you cite to Kannan, Exhibit 1007, page 10,
11 lines 16 to 18; is that right?
12 A So when I have 1007 at 10, 16 through 18, is
13 that page 10?
14 MS. MAYS-WILLIAMS: I can help you get there.
15 THE WITNESS: 1007 is the WO; 10, 16 through
16 18.
17 BY MR. ARMENIO:
18 Q Do you see the cited text?
19 A Yes.
20 Q Did you find that cited text in Exhibit 1007,
21 or did someone point you to it?
22 MS. MAYS-WILLIAMS: I'm going to object and
23 instruct the witness not to reveal any attorney-client
24 communications in your response. If and only if you can
25 answer the question without revealing the substance of

any attorney-client communications in your response, you may do so.

THE WITNESS: That -- this was the sentence I noticed and referred to when we were doing the '286 and Kannan about that one sentence saying, "You can go neutral to charge."

BY MR. ARMENIO:

Q Understood.

My question is, in your preparation of your declaration, did you find that statement in Kannan 1007 by yourself?

MS. MAYS-WILLIAMS: I'm going to give the witness the same caution, and I'm going to instruct you not to reveal any attorney-client communications in your response. If and only if you can answer the question without revealing the substance of any attorney-client communications in your response, you may do so. If you can't answer without revealing the substance of any attorney-client communications, you may do so.

THE WITNESS: I honestly can't remember. It's so long ago.

BY MR. ARMENIO:

Q And is that a statement that you recall ever seeing or reading during your normal non-patent proceeding involvement work as a scientist?

A Is the question did I ever see that sentence before I ever started any of this?

Q Correct.

A Not that I remember.

Q And this sentence that is cited in your declaration, page 10 of Exhibit 1007, it doesn't say anything about the hydrophobic core of the CH3 domain, right?

A The statement is "This strategy can also be extended to modifying uncharged residues to charged residues at the CH3 domain interface."

And we've already established the CH3 domain interface.

Q Right.

And as you've explained, the CH3 domain interface has a periphery and it has a hydrophobic core, right?

A And according to this statement, you could do it at either place.

Q My question is, in Kannan Exhibit 1007, it doesn't say anything about the hydrophobic core. It doesn't say you can or cannot, in this cited piece, say anything about the hydrophobic core of the CH3 domain, right?

A In the entire --

MS. MAYS-WILLIAMS: Objection.

THE WITNESS: Sorry.

MS. MAYS-WILLIAMS: Asked and answered.

But go ahead.

THE WITNESS: You mean in the entire WO -- in the entire 1007?

BY MR. ARMENIO:

Q I'm looking at where you cited. So page 10, lines 16 to 18, there's nothing in what you cited to that mentions one way or another the hydrophobic core of the CH3 domain, correct?

A My answer is the same. The last part of that sentence, "This strategy can also be extended to modifying uncharged residues to charged residues at the CH3 domain interface."

That includes the hydrophobic core, the charged periphery.

Q We can agree this far, the words "hydrophobic core" do not appear in the section you cited from example -- excuse me -- Exhibit 1007, the Kannan published application?

MS. MAYS-WILLIAMS: Objection. Asked and answered, misleading, and you're attempting to mischaracterize his testimony.

MR. ARMENIO: Counsel, I don't appreciate

that. I view that as a personal attack on me. I object to it. I asked whether words appear on a page. Your attempt to vilify that is not well taken.

Q Doctor --

MS. MAYS-WILLIAMS: I'm truly not trying to attack you, but I do think you're trying to trick the witness.

MR. ARMENIO: No, clearly not.

Q On page 10, can we agree simply in the text that you cite the words "hydrophobic core" do not appear?

MS. MAYS-WILLIAMS: Objection. Asked and answered, misleading, and mischaracterizes the witness's testimony.

THE WITNESS: Let me rephrase what I said before.

It does not specifically, in that sentence, refer to the hydrophobic core; however, CH3 domain interface implicitly includes the hydrophobic core. So they didn't repeat themselves.

BY MR. ARMENIO:

Q In Exhibit 1012 -- this is the Kannan paper that came later in June 2010 -- they did specifically discuss the hydrophobic core of the CH3 region, correct?

A Can you point me to that --

Q Sure.
A -- where they're talking about that?
Q Page 4 of 22, right-hand column, five lines in.
A Page 4, and then what?
Q Five lines down in the right-hand column.
A Right-hand column.
Q And this is where Kannan tells us, quote, "It has long been established that the hydrophobic core of protein domains play an important role in protein folding and stability," and he cites reference 17; is that right?
A We went over this with the '286. This -- it's -- it is stating a generality.
Q And Exhibit 17, the Matthews paper that we reviewed earlier, that was from 1995; is that right? We can either look at Matthews or you can look at the citation for 17 in the end notes included here.
A Matthews 1995, "Advances in Protein Chemistry."
Q So according to Gunasekaran Kannan, who's both the author of Exhibit 1012 and the first named inventor on Exhibit 1007, it had been -- long been established, citing a 1995 paper, that the hydrophobic core of protein domains plays an important role in protein

1 folding and stability, right?
2 A Again, this is a -- it's a general
3 observation.
4 Q Now, in your '859 declaration, you're using
5 Kannan Exhibit 1007 to suggest that you could flip the
6 charges at 364 and 368 seen in Lazar; is that right?
7 Is that its purpose in your declaration?
8 A Where is that at in the declaration?
9 Q It's actually a pretty substantial part of the
10 whole declaration.
11 MS. WILLIAMS: You can take your time to find
12 it.
13 BY MR. ARMENIO:
14 Q You can see you discuss Kannan at 101,
15 including -- and 102, including paragraph 180. And then
16 paragraph 207, page 117, you talk about Kannan, in your
17 view, teaching swapping positive and negative charges.
18 Do you see that?
19 A Where is that again?
20 Q 207, paragraph 207, page 123 of 143.
21 A Do I have a copy of Lazar?
22 MS. MAYS-WILLIAMS: You do, right --
23 BY MR. ARMENIO:
24 Q It's Exhibit 1004.
25 A Okay.

Q So if you look at, for example, your paragraph 204 on page 123 of 143 of your declaration, you're citing Kannan for potentially swapping 364E, 368K, to be opposite charges, right?

A 1007 at 3, 1 through 4, is that page -- no.

Q So right now, I'm looking at paragraph 204. It's in your declaration, Exhibit 1002.

And in that paragraph, am I reading it correctly that you are using Kannan to suggest that a person of ordinary skill in the art might take the 364E, 368K, that you say is in Lazar, and turn it into a 364K, 368E?

MS. MAYS-WILLIAMS: Objection. Mischaracterizes the declaration.

THE WITNESS: No. My question is, in paragraph 204, it says, "Exhibit 1007, F3, dash, 1 through 4."

I'm trying to find 3:1-4. It can't be page 3.

MS. MAYS-WILLIAMS: Is this what you're looking for?

THE WITNESS: Okay. Is that 1007? Oh, yeah.

Okay. Let me do 204 once again here. I'm getting there.

So we are considering paragraph 204?

///

BY MR. ARMENIO:

Q Yes, sir.

A "Based upon Kannan's disclosures, a person of ordinary skill would have good reason to swap the charges of Lazar's 'preferred' 'S364E'/'L368K' heterodimer."

Q And you cite as the basis for that statement -- the next sentence, you cite Exhibit 1007 at 3:1 to 4; is that right?

A That's -- 1007 is the Kannan. Right. Okay.

Q And in the very next sentence after your cited Exhibit 1007 at 3:1 to 4, the Kannan published application, Exhibit 1007, says, quote, "By reversing the charge of the amino acid, homodimer formation is reduced," closed quote.

Do you see that?

A Where are we at again?

Q In the Kannan published application, Exhibit 1007.

A Oh, there. Okay.

Q Immediately after the words you rely upon and cite at 3:1 through 4, the very next sentence says, quote, "By reversing the charge of the amino acid, homodimer formation is reduced," closed quote, correct?

A "By reversing the charge of the amino acid,

homodimer formation is reduced."

Q And that statement is only true if you're reversing the charge in the native-occurring chain, correct?

THE WITNESS: Please repeat that, the last question.

(Record read as follows:

"Question: And that statement is only true if you're reversing the charge in the native-occurring chain, correct?")

THE WITNESS: That was their observation in their charge swapping experiments.

BY MR. ARMENIO:

Q Let's take a look at Xencor Exhibit 1038.

A Before we go there, we were looking at 204. And earlier in 198, I'm also discussing why -- the swapping of charges at a specific pair.

"And while Table 1 of Lazar identifies a heterodimer incorporating CH3 domains substituting in 364E (negatively charged) on a first CH3 domain and 368K (positively charged) on the second CH3, Lazar would have provided a person of ordinary skill in the art good reason to pursue amino acid substitutions with opposite charges. For example, 364K and 368E."

Q So in that table you just cited me to -- it's

on page 120 of 143 of your declaration -- if you look at No. 17, S364R --

A Where are we at now?

Q Exactly where you were pointing me to, page 120 of 143.

A 120 of -- okay.

Q And if you look at the Figure 5 you include in this page, row 17, S364R, K370D has a lower heterodimerization percentage than S364E, Y349K, correct?

A I have the 17. What lane are you referring to for the second set?

Q The heterodimerization percentage for lane 17, which corresponds to S364R, K370D is 59 percent, correct?

A Correct.

Q And we can agree that is lower than S364E, Y349K, which is reported to heterodimerize at 75 percent, correct?

A That's what the numbers are. I don't see the connection.

Q And for the 364 residues that you're talking about in this figure on page 120 of 143 of your declaration, they appear in the empty Fc column, right?

A For the ones you quoted, S364 are in the empty

Fc.

Q And we looked already earlier today at Lazar, and we saw the empty Fc construct in Figure 1 in Lazar, correct?

A Yes.

Q Let's take a look at Xencor 1038. Just watch these staples. They didn't go in quite right. I don't want you to stab yourself. Careful with the staples.

Did you review Exhibit Xencor 1038 in connection with your '859 declaration?

A I don't remember.

Q You see on the first page that this is an article by Xencor authors?

A The first page, these are Xencor authors.

Q And do we see on the first page, right-hand column, first full paragraph, first sentence, the Xencor authors state, "A vast array of bispecific formats have been suggested," right?

A Where is this at, please?

Q Right-hand column, first full paragraph, first sentence, quote, "A vast array of bispecific formats have been suggested," right?

A I see that statement.

Q The Xencor authors then walk through some of the approaches.

If we look at page 2 of 13 of the exhibit, they first cite, in the left-hand column, line 6, quote, "Pioneering work by Carter and colleagues identified 'knob-into-hole' approaches successful in promoting heterodimer formation at yields over 85 percent," closed quote.

And Carter and colleagues, that's you, right, with the knob-in-hole work?

A That is our papers.

Q If we go five lines down from there, Xencor states, quote, "Other early approaches to Fc heterodimerization introduced complementarity in different manners, either by charge inversions (electrostatic steering) or multiple IgA substitutions (strand-exchange engineered domain, or SEEDbody)."

Do you see that?

A Yes.

Q And then Xencor said, quote, "These 'first generation' approaches were successful in promoting heterodimer formation at relative yields over 85 percent," right? That's what they say?

A Which is followed by, "However, the thermostabilities of their heterodimeric CH3 regions were reduced compared to those of IgG isotypes."

Q My focus is -- they talk about "early

1 approaches" and "first-generation approaches," and then
2 two lines down from that, they talk about "our own
3 first-generation efforts."
4 Do you see that?
5 A "Our own first-generation efforts to generate
6 a heterodimeric Fc resulted in an IgG1 variant capable
7 of promoting heterodimer formation that yields up to
8 89 percent."
9 Q Later in the paper, Xencor describes
10 substitutions at 3S to 364K and L368D. We see that on
11 page 5 of 13, correct?
12 THE WITNESS: Could you read back that last
13 question, please?
14 (Record read as follows:
15 "Question: Later in the paper, Xencor
16 describes substitutions at 3S to 364K and L368D.
17 We see that on page 5 of 13, correct?")
18 THE WITNESS: I'm still not seeing --
19 BY MR. ARMENIO:
20 Q If you look at the illustrations on page 5 of
21 13, do you see that they're -- in the bottom left
22 illustration, there's an S364K substitution and an L368D
23 substitution?
24 A Right. And that's the same as in Table 1,
25 version 4.

Q Xencor didn't discuss any possibility of obtaining the same results swapping where -- which residue has the K and which residue has the D, correct?

MS. MAYS-WILLIAMS: Objection. Scope.

THE WITNESS: A POSA would understand that you could try different charge pairs.

MR. ARMENIO: Objection. Motion to strike.

Q My question is a little different, Doctor.

It's in this paper, Xencor is providing detailed information about S364K and L368D, and is nowhere citing you could get equivalent results with S364D and L368K, correct?

MS. MAYS-WILLIAMS: Objection. Asked and answered. Also, compound.

THE WITNESS: I do not see that they made that particular variant.

BY MR. ARMENIO:

Q If we look at page 6 of 13 of Exhibit 1038, left-hand column, first paragraph under subheading 3.2, do you see Xencor states that its design process began with a study of first-generation Fc heterodimer solutions?

A The first sentence under 3.2?

Q Yes, sir.

A Yes.

Q And they list as the first-generation Fc heterodimer solutions "increasing/decreasing, side chain volume," which has a parentheses, "knob-into-hole," "charge inversions," which has a parenthetical, "electrostatic steering," "or multiple IgA substitutions," which has a parenthetical, "SEEDbody," right?

A That's the first sentence.

Q Xencor does not list neutral to charge substitutions as a first-generation Fc heterodimer solution, correct?

A They don't list that as their first generation.

Q Let's look back at Exhibit 1036. We saw that earlier today. It will either be in front of you -- it's the Xencor '427 patent. If it's not in front of you, it will be on the stack on the side table.

A Okay. I don't see that one.

Oh, the Desjarlais. Okay.

Q And the Xencor '427 patent, Exhibit 1036, we looked at earlier today, this claims the S64K, L368D substitutions in certain monomers, right?

A Could you say that again, please?

Q Sure.

If we look at the second-to-the-last page, we

1 can see claim 1, right?
2 A Yes.
3 Q And that talks about a first monomer with a
4 first variant Fc domain and a second monomer comprising
5 a second variant Fc domain.
6 Do you see that?
7 A Claim 1, yes.
8 Q And then it says, "Wherein said first and
9 second variant Fc domains comprise amino acid variant
10 set L368D and S364K according to the EU index as in
11 Kabat," K-A-B-A-T, correct?
12 A That's claim 1, part B.
13 Q And we don't see, or you don't cite to us
14 anything in the Xencor '427 patent that says you could
15 get similar results with an L368K and an S364D
16 substitution.
17 You don't cite anything like that from the
18 '427 patent in your declaration, correct?
19 MS. MAYS-WILLIAMS: Objection. Compound.
20 BY MR. ARMENIO:
21 Q So I see you looking in the '427 patent. My
22 question is whether you cite it in your declaration,
23 anything about the '427 patent, that said you could
24 switch those claimed residues.
25 MS. MAYS-WILLIAMS: By the way, as you're

1 considering the question, feel free to consult any
2 material you'd like.
3 THE WITNESS: Repeat the question again,
4 please.
5 MR. ARMENIO: Sure.
6 (Record read as follows:
7 "Question: And we don't see, or you don't
8 cite to us anything in the Xencor '427 patent that
9 says you could get similar results with an L368K
10 and an S364D substitution. You don't cite
11 anything like that from the '427 patent in your
12 declaration, correct?")
13 MS. MAYS-WILLIAMS: Objection. Compound.
14 BY MR. ARMENIO:
15 Q Okay. I'll withdraw the question. We can
16 read your declaration and see what it says.
17 So if we look at the '427 patent with its
18 claim 1, we already noted earlier today that this patent
19 was issued over the Lazar published patent application
20 2011/0054151, which is Exhibit 1004, correct?
21 And we did that by looking at page 2 of 144 in
22 the '427 patent. In the right-hand column, we counted
23 up 14, and we see Lazar 2011/0054151 in the references
24 cited for the '427 patent, and that's the same published
25 patent application as the Xencor Exhibit 1004, correct?

A Wait. I need to orient myself for all the numbers you're giving me.

Q Sure. First things first.

The '427 patent, that's Exhibit 1036.

A Yes.

Q Okay. Let's turn to page 2 of 144, please.

A Page 2? Yes.

Q On this page, there are references cited that were considered before this patent was granted. If we look in the right-hand column, 14 lines up from the bottom, we see a citation to Lazar 2011/0054151, correct?

A I see that.

Q And that is the same Lazar as the Xencor Exhibit 1004 we've been talking about today if we compare the numbers?

A That's the same.

Q In connection with your work on your '859 declaration, did anyone tell you that the Kannan published patent application, Xencor Exhibit 1007 that we've been discussing, issued as a U.S. patent?

So 1007, the Kannan published patent application that is Xencor Exhibit 1007, WO 2009/089004, that's the one we're going to start with.

MS. MAYS-WILLIAMS: And, Dr. Presta, you

can answer that question "yes," "no," "I don't recall."

BY MR. ARMENIO:

Q I think right now the question is, do you have Exhibit 1007 in front of you?

MS. MAYS-WILLIAMS: I wasn't sure. There were a few questions pending. So if that's the question, I'll withdraw the objection.

THE WITNESS: I have to find it in the pile.

BY MR. ARMENIO:

Q Okay. It looks like this one.

A Okay. 1007.

Q And Exhibit 1007 was part of your analysis in your '859 patent declaration, correct?

A Yes.

Q Did anyone inform you that this published patent application, Xencor Exhibit 1007, actually issued as a U.S. patent?

MS. MAYS-WILLIAMS: And, Dr. Presta, I will just instruct you that you may answer that question "yes," "no," "I don't recall," or "I don't know."

THE WITNESS: 1007 is what I looked at. The patent came later. I don't remember looking at it.

BY MR. ARMENIO:

Q Were you ever told that the same disclosure in

1 Xencor Exhibit 1007 issued as U.S. Patent 8,592,562?
2 MS. MAYS-WILLIAMS: Dr. Presta, I'll instruct
3 you that you may answer that question "yes," "no," "I
4 don't recall," or "I don't know."
5 THE WITNESS: I don't recall.
6 BY MR. ARMENIO:
7 Q If you look on page 2 of the '427 patent that
8 we looked at just a minute ago, if we look at the
9 left-hand column, four lines up from the bottom, do you
10 see that one of the references cited is U.S.
11 Patent 8,592,562 to Kannan, et al.?
12 A That's in the list.
13 Q And did you review that patent, 8,592,562, in
14 connection with your '859 patent declaration?
15 MS. MAYS-WILLIAMS: Objection. Scope.
16 THE WITNESS: That is not on my list of what I
17 looked at.
18 BY MR. ARMENIO:
19 Q Did anyone inform you when you were preparing
20 your '859 declaration that the U.S. Patent Office issued
21 the '427 patent with its claims, including claim 1 that
22 we've looked at now several times, over the same Lazar
23 and Kannan disclosures that you cite in your
24 declaration?
25 MS. MAYS-WILLIAMS: And I will instruct you,

Dr. Presta, that you may answer that question "yes," "no," "I don't recall," or "I don't know."

THE WITNESS: Could you repeat the question, please?

(Record read as follows:

"Question: Did anyone inform you when you were preparing your '859 declaration that the U.S. Patent Office issued the '427 patent with its claims, including claim 1 that we've looked at now several times, over the same Lazar and Kannan disclosures that you cite in your declaration?")

MS. MAYS-WILLIAMS: And again, Dr. Presta, I will instruct you that you may answer that question "yes," "no," "I don't recall," or "I don't know."

THE WITNESS: I don't understand the question. I was given '427.

BY MR. ARMENIO:

Q And '427, in the claims -- we've talked about it now multiple times -- that's got substitution 364K and L368D, right? Claim 1, for example.

A Claim 1.

Q And Xencor was granted this patent, right? It's an issued patent, Exhibit 1036, right?

MS. MAYS-WILLIAMS: Objection. Compound.

THE WITNESS: I can see the patent was issued.

BY MR. ARMENIO:

Q And in the big list of references cited, we've walked through and we've pointed out Lazar and Kannan, right?

A The Kannan is the 8,592,562?

Q Yes, sir.

A And the Lazar was which one?

Q 2011/0054151.

A Yeah. Neither of those are in my list.

MR. ARMENIO: So why don't we take a few-minute break.

MS. MAYS-WILLIAMS: If you got confused, you can say.

THE WITNESS: 1004?

MR. ARMENIO: Let's continue until we resolve this, and we can take a break when we've resolved it one way or the other.

THE WITNESS: So the '151, yes. I don't see the Kannan 8,592,562.

BY MR. ARMENIO:

Q So now in the Merus '859 patent that you were declaring about, it talks about having a 364K substitution and a 368D substitution.

And we see that, for example, in claim 3 of the '859 patent, right?

A "The heterodimeric antibody of claim 2, wherein said positively charged amino acid residue at position 364 comprises a lycine (K) residue, and wherein said negatively charged amino acid residue at position 368 comprises an aspartic acid (D)."

Q And in your declaration, you tell us you believe those limitations are disclosed in a combination of Lazar and Kannan, right?

You can look back at 204 in your declaration as a perfect example of somewhere where you say that.

A What was the question again?

Q For the Merus '859 patent with those claim substitutions, you, in your declaration, suggest that they're disclosed by the combination of Lazar and Kannan.

That's what you say in the declaration, right?

MS. MAYS-WILLIAMS: I think earlier he pointed you to 204. So review what you need to review, but also review 204.

THE WITNESS: So from paragraph 204, "For instance, Kannan teaches that the positively charged lysine (K) at position 368 'may be replaced with a negative charged amino acid in the first CH3 domain' and the negatively charged glutamic acid (E) at position 364

1 'may be replaced with a positive-charged amino acid in
2 the second CH3 domain.'"
3 BY MR. ARMENIO:
4 Q And so in that paragraph, you're talking about
5 Lazar and Kannan references. And you make the
6 statements that are set forth in your declaration
7 regarding those references, right?
8 A I'm sorry. I still don't understand the
9 question.
10 Q We'll try it another way.
11 The '427 patent to Xencor, it's Exhibit 1036.
12 Do you still have that in front of you?
13 A Yes.
14 Q Claim 1, it has S364K, L368D, right?
15 A Claim 1, yes.
16 Q And the patent office issued that patent with
17 that claim over the Kannan and Lazar references that we
18 pointed out on the "References Cited" table, right?
19 A What does the phrase "over" --
20 Q The patent office knew about Kannan and Lazar
21 references, as we've pointed out on the "References
22 Cited" table, when it issued the '427 patent, Xencor
23 Exhibit 1036, with its claimed L368D and S364K, correct?
24 MS. MAYS-WILLIAMS: Objection. Scope.
25 THE WITNESS: I have to look into that.

1 That's not -- that's legal stuff.
2 BY MR. ARMENIO:
3 Q And that's not something you looked at or
4 looked into in preparing your '859 declaration for this
5 case, correct?
6 A As we previously established, the Lazar
7 reference, yes; the Kannan 8,592,562, as far as I can
8 recall, no.
9 MR. ARMENIO: So why don't we take a break.
10 I'll see what, if anything, I have left, and we could be
11 close to completing at least my portion of the
12 proceeding.
13 (Recess, 4:52 p.m. - 5:03 p.m.)
14 BY MS. MAYS-WILLIAMS:
15 Q During the breaks today, Doctor, did you talk
16 about the substance of your testimony with anyone?
17 A No.
18 MR. ARMENIO: With that, I have no further
19 questions for you at this time, pending any examination
20 by counsel for Xencor.
21 I want to thank you for your time and
22 participation in the proceeding, Doctor. I pass the
23 witness.
24 MS. MAYS-WILLIAMS: I appreciate that. We're
25 just going to need to go off the record and take a

moment and figure out if we're going to ask any questions.

(Recess, 5:03 p.m. - 6:22 p.m.)

MR. ARMENIO: Let's go back on the record.

For the record, I'm going to object to the extended conference that the witness had with counsel. It was an hour-and-20-minute break.

The only reason I didn't object, because counsel for the petitioner said they were going to take a moment and decide whether there's any redirect. And they then had a one-hour-and-20-minute conference with the witness. I object to it.

I was not able to contact the board to voice my objection because the break started at 5:03 Pacific Time. And given the hour, the board is not available to voice my objection.

But I object to any and all redirect after that extended conference with counsel.

EXAMINATION

BY MS. MAYS-WILLIAMS:

Q Okay. I have a few questions.

Dr. Presta, earlier in the day, previously, you were asked the question, "You and your co-inventor state, 'There remains significant technical difficulties in construction, expression, and production of

1 bispecific antibodies.' Was that a true statement when
2 you and your inventors made it in September 2013?"
3 That was the question you were asked, right?
4 A Yes.
5 Q You noted both that is a general statement
6 that could be generally true, and that there are
7 statements that are very general and very true, but no
8 one -- excuse me -- but one also has to consider the
9 context when you are trying to come up with specific
10 examples, right?
11 MR. ARMENIO: Objection. Completely leading.
12 Also, objection given the extended preparation
13 and conference between counsel and the witness.
14 BY MS. MAYS-WILLIAMS:
15 Q We're going to add that context now, okay?
16 A Okay.
17 Q If you were going to try to change -- if you
18 were going to try changes and combinations that are
19 already in the references that we have been talking
20 about, including patents, would you have confidence that
21 has a good chance of working?
22 A Yes.
23 MR. ARMENIO: Objection. Asked -- excuse me.
24 Objection. Leading. Objection to the extended
25 conference between counsel and the attorney.

One hour and 20 minutes of practicing a redirect answer does not lead to reliable testimony. I object.

BY MS. MAYS-WILLIAMS:

Q We were previously looking at claim limitation 1 of the '286 patent. Let's get the '286 patent out.

A That may be in that.

Q It might be.

MR. ARMENIO: Doctor, please give me a chance to object between counsel's question and your answer, please.

THE WITNESS: I understand.

MR. ARMENIO: Thank you.

THE WITNESS: What are you looking for?

MS. MAYS-WILLIAMS: Just pull it up for me.

THE WITNESS: Are you looking for '286?

MS. MAYS-WILLIAMS: You keep it.

Q Can you read portion -- in claim 1, portion 1B of the '286 patent into the record?

A Claim 1B?

Q 1B.

A Okay. "Culturing said host cell and allowing for expression of said two nucleic acid molecules to produce said first antibody heavy chain and said second

antibody heavy chain, wherein the at least one positively charged amino acid residue substituted in the CH3 domain of said first antibody heavy chain interacts with the at least one negatively charged heavily amino acid residue substituted in the CH3 domain of said second antibody heavy chain in the interface between said first and second antibody heavy chains to produce a heterodimeric antibody, and..."

Q Does claim limitation 1B require that the interaction by itself is what produces the heterodimeric antibody?

MR. ARMENIO: Objection. Leading. Objection to the one-hour-and-20-minute conference between the witness and counsel to practice an answer. Such testimony is not reliable and is inherently suspect.

BY MS. MAYS-WILLIAMS:

Q Dr. Presta, you may answer.

A Can you ask the question again?

Q Does claim limitation 1B require that the interaction by itself is what produces the heterodimeric antibody?

MR. ARMENIO: Same objections. Also object to the extent you're now asking the witness for claim construction, which is a legal -- purely legal matter.

MS. MAYS-WILLIAMS: Now you're being

1 obstructionist.
2 MR. ARMENIO: Not at all. Stating my
3 objections.
4 MS. MAYS-WILLIAMS: You are. You are. He
5 can't even remember the question.
6 Q I'll do it again, Dr. Presta.
7 A Thank you.
8 Q Does claim limitation 1B require that the
9 interaction by itself is what produces the heterodimeric
10 antibody?
11 MR. ARMENIO: Same objections.
12 THE WITNESS: No.
13 BY MS. MAYS-WILLIAMS:
14 Q You testified earlier today about KIH and
15 other modifications.
16 Do you recall that?
17 A Yes.
18 Q Using KIH, people, including yourself, could
19 get very high heterodimers, right?
20 MR. ARMENIO: Objection. Leading. Objection
21 to the conference with counsel.
22 BY MS. MAYS-WILLIAMS:
23 Q You can answer. I can ask again if you've
24 forgotten after the --
25 A Yes.

Q Would a POSA be motivated to combine KIH with charge changes?

MR. ARMENIO: Objection. Leading. Objection to the conference with counsel. Objection. Also outside the scope of the witness's declaration.

MS. MAYS-WILLIAMS: It's absolutely not.

Q And if you've lost the question, I'm happy to ask it again.

A Please do it again.

Q Would a POSA be motivated to combine KIH with charge changes?

MR. ARMENIO: Same objection.

THE WITNESS: Yes.

BY MS. MAYS-WILLIAMS:

Q Why?

MR. ARMENIO: Same objections.

THE WITNESS: These are all things that worked in the literature, as we've covered. And they would be -- the POSA would be modified -- sorry, not modified -- would want to combine to try and improve the percent heterodimer.

BY MS. MAYS-WILLIAMS:

Q You talked earlier about whether Kannan taught charge changes in wild-type IgGs. Would a POSA understand that a charge swap could apply to

1 non-wild-type formats?
2 MR. ARMENIO: Objection. Leading. Objection
3 to the conference of an hour and 20 minutes between the
4 witness and counsel.
5 BY MS. MAYS-WILLIAMS:
6 Q You can answer the question if you can
7 remember it. And if you need me to read it again, I'm
8 happy to do so.
9 A Read it again, please.
10 Q Would a POSA understand that a charge swap
11 could apply to non-wild-type formats?
12 MR. ARMENIO: Same objections.
13 THE WITNESS: To non-wild-type?
14 BY MS. MAYS-WILLIAMS:
15 Q To non-wild-type formats.
16 MR. ARMENIO: Same objections.
17 THE WITNESS: A POSA would understand that.
18 And, in fact, in Lazar, we had examples with their test
19 system.
20 BY MS. MAYS-WILLIAMS:
21 Q Later published in 2010, Kannan said, "It has
22 been long established that the hydrophobic core plays an
23 important role in protein folding and stability."
24 If you're going to try to -- if you're going
25 to try changing the combinations that are already in the

1 references that we've been talking about, including
2 patents, and including those in the hydrophobic core,
3 would you have confidence that there would be a good
4 chance of those working?
5 MR. ARMENIO: Objection. Leading, compound,
6 extended conference between counsel and the witness.
7 BY MS. MAYS-WILLIAMS:
8 Q You may answer the question.
9 A If these were done before, I would have
10 confidence that there would be a high probability that
11 they would work.
12 Q You were asked earlier whether Lazar and
13 Arathoon take two different approaches to bispecific
14 antibody formation. You answered yes.
15 Would a POSA have found those formats to be
16 incompatible?
17 MR. ARMENIO: Objection. Leading. Objection
18 to the extended conference between the witness and
19 counsel that leads to inherently suspect and unreliable
20 testimony.
21 BY MS. MAYS-WILLIAMS:
22 Q You may answer the question.
23 A No.
24 Q Could different methods of forming
25 heterodimers be combined?

1 MR. ARMENIO: Objection. Leading. Objection
2 to the extended conference between counsel and the
3 witness.
4 THE WITNESS: Yes. In fact, Cabrera is an
5 example of that.
6 BY MS. MAYS-WILLIAMS:
7 Q Earlier, you said that when wild-type
8 chains interact, that doesn't necessarily mean that when
9 you make a substitution, those substitutions will
10 interact.
11 That's not true with respect to changes that
12 were already made and taught by the literature; is that
13 fair?
14 MR. ARMENIO: Objection. Leading. Objection.
15 Contradicting the witness's own testimony. Objection.
16 Pure, clear result of coaching by counsel during the
17 break. I object.
18 BY MS. MAYS-WILLIAMS:
19 Q You may answer the question.
20 A Could you repeat the question?
21 Q Earlier, you said that when wild-type chains
22 interact, it doesn't necessarily mean that when you make
23 a substitution, the substitutions will interact.
24 That's not true with respect to changes that
25 were already made and taught in the literature.

1 MR. ARMENIO: Same objections.
2 THE WITNESS: If the changes were already in
3 the literature and were successful, I would assume that
4 they would interact.
5 BY MS. MAYS-WILLIAMS:
6 Q You'd expect them to interact?
7 MR. ARMENIO: Same objections.
8 THE WITNESS: Yes.
9 BY MS. MAYS-WILLIAMS:
10 Q Okay. Earlier, you were discussing whether
11 the provisional application to the '859 patent, which is
12 provisional 61/635935 described the antibody.
13 Let's go to your report for a moment.
14 A So which report is this?
15 Q '859.
16 A '859. Okay.
17 Q Can you read paragraph 109 out loud?
18 A Paragraph 109. "Provisional Application
19 No. 61/635,935 ('the '935 application') (Exhibit 1030)
20 was filed on April 20, 2012. (Exhibit 1001 at Cover.)
21 And while the '935 application is listed on the face of
22 the '859 patent, it does not describe a heterodimeric
23 antibody with the specific pair of amino acid insertions
24 on a first and second CH3 domain at positions 364
25 and 368, respectively, recited in the claims of the

1 issued '859 patent."
2 Q Do you stand by the statement that the
3 provisional did not describe the claimed heterodimeric
4 antibody with a pair of mutations at positions 364 and
5 368 respectively?
6 MR. ARMENIO: Objection. Leading. Objection
7 to the extended conference with counsel.
8 THE WITNESS: With a specific pair of amino
9 acid insertions, I stand by it.
10 BY MS. MAYS-WILLIAMS:
11 Q Earlier, you were discussing Exhibit 1038.
12 I'm just going to get it in front of you.
13 Do you have 1038 in front of you?
14 A That's the Moore methods.
15 Q I think earlier, you said that you didn't
16 remember this.
17 MR. ARMENIO: Objection. Leading.
18 BY MS. MAYS-WILLIAMS:
19 Q Can you turn to paragraph 79 of your '859
20 declaration?
21 A Paragraph 79.
22 Q Do you remember Moore now?
23 MR. ARMENIO: Objection. Leading. Objection
24 to the extended conference with counsel.
25 ///

BY MS. MAYS-WILLIAMS:

Q You can answer the question.

A I remember it now. Before I was thinking Moore was the patent.

Q Can you turn to paragraph 153 of your report?

A Paragraph 153.

Q Can you read paragraph 153 out loud?

A "In addition to understanding that Desjarlais teaches every limitation of claims 1 through 7 of the '859 patent, as discussed above in Section XI, it is my opinion that a person of ordinary skill in the art would have understood that Moore teaches every limitation of these same claims, as arranged in the claims."

Q And do you stand by those opinions, Dr. Presta?

MR. ARMENIO: Objection. Leading. Objection to the extended conference with counsel.

BY MS. MAYS-WILLIAMS:

Q You may answer.

A Yes.

MS. MAYS-WILLIAMS: Pass the witness.

FURTHER EXAMINATION

BY MR. ARMENIO:

Q Dr. Presta, did you talk with anybody about the substance of your redirect testimony in the

one-hour-and-20-minute break between the end of my cross-examination and the beginning of counsel's redirect questioning?

MS. MAYS-WILLIAMS: And Dr. Presta, you may answer that question "yes" or "no."

THE WITNESS: Yes.

BY MR. ARMENIO:

Q And did you talk with any lawyers for Xencor about the substance of your testimony on redirect during the break between when I ended my questions on cross-examination and when counsel began her questions of you on redirect examination?

MS. MAYS-WILLIAMS: You may answer that question "yes" or "no."

THE WITNESS: Repeat the question, please.

(Record read as follows:

"Question: And did you talk with any lawyers for Xencor about the substance of your testimony on redirect during the break between when I ended my questions on cross-examination and when counsel began her questions of you on redirect examination?")

MS. MAYS-WILLIAMS: Same caution. You may answer that question "yes" or "no."

THE WITNESS: I would like a clarification in

that we have two types of lawyers here: two from Xencor, two from Paul Hastings.

So are you asking me, did I talk to one or both of the people from Xencor about this?

MS. MAYS-WILLIAMS: And you may only answer that "yes" or "no."

BY MR. ARMENIO:

Q So let me withdraw the prior question and reask to address your requested clarification.

In the one-hour-and-20-minute break between the time I ended my cross-examination and when counsel began her redirect examination, did you talk to any lawyer for Xencor, either from Paul Hastings or internal to Xencor or consulting for Xencor -- any of the four people sitting at the table on the Xencor side of the table -- did you talk to any of them during that one hour and 20 minutes about the subject of your redirect testimony?

MS. MAYS-WILLIAMS: You may answer that question "yes" or "no."

THE WITNESS: Yes.

BY MR. ARMENIO:

Q Doctor, during that one-hour-and-20-minute break where you talked about the substance of your redirect testimony with counsel for Xencor, did you

1 practice your answer to questions they were going to ask
2 you during redirect?
3 MS. MAYS-WILLIAMS: And Dr. Presta, I'm going
4 to instruct you not to answer that one.
5 BY MR. ARMENIO:
6 Q Dr. Presta, during the one-hour-and-20-minute
7 break you had, did counsel tell you in advance the
8 questions they were going to ask you on redirect?
9 MS. MAYS-WILLIAMS: Dr. Presta, I'm going to
10 instruct you not to answer that question.
11 BY MR. ARMENIO:
12 Q For the two instructions you just received to
13 the prior two questions, Doctor, are you going to follow
14 those instructions?
15 A Follow the instructions? Yes.
16 Q If counsel did not instruct you on those two
17 questions, could you have answered my questions and told
18 me whether someone gave you the questions in advance and
19 whether you practiced the answers in advance with
20 counsel?
21 MS. MAYS-WILLIAMS: I'm going to instruct you
22 not to answer that one.
23 THE WITNESS: I will follow instructions.
24 MR. ARMENIO: So you won't let the witness say
25 whether he could have answered my questions if you

allowed him?

MS. MAYS-WILLIAMS: I'm not going to let him answer any questions about the substance of any communications.

MR. ARMENIO: That's not the question.

Let's just be very clear because this is establishing --

MS. MAYS-WILLIAMS: Are you asking me or are you asking him? I'm not the witness.

MR. ARMENIO: Counsel, you and I are framing a discovery dispute, and I'm trying to explain to you that my question is not asking him for the substance of the communication.

Right now, it's asking whether he, right now, has the knowledge to answer my questions about whether questions were presented to him in advance and whether answers were practiced, whether he had the capacity and knowledge to answer that question but for your instruction. And that frames what the motion to compel, motion to strike, will look like, okay?

Q So with that explanation, I'll ask you again.

If counsel for Xencor did not instruct you not to answer, could you have answered my questions about whether your redirect questions from counsel were presented to you in advance and whether your redirect

answers to those questions were practiced in advance?

Would you have been able to answer my questions if counsel did not instruct you not to answer?

MS. MAYS-WILLIAMS: And I'm going to instruct you to answer this question either "yes" or "no."

THE WITNESS: So can you give me the question again?

(Record read as follows:

"Question: If counsel for Xencor did not instruct you not to answer, could you have answered my questions about whether your redirect questions from counsel were presented to you in advance and whether your redirect answers to those questions were practiced in advance? Would you have been able to answer my questions if counsel did not instruct you not to answer?")

MS. MAYS-WILLIAMS: You may answer that question "yes" or "no," if you can.

THE WITNESS: I still don't understand the question.

BY MR. ARMENIO:

Q I'll take another try.

I inquired -- I asked a question whether you were given the redirect questions in advance during the break. Your counsel instructed you not to answer.

1 Do you remember that question and objection
2 and instruction?
3 A Yes.
4 Q I asked you whether you practiced your answer
5 to the redirect questions in advance during the break,
6 and your counsel, counsel for Xencor, objected and
7 instructed you not to answer.
8 Do you remember that question, objection, and
9 instruction?
10 A Yes.
11 Q And what I'm asking is, from your memory,
12 could you remember whether you were given redirect
13 questions in advance and practiced redirect answers in
14 advance during the break, if your memory would allow you
15 to answer those questions, but the instruction from
16 counsel is what's preventing you from providing an
17 answer. Is that true?
18 MS. MAYS-WILLIAMS: I object to the question.
19 It's compound.
20 You may answer "yes" or "no."
21 THE WITNESS: I'm sorry. I still do not
22 understand what the question is.
23 BY MR. ARMENIO:
24 Q We'll give it one last try. I'm trying to
25 frame what's going to end up being a dispute that the

1 lawyers have to have, okay?
2 So when there's a dispute like this -- I want
3 to know the answer to a question on behalf of Merus;
4 counsel for Xencor instructs you not to answer my
5 question -- part of the due diligence the lawyers owe to
6 the board is to find out whether the witness could have
7 answered the question but for the instruction happening.
8 And so I'll ask it this way: Your memory is
9 good enough to know what happened during the
10 hour-and-20-minute break between the cross-examination
11 and the redirect, right?
12 MS. MAYS-WILLIAMS: You may answer that "yes"
13 or "no."
14 THE WITNESS: Yes.
15 BY MR. ARMENIO:
16 Q And if questions were presented to you during
17 that hour and 20 minutes and answers were practiced, you
18 would be able to remember that one way or the other,
19 right?
20 MS. MAYS-WILLIAMS: You may answer that "yes"
21 or "no."
22 THE WITNESS: Yes.
23 BY MR. ARMENIO:
24 Q And when I'm asking you, please tell me all
25 the redirect questions that were presented to you in

advance during the one-hour-and-20-minute break, the only thing preventing you from telling me is Xencor's counsel's instruction, right?

MS. MAYS-WILLIAMS: You may answer that "yes" or "no."

THE WITNESS: Yes.

BY MR. ARMENIO:

Q And similarly, for whether you practiced answers to redirect questions during the one-hour-and-20-minute break between cross-examination and redirect, your memory is good enough to tell me the answer to that question, but because of counsel's instruction, you're not telling me the answer, correct?

MS. MAYS-WILLIAMS: You may answer that "yes" or "no."

THE WITNESS: Yes.

MR. ARMENIO: I have no further questions.

I apologize, Doctor. I know going through some of the lawyer questioning -- I apologize -- it's just necessary for us to do it for the procedure.

No further questions on redirect.

THE REPORTER: Counsel, would you like a rough draft or just the final?

MS. MAYS-WILLIAMS: A rough.

And before we go off the record, thank you to

you.

MR. ARMENIO: Certainly thank you to you, Carla. And thank you, Dr. Presta.

MS. MAYS-WILLIAMS: Thank you as well to the witness on the record, please.

MR. ARMENIO: From both of us, for sure.

MS. MAYS-WILLIAMS: Yes.

(TIME NOTED: 6:50 p.m.)

--o0o--

I, LEONARD G. PRESTA, Ph.D., do hereby declare under penalty of perjury that I have read the foregoing transcript; that I have made any corrections as appear noted, in ink, initialed by me, or attached hereto; that my testimony as contained herein, as corrected, is true and correct.

EXECUTED this _____ day of _____, 2025, at _____, _____.

(City) (State)

_____

LEONARD G. PRESTA, Ph.D.

I, the undersigned, a Certified Shorthand Reporter of the State of California, do hereby certify:

That the foregoing proceedings were taken before me at the time and place herein set forth; that any witnesses in the foregoing proceedings, prior to testifying, were administered an oath; that a record of the proceedings was made by me using machine shorthand which was thereafter transcribed under my direction; that the foregoing transcript is a true record of the testimony given.

Further, that if the foregoing pertains to the original transcript of a deposition in a Federal Case, before completion of the proceedings, review of the transcript [ ] was [ ] was not requested.

I further certify I am neither financially interested in the action nor a relative or employee of any attorney or any party to this action.

IN WITNESS WHEREOF, I have this date subscribed my name.

Dated: December 10, 2025.

Carla Soares

CARLA SOARES

CSR No. 5908

1 ERRATA SHEET
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3 DATE OF DEPOSITION: 12/5/2025
WITNESSES' NAME: Leonard G. Presta , Ph.D.
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Federal Rules of Civil Procedure

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