

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AJINOMOTO CO., INC.,
Petitioner,

v.

ABTIS CO., LTD.,
Patent Owner

IPR2025-00283
Patent 11,896,657

Record of Oral Hearing
Held: May 8, 2026

BEFORE: JEFFREY N. FREDMAN, JO-ANNE M. KOKOSKI, and
LILAN REN, Administrative Patent Judges.

IPR2025-00283
Patent 11,896,657

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The above-entitled matter came on for hearing on May 8, 2026,
commencing at 9:00 a.m., via video teleconference.

P R O C E E D I N G S

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JUDGE REN: We're going on the record. Good morning. Today we'll hear arguments in IPR2025-00283, concerning U.S. Patent Number 11,896,657. I'm Judge Ren. And I'm joined here today by Judge Fredman and Judge Kokoski. Let's start with appearances, beginning with Petitioner.

MR. MOCK: Good morning, Your Honors. My name is Jason Mock, appearing on behalf of Petitioner. And I have here with me my cocounsel, Steve Maebius and Liane Peterson.

JUDGE REN: Thank you. And who do we have with the Patent Owner?

MR. ENGEL: Good morning, Your Honor, Jason Engel, lead counsel to the Patent Owner. With me are my colleagues, Rebekah Hill and Peter Giunta, they'll be arguing today.

JUDGE REN: Thank you. Before we begin, I would like to remind the parties that we each have a copy of the demonstrative exhibits you provided. During your argument, please identify clearly and specifically the demonstrative referenced by slide or screen number so that everyone can follow along and to ensure clarity and accuracy of the court reporter's transcript.

As set forth in our hearing order, the Petitioner will have 60 minutes to present the arguments. Petitioner will proceed first and may reserve time for rebuttal. How much time would you reserve?

MR. MOCK: Fifteen minutes, please.

JUDGE REN: Fifteen minutes.

1 And I understand we have a LEAP practitioner for Patent Owner
2 today, Ms. Hill. And you will have 75 minutes total to present your case.
3 Would you like to reserve surrebuttal time?

4 MR. GIUNTA: Yes. We'd like to reserve 15 minutes, Your
5 Honor.

6 JUDGE REN: Thank you. Petitioner, if you're ready, you may
7 proceed, please.

8 MR. MOCK: Okay. Thank you. Good morning again. Thank
9 you for taking the time today. I will dive right in because we have several
10 grounds to cover. Today we're going to walk through a couple 112 grounds
11 relating to written description enablement of the proposed substitute claims.
12 There is an anticipation ground based on intervening art as a result of those
13 112 grounds, as well as few 103 challenges.

14 Should it please the Court, I'm going to go ahead and start with the
15 112 as I think the -- some of the issues with that actually permeate through
16 the discussion of not only the anticipation ground but also the obviousness
17 grounds as well. And so just for table setting, I think it's important to walk
18 through the basis of that ground and the technology.

19 So, the '675 Patent discloses a technology for modifying lysine
20 residue, specific lysine residue 248, in IgG1 antibodies. This is done using a
21 reagent that is referred to as a site-specific antibody interactome or SSAI.
22 The SSAI functions by binding a particular site on the Fc domain of these
23 IgG1 antibodies around and adjacent to the lysine being modified -- in this
24 case, 248 -- to bring a molecule to be labeled to reactive group in close
25 proximity to that lysine being modified such that the chemical reaction can
26 occur.

1 The '675 Patent explains that there are a subset of site-specific
2 antibody interactomes called site specific Fc interactomes or SSFI. But it is
3 noteworthy that the '675 Patent does not provide any examples or
4 demonstration or discussion of sequences for an SSAI generally, rather, the
5 only thing that it discloses are SSFI that are used for binding to the Fc
6 domain of human IgG1 antibodies. It is worth noting too, just for the sake of
7 clarity, that that sequence, the target sequence so to speak of those disclosed
8 SSFI is SEQ ID NO: 1.

9 That sequence is repeated multiple times throughout the
10 specification but with different nomenclature, including formula 8-1, 8-2, 8-
11 3, 7-1, 7-2, 7-3, and 10-1, 10-2, 10-3. In each case, it is the same base amino
12 acid sequence. It's just in each case the -1 version is unmodified or has a
13 modification at 246, the -2 version shows a modified lysine at 248, and the -
14 3 version shows modified lysines at both of those positions.

15 The sequence specificity and the sequence requirements of this
16 technology are outlined in the figures and graphically displayed there. And
17 they note that the precise sequence is going to be required because it needs
18 to bind closely to this particular cleft within the Fc domain, such that the
19 reactive groups are extremely close to lysine 248. It even notes that the Fc
20 domain may become unstable and the reaction may not work if there is not a
21 favorable reaction between an SSFI and an Fc domain. In other words, no
22 labeling or no modification of the 248 lysine may occur.

23 JUDGE FREDMAN: Can you point to where the spec says that?

24 MR. MOCK: Yes. That is in columns 14, 41 through 42; and 33
25 -- column 37, lines 35 through 39 are the portions that discuss --

26 JUDGE FREDMAN: In 14 it just talks about the structure. So, it's

1 on 37?

2 MR. MOCK: Let me pull up the update of the --

3 JUDGE REN: Also, let the record reflect that we're on Slide
4 number 5.

5 MR. MOCK: Oh, yes, my apologies to the Court. I don't know
6 where I put my copy of the patent.

7 JUDGE FREDMAN: Column 37 does give some guidance on
8 which amino acids can be used in that region functionally, with regard to
9 histidine and other amino acids.

10 MR. MOCK: Excuse me, what --

11 JUDGE FREDMAN: When you're quoting column 37, column 37
12 does give some guidance as to other amino acids that can be used and how
13 the topology can be addressed.

14 MR. MOCK: Right. But it is still a sequence-specific reaction,
15 and I think that's illustrated well within these figures. Turning to Slide 6,
16 where this is shown, you have your base sequence, the linear sequence of
17 that target of the Fc region in the IgG1. In Figure 2, you can see the three-
18 dimensional architecture, how you get this cleft there with lysine 248, right
19 there squarely at the center of it. And Figure 7 shows the SSFI binding in
20 this region, such that the Xa1 portion, which is the portion that --

21 JUDGE FREDMAN: Right. You're showing us the three-
22 dimensional structure in a ribbon-type diagram. I'm not entirely sure what
23 your point is.

24 MR. MOCK: The point is just underscoring that this is a
25 sequence-specific process. And so, the binding affinity of an SSAI or SSFI
26 is going to impact the functionality and essentially the entire foundation of

1 whether this reaction is going to occur without binding in close proximity --

2 JUDGE FREDMAN: So, in the context of an antibody, are the Fc
3 regions usually constant or are they variable like the variable regions?

4 MR. MOCK: So, the Fc regions are going to be common in
5 certain isotypes of antibodies. And in this case, the sequence that is the
6 target sequence here, SEQ ID NO: 1 for Formulas 8-1 through 8-3, that is an
7 Fc sequence that is common to human IgG1s, IgG2s, and IgG4s. That is not
8 a sequence that is common to all antibody isotypes, let alone other proteins.

9 JUDGE FREDMAN: Your argument is that the claims as written,
10 because they don't specifically mention the isotype lack written description?

11 MR. MOCK: Both written description and enablement because --

12 JUDGE FREDMAN: We know the sequence is the IgG1, say,
13 isotype, then we know which ones will work. So that doesn't seem to be an
14 enablement problem. That's a Capon issue, right? So, it seems like you're
15 -- your description argument's a little bit better there because at least you're
16 arguing that we haven't described all of them.

17 MR. MOCK: Well, certainly not all of them are described. But I
18 think there are limitations in terms of whether this would function across the
19 entire scope of the claims too, including other isotypes, and therefore
20 enabling them. Just because a certain subset of them will work, it doesn't
21 mean that the -- in this case, really the majority of things that would be
22 encompassed by the claims will not function.

23 JUDGE FREDMAN: But if it's predictable, does that matter? In
24 Capon, which was an antibody case too, there were things that wouldn't have
25 worked. I don't think there's really any doubt about that. It was a nucleic
26 acids and antibody case, sort of. So, I think that the fact that there was some

1 level of unpredictability alone is not sufficient. It has to be -- the ordinary
2 wouldn't have been able to do it.

3 MR. MOCK: So, I'm actually glad you bring up predictability
4 because that is something that both our expert, Dr. Tumey and Dr. Zhou, the
5 expert for Patent Owner, have touched on. In particular, in Exhibit 2004,
6 Dr. Zhou's first declaration, he referred to the field of ADC modification as
7 inherently unpredictable, in paragraph 40, and said, "Given the structural
8 diversity and highly variable chemo-physical properties of antibodies, a
9 POSA could not predict with confidence whether a modification that
10 succeeded for one antibody would also succeed for another."

11 So here, Patent Owner's own expert has said that just because this
12 works for one antibody doesn't mean it's going to work for another.

13 JUDGE FREDMAN: Can you repeat the cite for me? I'm sorry.

14 MR. MOCK: That is 2004, Exhibit 2004, at paragraph 40. In that
15 same exhibit, at paragraph 39, he says, "Achieving selective modification,
16 particularly at specific lysine residues such as lysine 248, is not a matter of
17 routine optimization but one of significant uncertainty." And in his second
18 declaration, Patent Owner and Dr. Zhou have doubled down on that position
19 in Exhibit 2008, at paragraph 8. He says, with respect to the PepTalk
20 references, that "regarding broad applicant applicability or potential across
21 antibody isotypes, this was merely aspirational and outcome oriented, and
22 that those references do not disclose the chemistry-specific information
23 necessary for a POSA to reasonably predict success of a particular
24 modification."

25 Now I think it's important, and I'd like to walk through that
26 particular comparison. Because while Dr. Zhou does reference the PepTalk

1 references, the PepTalk Poster, and PepTalk Presentation with respect to this
2 aspirational goal of modifying other isotypes, the PepTalk references and the
3 '675 Patent disclose effectively the same amount of technical information in
4 terms of modification. Both of those references, the PepTalk references
5 -- and I'll just refer to the PepTalk Presentation since the slide numbers are a
6 little bit easier than pulling through the full poster.

7 But both of those references disclose what they refer to as an
8 affinity peptide, which is a corollary to the SSFI. It's a peptide that has a
9 reactive group on it that binds to this specific target sequence in proximity to
10 lysine 248, such that a reaction can occur. Slide 14 of the PepTalk
11 Presentation shows that that affinity peptide, the sequence of it, its structure,
12 the reactive groups that can be on it. Slides 16 through 18 show site-specific
13 functionalization of trastuzumab at lysine 248. And that was confirmed
14 through mass spectrometry in those slides, that that particular residue 248
15 was modified.

16 And notably, trastuzumab is the same antibody that was used in the
17 only working examples in the '675 Patent. That is the only example that
18 they showed of modification using their SSFI in their system. It is a human
19 IgG1 antibody. That is all they showed. So, we have performed the same
20 type of proof of concept in the prior art. And when the prior art says that
21 this could be applicable at least to IgG2 and IgG4, Dr. Zhou says, no, you
22 couldn't predict that, you have not given the site specific chemistry that's
23 needed, and that applying any sort of platform technology like this across
24 isotypes is inherently unpredictable.

25 That seems to be at odds with their position here. If it doesn't work
26 with the PepTalk references, why would the same proof of concept in the

1 '675 Patent be enabling or show possession for '675? To me that is an
2 irreconcilable position within the record in relation to the support for these
3 claims. Of note, with respect to this, not only the sequence specificity, but
4 as Dr. Tumey testified both in his first and second declarations, referring to
5 Slide 7 here, there are a wide array of antibody isotypes out there.

6 And in this particular situation, the '675 Patent itself defines
7 antibody as including all naturally occurring immunoglobulins as well as
8 recombinant proteins, fusion proteins, chimeric proteins, and the like that
9 have the same or similar structures. That includes both human and
10 nonhuman, which can also vary. But here, if we're looking at IgG1, IgG2
11 and IgG4, even those have variant forms that do not include SEQ ID NO: 1,
12 Formulas 8-1 through 8-3.

13 So even those might not predictably work with these SSFI that are
14 disclosed in the '675 Patent, let alone when you look at the array of different
15 constructions that you have here. The claims, as we've noted in our briefing,
16 say one or more modified heavy chain. Well, there are lots of different
17 antibody types that have more than two modified heavy chains. And at best,
18 they showed an IgG1 that has two modified heavy chains.

19 But they have not shown in any way how one could modify the
20 pentamers of IgM to get up to 10 modified heavy chains. They have not
21 shown how to modify the dimers of IgAs that would have up to four
22 modified heavy chains because those have different Fc sequences. They
23 would necessarily require a different SSAI or SSFI that is not disclosed, that
24 is not tested, and that is in no way predictable based on Dr. Zhou's own
25 testimony in the disclosure in the '675 Patent.

26 So far from teaching how to make and use the full scope of claims,

1 they show a very, very small subset is operable within the technology that's
2 disclosed. And they certainly do not show possession across the entire scope
3 of the claims.

4 JUDGE REN: Is it your position, Counsel, that what's claimed
5 beyond what Claims 14 through 16 recites is unenabled and unsupported? Is
6 what you're saying that the claim is -- the claims are broader than the
7 structures specifically recited and therefore they're not enabled?

8 MR. MOCK: Precisely.

9 JUDGE REN: Okay.

10 MR. MOCK: Because here we do have a situation where the only
11 SSFI that are disclosed, the only structures, the only reagents that they have
12 disclosed will only work for IgG1, possibly IgG2 or IgG4. But Patent
13 Owner's own expert cast doubt on the operability of that as well. And so,
14 when you look at the full scope of these claims, it's all naturally occurring
15 immunoglobulins, both human and nonhuman, all recombinant proteins,
16 fusion proteins, chimeric proteins that have the same or similar structure.

17 That is massive, truly massive, without being hyperbolic genus that
18 is not disclosed or would not function or be operable with the technology
19 that's disclosed here.

20 JUDGE REN: But Counsel, that's exactly why when we review a
21 patent or we understand a claim the POSITA knowledge comes in. I see that
22 in your sur-reply you have this argument that the specification contains no
23 guidance or teaching how to introduce a lysine at a 248 position in proteins
24 that lack it. But that's not the issue here, is it? A POSITA would know that,
25 oh, if the protein that doesn't have the lysine at 248, then the claim is not
26 -- the structure is not applicable. We're not saying that the claim applies to

1 proteins that don't even have lysine at this 248 position.

2 MR. MOCK: I think the construction of the claim should be such
3 that it could apply to that because there's no limitation on antibody; rather it
4 purposefully says all naturally occurring immunoglobulins, some of which
5 may have a lysine at 248 some of which may not. There are going to be
6 technologies in the art to make amino acid substitutions. That is something
7 that could be done, but it is nowhere taught here.

8 And even if a substitution was made and one of those other
9 isotypes could get a lysine at 248, because the flanking sequences, the
10 surrounding area is distinct and does not have the same sequence as IgG1, 2,
11 or 4 Fc domain, you would still require a separate SSFI or SSAI. Here the
12 specification provides an explicit, very broad definition on purpose. And
13 under Phillips, when an Applicant or a Patentee defines a term that is
14 controlling, that is what's supposed to govern.

15 And so, I do not think it is proper or permissible for Patent Owner
16 to walk back that construction now and say, oh, well, when we say antibody,
17 we don't mean antibody as we've defined it. We mean antibody only when it
18 works, only when it works in our favor here. Because I think --

19 JUDGE FREDMAN: Just to clarify, so you arguing that you
20 couldn't put position 248 as a lysine; is that right?

21 MR. MOCK: No. You might be able to with this other antibody --

22 JUDGE FREDMAN: You keep using might, is that really a
23 statement that you want to tie down to? Well, you could. Any ordinary
24 artisan would realize you could -- we could go out right now to NIH; and if
25 we borrowed a machine, we could do it. At the time you could have done it.
26 That's not a reasonable position with PCR amplification of the sequences

1 and then just cloning it into a gene. I mean, that's not persuasive. Now if
2 you're arguing that the surrounding sequence, that's a different argument.

3 MR. MOCK: Well, the surrounding sequence is what would
4 matter.

5 JUDGE FREDMAN: It would be part of what might matter,
6 depending on the circumstance, right?

7 MR. MOCK: I think it would --

8 JUDGE FREDMAN: Because it's the folding that matters.

9 MR. MOCK: It would entirely matter. Because if you had a
10 lysine at 248 of an IgM, for instance, that has an entirely different flanking
11 sequence --

12 JUDGE FREDMAN: It might not work.

13 MR. MOCK: -- then it's -- yeah, it's not going to work that. Just
14 like antibody --

15 JUDGE FREDMAN: Have you tested that? Do you know it won't
16 work?

17 MR. MOCK: We have not tested that, but neither has Patent
18 Owner.

19 JUDGE FREDMAN: So, you're speculating it wouldn't work
20 there. Do you have any evidence that it wouldn't work? Have you done any
21 folding studies or anything else?

22 MR. MOCK: We have Patent Owner's own testimony that -- from
23 their expert that says it was inherently unpredictable.

24 JUDGE FREDMAN: That's a different statement than it wouldn't
25 work.

26 MR. MOCK: I don't think it is. He said that this type of --

1 JUDGE FREDMAN: Do you say that he tested IGMs and they
2 didn't work -- or IgAs or any other type of anybody?

3 MR. MOCK: No, he did not.

4 JUDGE FREDMAN: Okay. So, there's no evidence on that point?

5 MR. MOCK: There's also no --

6 JUDGE FREDMAN: No argument on both sides?

7 MR. MOCK: There is no evidence in the '675 Patent that it would
8 work in the sequence --

9 JUDGE FREDMAN: I understand. That's correct, yes.

10 MR. MOCK: But there is also a juxtaposition here that I think is
11 difficult to address. That is what I was alluding to with respect to the 112
12 and the other prior art grounds as well, when we have statements from
13 Patent Owners about the teachings in the prior art. With respect to all of the
14 art that's been cited against them, they have interpreted it such that it should
15 only be applicable to the very precise confines of what is taught there. They
16 say that Yamada's disclosed compounds are limited, and so the chemistry
17 taught there should be limited to what they have shown.

18 They say that importing other chemistry, relying on what might
19 have been known out there, was not something would have that would have
20 been routine or obvious with respect to the PepTalk references and what
21 they show of the AJICAP platform that also modifies lysine 248 using an
22 affinity peptide. They say that this does not demonstrate that site-specific
23 chemistries were predictable and that it can't be applied outside of this.

24 So, we're stuck with a position here where Patent Owner says, on
25 the one hand, all of the art that is prior art to our application must be limited
26 only to what is shown there. It can't be applied more broadly. But our

1 specification of course is going to be applied more broadly and would enable
2 us, would show possession of all these different isotypes, varying different
3 chemistries, even though that's not the case for prior art that showed
4 effectively the same thing.

5 Yamada, like the '675 Patent, discloses lots of different affinity
6 peptides. It shows multiple working examples modifying different
7 antibodies, as is Matsuda. In many cases, it is trastuzumab, the same
8 antibody. It's the same amount of technical information there in those
9 references with respect to the teachings. But there is this sort of
10 irreconcilable friction there that Yamada and Matsuda should be, according
11 to Patent Owner, interpreted as a POSA to could do nothing with that
12 beyond what is expressly taught versus the '675 Patent.

13 In order to be properly enabled, in order to have written
14 description, it necessarily must be interpreted as you would be able to take
15 these teachings and run with them. And I think that is an incongruity here --

16 JUDGE FREDMAN: You're essentially arguing with the -- what
17 an examiner would do. I don't know if you did prosecution or not, where
18 they squeeze using a 112 and a 103.

19 MR. MOCK: Certainly. I think it is a bit of a squeeze here. I
20 don't think those things can be true. I don't think that you can have this
21 inherently unpredictable and tremendously confusing prior art that would not
22 allow any further application but also be enabled across a large scope of
23 antibodies as defined by the '675 Patent.

24 And this is referring to demonstrative Slide 10, while Patent
25 Owner has argued and asserted in their response that a POSA would just
26 need to recognize antibodies that have a heavy chain, an Fc domain can be

1 substituted here. That in my opinion, as I was saying to Judge Ren, in is not
2 a proper construction. This is not a case where they can walk back the
3 expressed, explicit definition in '675 Patent now and say, oh, it works. They
4 need to show, in order for proper 112 support, that this technology they
5 would be able to modify.

6 And we're in possession of modified antibodies across the entire
7 scope of the claims, regardless of the flanking sequences around lysine 248,
8 regardless of whether the amino acid at lysine 248 -- at 248 was a lysine, and
9 regardless of how many heavy chains there are in the antibody. And that is
10 --

11 JUDGE FREDMAN: It has to be a lysine. That's not really an
12 issue. The things all require that.

13 MR. MOCK: Certainly. But for the sake of argument, there could
14 be a case where there's not a lysine, but you modify the antibody before this
15 reaction to place a lysine here in those instances.

16 JUDGE FREDMAN: But there has to be a lysine when you're
17 making it. It's certainly not an issue. You're claiming it's a flanking
18 sequence really is the biggest argument I think you have.

19 MR. MOCK: Sure, yes. I think that predominantly covers our 112
20 position. If you have any other questions, I'm happy to address them to the
21 best I can. Otherwise, I'll quickly turn to anticipation and then run through
22 the 103.

23 Okay. Well, in this case, anticipation is really simple. In the event
24 that the claims are found to not have proper written description and/or
25 enablement in the specification of the '675 Patent, then they also would not
26 be entitled to priority beyond the filing date of the '998 Patent from which

1 -- the '998 application from which the '675 Patent issued. That application
2 was filed on January 16th, 2023. And that means the Canadian national
3 publication, the 959 publication that is part of this same family, would be
4 prior art. It was published enough in advance of the filing date in 2023 that
5 there are no exceptions.

6 While I know Patent Owner has thrown out the potential for a
7 102B exception, that would only be if the '675 Patent was accorded an
8 earlier filing date than the '998 applications filing date. But in this case, if
9 there is no written description support in the '675 Patent and there's no
10 enablement in the '675 Patent, then that means the 503 application, the
11 earlier parent necessarily would also lack that. And so, the priority chain
12 breaks at the outset. It's only the filing date of the '675 Patent that it is
13 entitled to, that is the only one that's important.

14 We don't need to belabor that point because it's a fairly simple 102,
15 with respect to the teachings here. The examples in the 959 publication and
16 the '675 Patent show modification of trastuzumab, which is one species, a
17 very particularized species within the much, much larger genus that is
18 claimed here. And so that species would anticipate the genus.

19 Turning to the obviousness grounds now. There are a lot of issues
20 to unpack here. So obviously, feel free to stop me and dive into whatever is
21 most pressing from your perspective. But in this case, all three of the
22 proposed substitute claims have the same lead-in with respect to a modified
23 antibody comprising a bioorthogonal click chemistry group, click chemistry
24 functional group, wherein the modified antibody comprises one or more
25 modified heavy chain, where in each of the modified heavy chains comprise
26 a modified lysine at 248 position of the heavy chain amino acid sequence,

1 where the 248 is determined by an EU numbering.

2 All of that, the initial part of the claim, is set forth in each one of
3 the prior art references, Yamada and Matsuda, and both of the PepTalk
4 references. I don't think there's really much of any debate there. All of
5 those are disclosing platform technologies for modifying lysine 248. They
6 all show reduction to practice. In many cases, the same reduction practice,
7 the same proof of concept as the '675 Patent. So that is all there.

8 The rub here, the thing that is being contested is whether a person
9 of skill in the art would have actually found obvious the particularized
10 sequences that are -- or structures that are depicted in the proposed substitute
11 claims. Claim 14 includes this azide group with a short linker. Claim 15 as
12 a norbornene with no linker between the tourmaline of the lysine group and
13 norbornene click chemistry group. And Claim 16 is a norbornene click
14 chemistry group with a short linker that is similar to the one in Claim 14.

15 JUDGE REN: Could I ask you why a POSITA will go and remove
16 this linker, for example, to arrive at the substitute Claim 15?

17 MR. MOCK: Sure. I will see if we have --

18 JUDGE REN: And I see that. I think your argument is supported
19 by expert testimony saying that there's an implicit motivation to keep
20 molecules simple based on the Ockham razor theory.

21 MR. MOCK: Correct.

22 JUDGE REN: Is that your only position to say that that's what a
23 POSITA will consider a reason to modify, to arrive at Claim 15?

24 MR. MOCK: So yes, I believe that is the reason that has been
25 presented. In this case, when you're in drug development, when you're
26 testing out these linkers, both Dr. Tumey and Dr. Zhou, I believe at different

1 times, have talked about the flexibility of the linker, how that can impact
2 downstream reactions for these groups. And Dr. Tumey's point was that
3 with respect to Claim 15, if you are going to do a controlled empirical study
4 of the impact of these linkers.

5 For instance, Patent Owner argues a lot about the impact of having
6 an ether group, this oxygen heteroatom. If you're going to do a controlled
7 study about the impact of that heteroatom, the links of the linkers, any of
8 those variables that can and are routinely adjusted, then the thing you're
9 going to compare it to is a modification with no linker. That is the perfect
10 control for that.

11 And so, I do not know and cannot say whether Patent Owner is
12 going to use that modified lysine for Claim 15 straight for drug development
13 or whether it is their in-house control. That I do not know. But for our
14 purposes today, I don't think that that necessarily matters because the
15 motivation for obviousness doesn't have to be the same as the motivation for
16 the inventor.

17 And here, I think Dr. Tumey has provided a very reasonable
18 explanation for why somebody would do that. These are scientists. This is a
19 development of a platform. There is a motivation to start --

20 JUDGE FREDMAN: How large is the chemical space that you
21 could put there?

22 MR. MOCK: Do what?

23 JUDGE FREDMAN: How large is the chemical space that you
24 could modify?

25 MR. MOCK: How?

26 JUDGE FREDMAN: Large is the chemical space that you could

1 modify.

2 MR. MOCK: Based on the examples in all of these --

3 JUDGE FREDMAN: Based on the examples -- because that's not
4 what they're looking at. Based on the prior art.

5 MR. MOCK: Yeah. Certainly, there's a there's a lot of ways that
6 this could be modified. There's a lot of literature that linkers --

7 JUDGE FREDMAN: Very large number of ways, I would
8 suggest.

9 MR. MOCK: Certainly. There are --

10 JUDGE FREDMAN: And you're arguing one particular way was
11 obvious.

12 MR. MOCK: Well, in this case --

13 JUDGE FREDMAN: It's the Occam's razor, based on a teaching
14 that this was a motivated modification rather than a person might have done
15 it.

16 MR. MOCK: In this --

17 JUDGE FREDMAN: That's essentially your argument.

18 MR. MOCK: Yes. But in this case, that Occam's razor, that
19 selection --

20 JUDGE FREDMAN: Occam's razor, I don't think, is a particularly
21 good argument for obviousness. I don't think I've ever seen it before.

22 MR. MOCK: In this case --

23 JUDGE FREDMAN: I've been doing this 30 years.

24 MR. MOCK: Semantics aside, we cannot refer to it as Occam's
25 razor. But calling it a control, this would be a good structure to select for a
26 control. Because while you mentioned there a plethora of different options

1 in terms of linkers, both in structure and composition and length that one
2 could try, this would be a control for all of those. You would know what
3 any of those variables are doing against all of those different options. So, I
4 would stand by that. I think there was implicit motivation to select a lack of
5 a linker, a direct conjugation to the modified lysine.

6 With respect to the other linkers, the ones from Claims 14 and 16,
7 Dr. Tumey has indicated that short linkers that allow for some flexibility but
8 not too much flexibility are preferred for that. That was pointed out both in
9 his first declaration as well as the second declaration, Exhibit 1059 of
10 paragraph 33 discusses this. And I don't think that there's much really
11 argument that -- in general, most of the examples in the art are going to be
12 short linkers.

13 Indeed, the linkers that are disclosed -- this is turning to Slide 15 of
14 the demonstratives. One of the linkers that's disclosed in the PepTalk
15 references and one of the linkers that's disclosed in Matsuda are both
16 roughly the same length as the linkers for Claim 14 and 16. The length of
17 the linkers in 14 and 16 actually fall within the range between the spacer in
18 PepTalk -- the PepTalk references and Matsuda.

19 JUDGE FREDMAN: So, they're not the same?

20 MR. MOCK: They are not the same. But just to take it in a
21 stepwise function, the length is within a range of a functionalist talk. The
22 difference here primarily is that beta heteroatom, the oxygen there in that
23 beta position. And I know that's something that you all would probably
24 want to discuss for our purposes.

25 The Patent Owner has said that we provide no motivation why
26 someone would select that. I don't believe that is an accurate representation

1 of the record. Dr. Tumey has explained in his specification again, at
2 paragraph 234 of Exhibit 1059, that oxygen heteroatoms were generally
3 thought of as nonreactive and expected to be stable. And so that lends itself
4 to a variety of different chemistries. If people are going to be trying out
5 different chemical conditions for carrying out these modification reactions, it
6 also provides a desirable ultimate product.

7 All of the claims here, the structures that are being claimed, are
8 essentially an intermediary or a pharmaceutical for an ADC, right? We have
9 the click chemistry group on this modified antibody. But eventually,
10 somebody is going to click on a drug, and that's the ultimate product. Well,
11 having an oxygen in the linker, as Dr. Tumey attest in paragraph 34 of 1059,
12 increases the polarity of the compound, which would likely increase
13 solubility. And he cites multiple references, including Exhibit 1048 and
14 1052, that support this proposition.

15 I will note that when Dr. Zhou, in his response has said, there's no
16 reason to do this, it doesn't work, there's never any supporting citations for
17 any of those assertions. And so, whether the Board wants to credit that or
18 not is certainly within your discretion. But here we have one expert who is
19 testifying to known desirable benefits for including an oxygen that are
20 supported by the literature and another who just says, no, trust me.

21 In further evidence, we also have noted that both the Yamada and
22 Matsuda include various heteroatoms within their linkers. And I think it's
23 important to note also --

24 JUDGE FREDMAN: Where is it supported in the literature when
25 you said that? Does the professor provide a support?

26 MR. MOCK: I would have to turn back to that.

1 JUDGE FREDMAN: You stated that, so I'm assuming you're
2 partly saying it.

3 MR. MOCK: Yeah. If I can finish this --

4 JUDGE FREDMAN: You expressly had quoted it in paragraph 34
5 there.

6 MR. MOCK: Certainly. I don't think it was a direct quote.

7 JUDGE FREDMAN: So, he doesn't cite anything. So, what is he
8 relying on for that? He points to Exhibit 1048, is that what you're relying
9 on?

10 MR. MOCK: Correct.

11 JUDGE FREDMAN: It just talks about hydrophobicity generally.

12 MR. MOCK: Right. Which is the property that he's --

13 JUDGE FREDMAN: That doesn't put you in the ether. That puts
14 you to something. That's not very particular to this molecule.

15 MR. MOCK: It may not be particular to this for this molecule, but
16 it is particular to oxygen. It would be particular to an ether linkage.

17 JUDGE FREDMAN: There are lots of oxygen linkages.

18 MR. MOCK: Certainly. But it is a reason to --

19 JUDGE FREDMAN: There are other elements that also would be
20 able to be not hydrophobic. It doesn't have to be oxygen. I think sulfur
21 might be a little bit hydrophilic too.

22 MR. MOCK: That is also one of two reasons that he provides
23 here, both desirability with the reaction chemistry. So, we --

24 JUDGE FREDMAN: There's some generic statement that you're
25 then pulling out one particular thing from.

26 MR. MOCK: I mean, I --

1 JUDGE FREDMAN: And that's essentially what he's doing. He
2 doesn't have any specific teaching to put this here. He's saying, well,
3 generally, you might put something there, so we're going to put this there.

4 MR. MOCK: Well --

5 JUDGE FREDMAN: That's essentially what I read to that. Is that
6 incorrect? And if so, why?

7 MR. MOCK: I think you have to give some credit to the fact that
8 he is a skilled person in this area. And if he's going to look at a reference
9 like that and say he could extrapolate this reasonably, have a --

10 JUDGE FREDMAN: Doesn't he have to give the basis for where
11 he extracts it than just say it?

12 MR. MOCK: Do what? Yeah. He's not going to just say it. All
13 of this was --

14 JUDGE FREDMAN: Well, he's just says it. He doesn't explain it.
15 In the paragraph he just says, yeah, it would have been obvious. He doesn't
16 really give a reason.

17 MR. MOCK: Certainly. But I think you got to consider that in the
18 broader context that, A, there was some underlying literature that would
19 suggest there were desirable properties for oxygen generally. If this person
20 who has decades of experience --

21 JUDGE FREDMAN: The burden is on the Petitioner, right?

22 MR. MOCK: -- within the ADC field says this is what I can glean
23 from that, then I think that should be given some weight. I also note that
24 with respect to Yamada, we laid this out in the petition, carried it forward in
25 our opposition to the motion to amend. There is this Formula IV in Yamada
26 that includes different variable groups and different combinations that can be

1 used in those variable groups.

2 We have shown from these formulas that there's more than one
3 way to follow through the steps of Yamada's Formula IV and arrive at
4 linkages with a beta heteroatom in oxygen. I would submit that if that was
5 completely undesirable and just antithetical to what a person of ordinary
6 skill in the art would have believed at the time, why would they have
7 included that in this patent? The pieces of the composition are there, the fact
8 that you could select a beta heteroatom -- an oxygen beta heteroatom for the
9 linker in Yamada is there. It's disclosed within Formula IV.

10 And we have shown that through Dr. Tumey's testimony that there
11 could have been -- there was motivation for a person to say, yeah, that's
12 reasonable, I would pick an oxygen there. I don't think that there's anymore
13 that it's required. Now Patent Owner has tried to cast doubt on this by
14 saying, well, the scheme in Figure 2 of Yamada would not function to
15 actually produce these, that the cleavage chemistry is not functional. It
16 wouldn't work.

17 But I think there are a few holes in that position that I think are
18 worth outlining. First is that under Beckman, there's precedent for saying
19 that even if a reference is allegedly inoperative, it's still prior art for all that it
20 teaches. And here it does teach formulas that encompass oxygen as beta
21 heteroatoms. Symbols Tech v. Opticon also says that non-enabling
22 references may qualify as prior art for the purposes of determining
23 obviousness under 103. So, if it was non-enabling, that should not be just a
24 kill all dead in the water position.

25 Because a person of ordinary skill looking at this can say there is
26 within the scope of Yamada disclosure of beta heteroatoms.

1 JUDGE FREDMAN: This is the Yamada 165; is that right?

2 MR. MOCK: Excuse me?

3 JUDGE FREDMAN: Heteroatoms were the 165 Yamada, is that
4 the correct one?

5 MR. MOCK: 165.

6 JUDGE FREDMAN: That's the English version; am I correct?

7 MR. MOCK: With the exhibit number?

8 JUDGE FREDMAN: The exhibit number, let me do that. This is
9 the Exhibit number 1011 --

10 MR. MOCK: Yes.

11 JUDGE FREDMAN: 1009.

12 MR. MOCK: Yeah, 1009.

13 JUDGE FREDMAN: And so, Formula IV is I think L1-B-R'-T;
14 that right?

15 MR. MOCK: Yes.

16 JUDGE FREDMAN: And you're saying that suggests an oxygen?

17 MR. MOCK: If you walk through those paragraphs, it starts in the
18 mid-600s and goes through several paragraphs there.

19 JUDGE FREDMAN: Okay.

20 MR. MOCK: If you step through those, you can get to that. But
21 additionally, even if the scheme in Yamada's Figure 2 would not work for
22 making these particular cleavage products, the expectation of success and
23 the motivation does not have to come from the reference itself. This is,
24 again, sort of harkens back to that disconnect in the 112 ground. There is an
25 argument that is permeated in Patent Owner's side saying that these
26 references, you just have to stick to what's in them. It's only what's in them.

1 JUDGE FREDMAN: You have about two and a half minutes left,
2 just so you know.

3 MR. MOCK: Thank you for the warning. But in this case, we
4 have presented some alternative chemical schemes that Dr. Tumey provided.
5 He walked through potential chemistry that could work, even cited
6 Matsuda's Figure 1 which shows a reaction in which if the linker and
7 reactive group on the end of those was changed would reasonably be
8 expected to result in the norbornene modifications claimed in Claim 15 and
9 16. Again, these are positions that Dr. Tumey put forth with some citation
10 showing that there was established chemistry for at least trying these things.

11 And while Patent Owner has come back and alleged that this
12 would not work -- again, note that Dr. Zhou provided no basis for his
13 opinion that it would not work. And to that end, for instance, he said that the
14 conditions in the prior art weren't compatible with antibody modifications.
15 He cited the reference showing what the conditions were, the temperature,
16 the pH, those type things. But there's nothing to support that those are
17 incompatible with --

18 JUDGE FREDMAN: But you don't accept his expertise. You
19 only accept your expert.

20 MR. MOCK: Our expert does have some citations to his. Again,
21 like --

22 JUDGE FREDMAN: His citations were quite generic.

23 MR. MOCK: When it comes to --

24 JUDGE FREDMAN: It's very generic, *In re Baird* would be upset.

25 MR. MOCK: When it comes to establishing the weight of each
26 examiner -- of each expert's testimony, I think it's still worth considering.

1 Same with respect to Dr. Zhou's arguments that dipolar elimination reactions
2 like the second scheme that Dr. Tumey provides, he says those are less
3 reactive than trifluoro, which may be true, but difluoro is still reactive. It's
4 sufficiently reactive for this purposes. It doesn't have to be the best or
5 optimized. It is just a way that this would reasonably work.

6 Finally, with respect to referencing the Matsuda is Figure 2, Patent
7 Owners says, well, you wouldn't -- nobody would make this substitution.
8 They haven't shown motivation for why somebody would make the
9 substitution to the norbornene in these linkers. As I've discussed earlier, I
10 think we have prevented some motivation for why somebody would do that,
11 in which case this is just a substitution of known elements in the field.
12 There's no argument --

13 JUDGE FREDMAN: You want to run into your extra time or not?

14 MR. MOCK: I can call it at that, unless you guys have any
15 questions.

16 JUDGE FREDMAN: Okay.

17 JUDGE REN: Patent Owner may proceed when you're ready.
18 Good morning.

19 MS. HILL: Good morning, Your Honors. I'm Rebekah Hill, on
20 behalf of Patent Owner Abtis. I will be discussing the written description
21 issue to start, and then I will also handle the anticipation issue. And then I'll
22 turn it over to Mr. Giunta who will discuss enablement and then explain why
23 the proposed substitute claims are not obvious based on the grounds
24 advanced by Patent Owner -- or sorry, by Petitioner.

25 So, starting with written description, written description asks
26 whether the original disclosure reasonably conveys possession of the

1 claimed invention, and it does not require a verbatim recitation of every
2 single claim limitation in the claim language and the limitations. All it
3 requires is that the specification conveys with reasonable clarity to a person
4 of ordinary skill in the art that the inventors were in possession of the
5 claimed invention.

6 JUDGE REN: Ms. Hill, the patent that you have here does specify
7 that, for example, the term antibody is an immunoglobulin molecule or
8 fragment thereof. And the patent goes on to say that it includes a variety of
9 molecules, including naturally occurring immunoglobulins and all
10 recombinant proteins. And according to the Petitioner, includes human and
11 nonhuman entities. So why should we limit the scope of antibody in the
12 claim to what you essentially have as just the recited structure?

13 MS. HILL: Sure. So, Dr. Zhou, in his second declaration, around
14 paragraph 46, he explains that -- and I'll point out that I'm on Slide 4 of the
15 presentation, which has each of the claims on the screen, just for reference.
16 But Dr. Zhou in paragraph 46 of his second declaration explains that a
17 person of ordinary skill in the art would understand that the claim limits
18 itself to the modified antibodies with the lysine at position 248. And that's
19 because of --

20 JUDGE FREDMAN: I think we agree with that. And I think
21 Petitioner kind of maybe conceded that slightly. But the question is, is that
22 enough? We have these other regions surrounding the lysine at 248 that are
23 apparently necessary to arguably -- to permit binding of the linker. So why
24 are we including antibodies that don't have those regions? Because that's the
25 breath issue.

26 MS. HILL: Right. Thank you. I'm turning to Slide 6 to discuss

1 the modified antibodies with the modified heavy chain. But also relevant is
2 in Dr. Tumey's original declaration, at paragraph 67, he provides his
3 understanding of the claimed term modified antibody. And he actually cites
4 to the intrinsic evidence and cites to a definition provided in the '675 Patent.
5 And Dr. Tumey admitted that based on the intrinsic record, a person of
6 ordinary skill in the art would understand modified antibodies to include any
7 antibody with the variety of heavy chains, for example. And he came to that
8 understanding based on the --

9 JUDGE FREDMAN: So heavy chains there's a lot of choices,
10 right? There's IgG1, IgG2, IgG3, I think there is one IgG4, there's one IgA,
11 IgM, IgE. Those are all encompassed here, right? So why is it not a
12 problem for description that you've only shown it works in essentially a
13 version of IgG1? I wouldn't dispute at least that you could modify any of
14 these for the lysine at position 248. I don't think that's a challenge. But I
15 don't know that they would actually bind, or at least that's the Petitioner's
16 petition -- position.

17 MS. HILL: No, I understand the point. I guess we would argue
18 that our -- the specification does provide a definition that we believe
19 encompasses more than just the IgG1. The definition you --

20 JUDGE FREDMAN: Clearly, it does. You're referring in
21 paragraph 580 I think in your slide, right?

22 MS. HILL: Yes. Here and then also in paragraph 209.

23 JUDGE FREDMAN: Right. It's not that you have more breadth.
24 The problem is that you have two more breadths. I mean, there's lots of
25 cases -- *Amgen v. Sanofi* is a case where having the -- that's not really the
26 exact same thing because you're having an antigen antibody reaction. But

1 knowing the antigen doesn't give you the antibody. Here, knowing that
2 position 248 is working doesn't necessarily tell you the rest of the
3 surrounding sequence will allow it to bind.

4 MS. HILL: Okay. So are you asking about the lack of specific
5 examples is the problem?

6 JUDGE FREDMAN: There's only that example. But it's really
7 more you haven't just said -- for example, your claim at your specification I
8 think has a description of three CKDs that do work. If they were in the
9 claim this would be a much weaker argument because then they would be
10 there, and that would be a limitation on the claim. And then you'd say, well,
11 now you'd have to argue with the rest of the three-dimensional structural
12 problem.

13 You can make that argument, I suppose. That would be harder for
14 them to make without that -- the surrounding amino acids could be anything
15 right now, I mean, 248 lysine but not everything else.

16 MS. HILL: Okay. Understood. I'm going to direct you to Slide 8,
17 which the claim Limitations 14C, 15C, and 16C further require that the 248
18 position is determined by an EU numbering system. And so those rely on
19 the same motif, which we believe, and our expert has testified, would further
20 allow a person of ordinary skill in the art to understand that these are --

21 JUDGE FREDMAN: So, is your argument that the motif is
22 required by simply the statement of lysine 248?

23 MS. HILL: That is determined by the EU numbering system.

24 JUDGE FREDMAN: Well, we understand that that would have to
25 be 248, amino acid.

26 MS. HILL: Okay.

1 JUDGE FREDMAN: I don't think that's, again, an argument. The
2 argument is, for example, you're showing paragraph 227 there, and there's a
3 sequence of the Fc domain that shows a series of amino acids with proline,
4 serine, valine, whatever. And then you eventually get to a couple lysines,
5 and then you get aspartic and onward, right? There are a couple lysines
6 there. I said one of those 248, but the rest of those amino acids aren't
7 required, right? Or are you arguing that they are in some way?

8 MS. HILL: Right. We're not arguing that they're required. And I
9 may let Mr. Giunta clarify if that was a misstatement. But he's also going
10 -- in the enablement portion, he's going to discuss a bit more about the lysine
11 and the other antibodies. But I guess our position for written description is
12 we provide an example of what we claim, and we believe that's enough to
13 satisfy the written description obligation.

14 JUDGE REN: And the issue is the Petitioner obviously disagrees
15 with you. And so what we're trying to figure out is why do you think one
16 example enables a skilled artisan to understand the entire scope of what
17 you're claiming?

18 MS. HILL: I'm sorry. I'm just looking through my notes --

19 JUDGE REN: Please.

20 MS. HILL: -- for a moment. We agree that there is only the one
21 example of IgG1 provided. I guess I would just have to point back to our
22 -- to Dr. Zhou's testimony that because of the further limitations in the claim,
23 including being limited to the -- including that claimed Limitations 14C,
24 15C, and 16C rely on the same motif. The chemistry would be relatively
25 predictable for the reactions in the same patent that Abtis has created, which
26 --

1 JUDGE FREDMAN: Does he says that? Can you point to where
2 he says that in the declaration?

3 MS. HILL: About the chemistry being the same or the --

4 JUDGE FREDMAN: About predictable. Otherwise, it's more of
5 an enablement concern, but --

6 MS. HILL: Right. I cannot turn to his --

7 JUDGE FREDMAN: Okay. We'll wait for your colleague on
8 enablement maybe.

9 MS. HILL: Okay.

10 JUDGE FREDMAN: Maybe he might do that for you.

11 MS. HILL: Okay. Thank you.

12 JUDGE REN: So, with that, I have -- the follow-up issue is that
13 what Petitioner argues is so why should we essentially rule in favor of your
14 expert on this enablement 112 issue and rule against Petitioner for the same
15 reason on the obviousness reason. Because your position is that your expert
16 -- or their expert is wrong in saying that a POSITA will look at the prior art
17 being Yamada and Matsuda and not understand how you could put the prior
18 art together and come down to this structure. So why should we believe
19 your expert on both of these issues and not credit Dr. Tumey on either one of
20 these issues?

21 MS. HILL: Sure. Mr. Giunta will go into detail on that. But just
22 to answer your question at a high level, we believe there's a difference
23 between Yamada as a completely separate patent reference from, for
24 example, Matsuda and just arguing that those who could be combined
25 without providing any reason based on the disclosures or otherwise to make
26 those changes. Whereas we're arguing that Dr. Zhou has looked at Abtis'

1 patent, looked at the chemistry, and is discussing modifications and
2 substitutions based on what is disclosed the singular Abtis patent, as
3 opposed to unrelated patent references. And that's a meaningful difference.

4 JUDGE REN: Okay. Thank you. I'll look forward to your
5 colleague's presentation. Please continue.

6 MS. HILL: So, for written description, it appears that the modified
7 antibody and the heavy chain is really the only disputed claim terms. So, I
8 don't want to walk through every limitation unless the Board has additional
9 questions, or if you would prefer me to --

10 JUDGE REN: Please proceed.

11 MS. HILL: Okay. So, I'll just remind the Board on page -- on
12 Slide 4 of our presentation that many of the claim limitations are identical,
13 except for the chemical structures that are indicated by the yellow, blue, and
14 orange boxes. So, the written description that applies to kind of the first half
15 of the limitations applies equally across all claim. And just for context, I am
16 -- all my citations are to the '998 application, as opposed to the '675 spec
17 specification.

18 So, starting with the claim limitations that are different, it's where
19 in the modified lysine has the following structure. And I will start here on
20 Slide 9 to discuss Claim 14D. And we want to point out that the '998
21 application in paragraphs 1290 through around 1293 discussed the synthesis
22 of antibody azide. And then the spec -- the '998 application in paragraphs
23 1318 and 1319 confirmed that the structure, as claimed, was actually -- it
24 was formed and created.

25 And then I will show paragraphs 575 of the '998 application. And
26 just highlighted in the -- by the blue boxes is the azide clock chemistry

1 functional group. Highlighted by the green box is the alkaline, which is also
2 defined in the '998 application as containing the ether spacer linker group.

3 And then similarly, for --

4 JUDGE FREDMAN: You're just showing that there's written
5 description for the particular --

6 MS. HILL: Yes. I was just showing you. If you would prefer I
7 skip, I'm happy to not waste your time.

8 JUDGE FREDMAN: I don't think that's been challenged. I don't
9 think it mattered.

10 MS. HILL: I'll move on then. So, if there are no questions for
11 written description, I can move on to anticipation --

12 JUDGE FREDMAN: Looking at Slide 11 for a second, I just want
13 to go back there. I'm sorry, Slide 10 actually. In Slide 10 you have an
14 example. It does show, for example, Formula 8-2, which is sort of again
15 where the -- I assume that's the region in the antibodies to which we're
16 binding, the IgG1 region, around position 248, probably the K with the caret,
17 probably the region where it's actually binding. Is there any indication that
18 there's any variability permitted here in the region other than, obviously, the
19 generic statements earlier in the patent? Do you have any discussion of
20 variability here?

21 MS. HILL: So, in paragraph 580, which is not on this screen, it
22 discusses that the -- it may be applied to the manipulated antibodies which
23 would provide variability in that sense.

24 JUDGE FREDMAN: Paragraph 580, okay. And this is in which
25 -- 2002, okay.

26 MS. HILL: And I have paragraph 580 --

1 JUDGE FREDMAN: Oh, you do?

2 MS. HILL: -- on the screen.

3 JUDGE FREDMAN: What slide is it, Slide 6?

4 MS. HILL: Slide 6.

5 JUDGE FREDMAN: That's fine. Thank you. Okay. But it
6 doesn't list any specific sequences of these or alternations -- alternatives for
7 amino acids. Thank you.

8 MS. HILL: Sure. So, I will advance to anticipation, unless there
9 are other questions.

10 JUDGE REN: Nothing further from me. Judge Kokoski and
11 Fredman?

12 MS. HILL: So, our ultimate point is that given we believe there is
13 adequate written description and support for the proposed substitute claims
14 and that the claims are enabled, that the 959 publication is not prior art, and
15 therefore cannot anticipate our proposed substitute claims. And as we've
16 mentioned, Mr. Giunta will discuss the enablement side of it a bit more.

17 Given the written description, we believe, is adequate and the
18 claims are enabled, the 959 publication has the same priority date as a '675
19 Patent because they claim back to the provisional, they have the same exact
20 inventors, and the 959 publication was published after the '675 Patent's
21 parent application. So given these reasons, in addition to the full story of
22 written description and enablement, we believe the 959 publication is not
23 prior art and therefore cannot anticipate the proposed substitute claims.

24 And with that, I will turn it to Mr. Giunta to discuss his arguments,
25 unless there are any additional questions.

26 JUDGE REN: No questions. Thank you.

1 MR. GIUNTA: Good morning, Your Honors.

2 JUDGE FREDMAN: Good morning.

3 MR. GIUNTA: Peter Giunta, representing the Patent Owner Abtis.

4 I'm going to discuss what else you need to know about written description,

5 enablement, and the obviousness issues. And so, I guess starting where we

6 kind of left off with the written description, these have a transition baked in.

7 So, I think what we need to do is start with the language of the claim itself.

8 Because I think that a lot of the written description positions are, one, not

9 really offered by their expert and, two, not really sticking to the claim itself.

10 And so, you had questions on what it means to have the lysine 248

11 position, what that means with regard to the DEQ ID. And you can see here

12 that the description here and what's relied on for the written description does

13 include that surrounding motif. So, I think that Your Honors' questions this

14 morning were around whether the lysine 248 position is with reference to the

15 environment that it would be in the Fc domain of IgG1. And the answer to

16 that is yes.

17 JUDGE FREDMAN: Are you conceding that the claim is limited

18 to the amino acid sequence recited in paragraph 227 in that slide?

19 MR. GIUNTA: So, I don't know that we would need to concede

20 that it'd be all of that. That environment is the point of saying lysine 248.

21 So, in other words, instead of going directly for a sequence, go somewhere

22 with all of it, and leaving off maybe the next amino acid down could change

23 and so on, it's claimed as lysine 248. But that's what's trying to be captured

24 there.

25 JUDGE FREDMAN: And the basis is this paragraph 227 is what

26 you're pointing to?

1 MR. GIUNTA: Well, it's throughout. So, if we were to go to the
2 patent document itself, if you just go to Figure 1, the same motif is there.
3 And I can try and bring it up on Ms. Hill's computer here.

4 JUDGE FREDMAN: Right. The motif is there as Figure 1. But
5 thing is it's not in the claim. And we tend not to read things into claims from
6 the specification. That's kind of black-letter law.

7 MR. GIUNTA: Well, that is what's meant by lysine 248 in the
8 claims, and that's their best --

9 JUDGE FREDMAN: That's how you're understanding it -- or your
10 expert is understanding. Does your expert say that?

11 MR. GIUNTA: Yes.

12 JUDGE FREDMAN: Where does he say that?

13 MR. GIUNTA: Well, that's what he means when he says it's lysine
14 248, that that motif is there.

15 JUDGE FREDMAN: Right. But I mean when you talk about
16 numbering of amino acids and antibodies, all antibodies share that common
17 numbering system of heavy chain. So that doesn't have to be g1. So,
18 position 248 in full-length antibodies is always there's going to be position
19 248. It may or may not be lysine natively, but ones could go on there always
20 even an IgA let's say.

21 MR. GIUNTA: So, I understood that from your question. So
22 that's not an argument that they've advanced. It's not an argument that their
23 expert has made, that what if you were to scramble the motif. I think the
24 point here is that --

25 JUDGE FREDMAN: Or if the motif just wasn't there because
26 you're looking at a different version. Because you say modified antibody

1 generally rather than IgG antibody, for example.

2 MR. GIUNTA: So yes, if you look at the definition in the patent
3 itself -- and I just jumped out of it. I'll jump back in. So, the patent itself in
4 column 23 has a definition of antibody. I believe that Ms. Hill referred you
5 to it, but let me get back there. And we've read it earlier today, but --

6 JUDGE FREDMAN: It's fairly broad. I'm looking at it right now.
7 According to the present invention, the term antibody refers to an
8 immunoglobulin molecule or fragment thereof. Immunoglobulins are
9 definitely well-known and have an ability to find a specific certain antigen.
10 However, because the antibody, according to the present invention, is a
11 concept that also encompasses a fragment thereof, fragments maybe are
12 different. The antibody doesn't have to show binding activity of a certain
13 antigen, as in the case of an Fc fragment.

14 In addition to the naturally occurring immunoglobulins, the
15 antibodies also encompass recombinant fusion proteins, chimeric proteins,
16 human immunoglobulins, nonhuman animal immunoglobulins, and the like.
17 Nonhuman animals would also presumably be different.

18 MR. GIUNTA: And so, I think the point there is that what they're
19 trying to capture is that structure that does occur in the Fc domain, that if
20 that's somewhere else, if it happens -- if that sequence occurs somewhere
21 else --

22 JUDGE FREDMAN: You're not saying the sequence is enforced
23 in this. You're not sort of reading the sequence into it, or you don't want to?
24 Because you have the sequence, as you say in Figure 1 --

25 MR. GIUNTA: And that's --

26 JUDGE FREDMAN: You can put that in the claim, I suppose, but

1 --

2 MR. GIUNTA: But that's what it's referring to. So, there was no
3 claim construction on this point. There was no explicit expert opinion on
4 this point that's --

5 JUDGE FREDMAN: In the absence of claim construction, when
6 we read it, the way that you define it I think, right, which it would be the
7 discussion of page -- column 23?

8 MR. GIUNTA: Right. But with reference to now we've identified
9 lysine 248, which is always given in the --

10 JUDGE FREDMAN: I don't think that's disputed, but maybe I'm
11 wrong. I want to hear from Petitioner if they dispute it later.

12 MR. GIUNTA: Right. And so, when referring to lysine 248,
13 they're referring to it as they've used it in the patent, which is in this
14 environment. So, you're asking whether I have to have the sequence. The
15 answer is yes, at least some of the sequence would be included in lysine 248.
16 That's what they're referring to. So, the Fc domain of IgG1 is exactly what
17 that lysine 248 is referring to. We haven't briefed claim construction, but
18 that was the reason for that.

19 Now, how much or how little of a sequence, if we want to use the
20 sequence? Sure, we could do that. And it wouldn't really be different,
21 except that you'd have to pick a place to begin and a place to end.

22 JUDGE FREDMAN: So, are you arguing that we should not read
23 the broad limitation -- the broad discussion in the specification of that
24 column 23, we should read it more narrowly? That's essentially what you're
25 saying I think.

26 MR. GIUNTA: I think that it's consistent. Because once we say

1 lysine 28 --

2 JUDGE FREDMAN: 248,

3 MR. GIUNTA: Sorry, 248. 248 and we say we're structurally
4 similar, the whole point of saying structurally similar there is let's say you
5 took the sequence of this motif and you were to put it on to -- you were to
6 make an IgG -- or sorry, an IgM or an IgD when you were to put the same
7 sequence on to some other --

8 JUDGE FREDMAN: Where does it say structurally similar? It
9 doesn't say that in the claim.

10 MR. GIUNTA: It's in that definition of antibody.

11 JUDGE FREDMAN: I don't think it says that there,
12 (INDISCERNIBLE) in Column 23.

13 MR. GIUNTA: Maybe it says, or similar structure. It's the last
14 few words in the definition.

15 JUDGE FREDMAN: Which are the same or similar structure.
16 Okay. But that's generic to all antibodies or proteins. It's not really --

17 MR. GIUNTA: That's the thinking, Your Honor, is that -- is
18 exactly that.

19 JUDGE FREDMAN: Your argument, that's fine.

20 MR. GIUNTA: And so, if you're thinking of ways to claim that,
21 how do you claim what it is that we're attempting to claim? Which is the
22 thing that our chemistry does. We're not trying to vastly expand things. All
23 we're trying to do is claim exactly what our chemistry does and what we
24 fully disclosed. And that's the way that we've described it. That's it. We've
25 described it as lysine 248, if somebody takes that same environment and
26 sticks it somewhere else, let's say --

1 JUDGE FREDMAN: Just on enablement for a second, just
2 because -- can you go through the predictability of this a little bit, making
3 this attachment to position 248 at -- obviously, if there's an IgG1, we expect
4 it to work I suppose. What about for other sequences around it?

5 MR. GIUNTA: That's right. So again, so for the enablement
6 point, I think it's worth noting that they offer no expert evidence on
7 enablement from their own expert, no affirmative position. Our expert
8 opined that it is fully enabled, and it's based on the chemistry in the
9 specification. And so, his point again with enablement is he points to this
10 lysine 248. When he does that, he's saying that there's an affinity peptide for
11 this motif.

12 JUDGE FREDMAN: It's clearly necessary, 248 is necessary. Is it
13 sufficient is the question I'm sort of trying to get at.

14 MR. GIUNTA: I'm sorry. Can you say that --

15 JUDGE FREDMAN: It's clear that lysine 248 is necessary for the
16 binding, the azide is going to bind to that, the immunoglobulin and the
17 lysine. Is it sufficient? That is, is it enough to simply have a lysine there, or
18 do we need the other sequence to enable the some of it or all of it or more of
19 it?

20 MR. GIUNTA: So, it's referred to in accordance with the Fc
21 domain. So, in other words, it's --

22 JUDGE FREDMAN: It's going to be an Fc domain, yes.

23 MR. GIUNTA: Right.

24 JUDGE FREDMAN: I'm taking about the immediate sequence
25 surrounding it.

26 MR. GIUNTA: And so, I think that we'd be satisfied with what

1 we've given here, which is this description of it, and what's in Figure 1,
2 which is that much of the motif, the sequence around it.

3 JUDGE FREDMAN: I don't know that they're arguing that that's
4 not enabled. They can come back and tell us if they're arguing that that
5 particular sequence is not enabled. I think the question is if someone
6 changes one or more of those amino acids, how many can you change and
7 still be enabled?

8 MR. GIUNTA: I don't know that that's intended to be what's
9 claimed. In other words --

10 JUDGE FREDMAN: I understand. You're not really claiming
11 that either. That's almost more of a description. But I mean to the extent
12 that even if an artisan could do this, I think -- I'm sort of thinking it against a
13 socially description point of view, but I'm using enablement language here.
14 I don't have as much of a problem because I think even an artisan know or
15 could figure out what regions would bind. My concern is sort of to use the
16 predictability to ask the question whether it's really described.

17 MR. GIUNTA: So, the chemistry here works. And so that's our
18 expert's opinion is that the chemistry here -- it's demonstrated in the patent.
19 It actually made it, not just hypothetical.

20 JUDGE FREDMAN: That's click chemistry. Click quick
21 chemistry is (INDISCERNIBLE).

22 MR. GIUNTA: Right. So, it's all there. And so, the point is that
23 with them offering no expert evidence and us pointing out that --

24 JUDGE REN: It is your burden, though, to show that your claims
25 are enabled.

26 MR. GIUNTA: Yes.

1 JUDGE REN: So, you do have to put forth evidence. You can't
2 just say they didn't put any evidence in there for you when --

3 MR. GIUNTA: Oh, of course. But I think it's important to note
4 that when they're talking about predictability, their expert never said that.
5 That's my entire point and saying about our expert versus their expert. And
6 so, a person of ordinary skill in the art, if you were to go to something else,
7 let's say you had a modified antibody or IgG6 or anything like that -- the
8 Wands case comes to mind, in re Wand, which is 858 F.2d 731, I think
9 everyone's very familiar with it. It's an antibody case.

10 It's also the case that says that enablement is not precluded by the
11 necessity for some experimentation, such as routine screening. And one
12 more point -- and let me just get to it here, let me back to the slides that go to
13 it -- is that they pointed to Dr. Tumey talking about all these various
14 antibodies. And they said that he -- and you touched on this, Your Honor, as
15 well that he goes through the isotypes. And he knows which ones do and
16 don't include a lysine 248. So, they know this. He says that the Fc domains
17 are different.

18 And that's kind of the point, that in advance you would know
19 whether or not that domain is there that the disclosed chemistry would work
20 with. So, if you know in advance whether or not something has an lysine
21 248, then you have a very good idea as to whether or not --

22 JUDGE FREDMAN: Okay. That's essentially a Capon argument,
23 right?

24 MR. GIUNTA: Yes.

25 JUDGE FREDMAN: *Capon v. Eshhar* where essentially the prior
26 art knew all these things, probably literally all these sequences, well before

1 any of this happened. We look at them, run an alignment, and figure out
2 which ones have 248 and 127 -- lysine at 248.

3 MR. GIUNTA: Exactly, Your Honor. And that's our position.
4 Our position is that if you would know in advance then -- and then you take
5 into account Wands, you would do a screening experiment. You'd take this
6 chemistry and you can try it. It's an incubation reaction. It takes not that
7 long.

8 JUDGE FREDMAN: Right. So that's for the ones that have it
9 already. What about for an IG, he shows in this same slide that you're
10 -- what about IgA, for example, an IgA might or might not have it, and it
11 might or might not have the surrounding region. And it's obviously
12 expressed very differently in the human body or it's not circulating. It's
13 usually in mucosal membranes. So, if the IgA doesn't have the lysine 248
14 and you put one in, let's say -- because I could do that -- will it work or not?
15 And how do I know?

16 MR. GIUNTA: Routine experimentation, Your Honor, that's our
17 position. And I don't think it would take that much. Again, the incubation
18 reaction is a fairly short, fairly straightforward reaction. And it's mild in
19 comparison to the amount of experimentation that, for example, Dr. Tumey
20 would do to try and recreate the Matsuda reaction on the prior art.

21 JUDGE FREDMAN: You mean the chemistry to actually make
22 the click quick chemistry compounds, yeah.

23 MR. GIUNTA: For these rotations on predictability, I think that a
24 lot of these are in a different context. I think that a lot --

25 JUDGE FREDMAN: What slide are you looking at, Slide 9?

26 MR. GIUNTA: This is Petitioner's demonstrative, Slide 9.

1 JUDGE FREDMAN: Okay.

2 MR. GIUNTA: And a lot of these are in a different context. I
3 think that they're talking about prior art. They're talking about different
4 aspects of the chemistry. Even if you look at the -- in Dr. Zhou's
5 declaration, which is Paper number 2004, and you look at the chemistry
6 -- you look at the paragraphs leading up to paragraph 40 that they touched
7 on, he's talking about these prior art references.

8 And so, the reference to one antibody versus another is a reference
9 to the PepTalk Poster where they talk about one generation of AJICAP
10 technology targeting lysine 248, and then another generation of AJICAP
11 technology using a second type of chemistry to target other sites on the
12 enzyme. If there are no other questions on written description or
13 enablement, I will move on to -- I think I might have closed my own
14 presentation, exited out of it by accident.

15 I so our expert, Dr. Zhou, and Petitioner's expert, Dr. Tumey, did
16 not disagree on the level of ordinary skill in the art, that the level of ordinary
17 skill in the art is a PhD with some amount of experience in antibodies or
18 ADCs, or alternatively a master's degree and a bit more experience with
19 antibodies or ADCs, and that the person would have familiarity gained
20 through the study, training, and/or or experience with the design
21 development of ADCs and antibody modifications. And Dr. Tumey noted
22 that people of ordinary skill in the art go to conferences.

23 And so, we've been talking about this technology for a while. So, I
24 don't want to belabor this too much. But the antibody portion here is the Y
25 shape in the middle, and the drug conjugate portion is the star. And so here
26 on Patent Owner's Slide 30, we break it down into the antibody residue, the

1 spacer that we've been talking about, the bioorthogonal click chemistry
2 group which here has already reacted, and then the attachment and payload
3 or cargo as the '675 Patent refers to it alternatively. And that would include
4 the drug molecule.

5 Again, another look at it on Patent Owner Slide 31, it's attached to
6 the antibody there. And if you look on the right, the more generic structure
7 shows just the attached group with the squiggly lines indicating where the
8 antibody, the Y shape or the other shapes, begin.

9 So, one of the references discussed is the Yamada reference. And
10 it's important to note that this is an Ajinomoto-assigned patent application.
11 And it names Yamada and Matsuda as inventors. The title is compound
12 having affinity substance to soluble protein, cleavable portion, and reactive
13 group or salt thereof. Now, as we discussed, Yamada discloses billions of
14 potential compounds. It does not identify the specific claimed compounds.

15 Petitioner assert that Formula IV, this L1-B-R'-T, discloses the
16 claimed compound permutations. So again, it goes through all -- this is
17 detailed in Dr. Zhou's declaration. You get to over 13 billion potential
18 compounds without even varying B, R', and T which can increase the
19 number. Dr. Tumey doesn't dispute the numbers. Their expert doesn't
20 dispute them. And Yamada does not provide any specific teaching or
21 motivation to go toward the claimed compounds.

22 Yamada does not disclose Claim 14. It does not specifically
23 disclose an ether spacer. It doesn't disclose -- well, it discloses a bunch of
24 alternatives for the lysine binding site. So, they would include lysine 248,
25 other lysine sites, tyrosine sites, tryptophan sites. Yamada discloses an azide
26 bioorthogonal group among many alternatives. It does exemplify it, but

1 never with the same spacer group. And Yamada does not disclose a method
2 of making the claim compounds. We'll get to that in a moment.

3 For Claim 15, Yamada does not specifically disclose the no-spacer
4 group. And even in all those permutations, Dr. Tumey never made the effort
5 to try and show that you could vary those in a way that would make the
6 compound of Claim 15. It also has this norbornene bioorthogonal click
7 chemistry group, which Yamada discloses among a group of many
8 bioorthogonal click chemistry groups, 21 in its narrowest depiction, and
9 even more elsewhere.

10 Claim 16 is combination of both. It's got the norbornene click
11 chemistry group and an ether spacer. And it does not disclose the ether
12 spacer. It does not specify any particular direction, although it does
13 exemplify other compounds at lysine 248. But it allows options for other
14 lysine sites, tyrosine, tryptophan, etcetera.

15 Now when we say that -- and that all goes to motivation. In other
16 words, it's pretty much an unlimited sort of selection process to get to the
17 claim compounds if you were trying to use Yamada. It's not even clear that
18 you could get to Claim 15 using Yamada. And so there really is no
19 motivation. That's what's really missing here, no teaching, no motivation
20 toward any group. And it's particularly not the spacer of the claim
21 structures.

22 But what's more limiting is that there would be no reasonable
23 expectation of success. And that is because, as the title suggests, Yamada
24 only discloses things with reference to this particular reaction scheme. Now
25 we're not limiting Yamada - we're not attempting to limit Yamada to only
26 its chemistry in a very specific way, the way that Petitioner's attorney

1 suggests. The way that Yamada as a patent document is written is in terms
2 of this.

3 So, in other words, it refers to this reaction scheme in Figure 2.
4 And I'm on Patent Owner Slide 37 here. You can see that Figure 2 shows
5 that this yellow box, which is compounds of Formula II, go through a
6 cleavage reaction to form the compounds of Formula IV. So, what's
7 required for Formula IV is that it must have cleaving from the L group to
8 form an L1 and an L2, And the L1 is what's in Formula IV. And Petitioner
9 admits that this scheme cannot make the claim compounds.

10 And the reason is that the claim compounds don't include
11 something that could have been cleaved to make an L. Dr. Tumey tried to
12 sort of create some in his last declaration, but there's really no indication that
13 that would work. And Dr. Zhou also opined that the chemistry, in all
14 likelihood, would not work to do that. And so, there's really nothing in
15 Yamada motto that would allow you to do that to make the claim
16 compounds. And that's why we read Yamada as so limited, that's really it.
17 That's how a person of ordinary skill would view it, and they would
18 understand it to be that.

19 Moving on, so Dr. Tumey says it in his declaration, says it in the
20 context of saying that, well, somebody would be able to come up with some
21 other way to do it. But he does say Yamada's synthesis scheme in Figure 2
22 could not be used to prepare the structures now recited in the proposed
23 substitute Claims 14 through 16. And so, how does he fill the gap?

24 Well, he starts with saying that Dr. Zhou's opinion that Yamada's
25 chemistry is scientifically infeasible to make the claim compounds is
26 incorrect because Abtis apparently made the claim compounds. And in fact,

1 Abtis making the claim compounds is the only synthesis on the record here
2 that shows that you can make the claim compounds.

3 Again, this image is where the billions of compounds come from.
4 And it looks like he's starting from Formula IV and making his way down to
5 claim compounds 14 and 16. But there's really no way to do that unless you
6 start from 14 to 16.

7 JUDGE FREDMAN: I'm just curious, this is probably not
8 relevant. But are there patents to the claimed compounds themselves? Are
9 there separate patents to this?

10 MR. GIUNTA: In the patent family, Abtis?

11 JUDGE FREDMAN: Yes.

12 MR. GIUNTA: So, these are the compound claim. The patent
13 you're seeing is the compound claim.

14 JUDGE FREDMAN: So, this is the only one. Okay.

15 MR. GIUNTA: Yeah. And that's the other point of it, that we are
16 talking a lot about enablement. We're talking a lot about the chemistry
17 because we're talking about enablement and so on. But this is a structural
18 claim. All three of these are structural claims. And so, if you just look at
19 the options in Yamada, all at one time there are about 10 different variables
20 here for option one.

21 On the left hand box here on Patent Owner's Slide 40, C1 can be at
22 least different possibilities. In the next box, which is sort of lower, mid
23 -- down underneath of a generic structure that the L1 is also pointing to, the
24 P -- he makes a selection of P, but that's from among 11 possibilities. He
25 makes a selection of X that's among three possibilities. He makes a
26 selection of Q that's among 11 possibilities. And he makes a selection for

1 R1, which is at least three. And it's unclear how many more possibilities
2 that could be.

3 And then for B, he makes a selection of Z, where X could be at
4 least three possibilities. He selects oxygen as Y, when Y could be at least
5 three possibilities. And for T, T could be at least three possibilities or more.
6 So, in other words, all these decisions get made. They all get made at once.
7 They don't get made for any particular reason that he discloses, other than
8 certain preferences for shorter spacer groups and so on.

9 And so here again there's an option two, and the same applies.
10 The claim compounds are at the bottom, but they appear to be the starting
11 point. And then he seems to locate them from all the various options. And
12 so, the gaps are -- there's no reason to select any of these. There's no
13 motivation. If there's no operative synthetic scheme, there's billions of
14 potential compounds.

15 For Claim 15, it was discussed he relies solely on Ockham's razor
16 to start with the simplest structure. And he's saying that if you preparing a
17 modified lysine with an norbornene as the terminal bioorthogonal click
18 chemistry group, you logically start by preparing the simplest structure,
19 which is the structure recited in proposed substitute Claim 15. He jumps to
20 the no-spacer group, and he also jumps to norbornene without any particular
21 reason for one or the other of them.

22 He also in the grounds combines Matsuda with Yamada, and they
23 don't really give any reason to combine them with each other. Ajinomoto,
24 again, is the Applicant. The inventors are again, Yamada and Matsuda,
25 among others. And those others are not completely overlapped. But
26 Matsuda here teaches away -- Matsuda discloses that beta heteroatom

1 spacious substituents, those are compounds 26 and 60 in the Matsuda
2 reference, their reactions which he groups together in the same comparative
3 example did not progress. And a person of ordinary skill in the art would
4 understand that Matsuda expressly teaches away from the spacer substituents
5 in proposed Claims 14 and 16.

6 The PepTalk references, same idea, Pep Talk references do not
7 disclose an ether spacer, they do not disclose norbornene, and they give
8 some variety as to the substituent sites that you would put it on the lysine.
9 And it's worth noting that on the PepTalk Poster itself, for its chemistry of
10 the first generation AJICAP technology, it cites to the Yamada reference.
11 And I can put it up. So, your footnote 4, which comes off of the first
12 generation AJICAP, that application, the number lines up with the Yamada
13 reference that we're discussing here. It has the same disclosure.

14 So given that none of these references disclose the claim
15 compounds, it's difficult to see how Dr. Tumey include that those -- the
16 invalid is obvious. These are just summary charts just basically depicting
17 that. Yes, Yamada has azide disclosed in an example. Matsuda, it discloses
18 it in with a bunch of things. But the ether spacer, Yamada does have an
19 ether spacer potentially disclosed within a bunch of things. Yamada
20 expressly teaches away the PepTalk references don't really offer you any
21 chemistry on that. Lysine 248, there's questions because they all offer
22 alternatives. And the synthesis, there's no synthesis that will work in
23 Yamada that Matsuda teaches away, and the PepTalk references are the
24 same.

25 Patent owner Slide 51, for the norbornene with no spacer, Claim
26 15 compound, Yamada, lots of options for the click chemistry group.

1 Matsuda, the same PepTalk references don't disclose norbornene. For the
2 no-spacer, nothing discloses it. And for lysine 248, again, there's options.
3 There's no operative synthesis for Claim 15 given, at least not according to
4 Dr. Tumey's opinion.

5 Claim 16, sort of a combination of both. This Slide 52 shows the
6 same, that they're taught away from with regard to the spacer. And that is
7 not expressly disclosed anywhere else. And with that --

8 JUDGE FREDMAN: I would say switching back to description
9 for a minute.

10 MR. GIUNTA: Yes.

11 JUDGE FREDMAN: I'm curious, have you read the case -- it's
12 really recently. It came out in April, *Teva v. Lilly*, Teva Pharmaceutical. It's
13 172 F.4th 1367. If you're not familiar with it, it's fine. In *Teva v. Lilly* what
14 happened was -- the question was whether the specification in that case
15 -- this was a represented number of species of the asserted humanized anti-
16 CGRP antagonist antibodies. In that case, the antibodies were being used to
17 treat headache.

18 And the Court basically found in that case that even though the
19 specification had just one antibody, one of them that was humanized, the
20 technology behind it was known. And so, this was a jury case. The Federal
21 Circuit and the jury reasonably found that it was enough to not have a
22 problem with written description. So, I'm just curious how you'd apply that
23 to your case if you wanted to. If you're not aware of it, it's hard. I'm sorry.

24 MR. GIUNTA: So, I am aware of it in the sense that we generally
25 go through these in terms of applying it to our case. From what I understand
26 is that there was only one example using a humanized antibody.

1 JUDGE FREDMAN: Right.

2 MR. GIUNTA: I do think that that's similar to the *In re Wands*
3 case itself, where there were only three examples of having made the
4 technology there. And so, in terms of written description and enablement, as
5 long as a person -- so written description first, I think that --

6 JUDGE FREDMAN: Yeah, written description.

7 MR. GIUNTA: -- positions sort of muddies the waters, but -- sorry
8 possession, as it gets discussed, can sometimes bleed over into enablement.
9 But if we think about it, is what is claimed in the spec? I think that's the sort
10 of hallmark. And you've been in this for 30 years, so you remember back
11 when you could use -- kind of like the using Yamada where you could kind
12 of use like an encyclopedia or phone book, just go to the spec, and if it's
13 there, then those words appear in the claim there.

14 JUDGE FREDMAN: It still said it in the repair -- I don't know. I
15 didn't write those rejections. But yeah, sure. But people may be dead.

16 MR. GIUNTA: It's a little bit different of an analysis, but this is
17 much closer -- this is much more tied than that. In other words, the
18 chemistry is there. The only places that they talk about lysine 248 are in the
19 context of that motif and are in that Fc domain. And so, the definition of
20 antibody happens to be broad shouldn't factor in -- or shouldn't take away
21 from the idea that all of it is disclosed there for what it would mean to a
22 person of ordinary skill in the art.

23 And so, I can agree with you that a person of ordinary skill in the
24 art would have no reason to think, and therefore it doesn't cut against written
25 description or enablement. But I have no reason to think that compounds or
26 antibodies that don't have the sequence that includes lysine 48 would work.

1 So, there's no mistake about that. Our position isn't that you would always
2 just kind of wing it, make it, try it. But there's a level of that that is accepted
3 because it's routine.

4 Like the Lily versus Teva case, when you go from human to these
5 other things or when you go from IgA to IgM, then there is a certain amount
6 of experimentation that you can do and still be enabled and still have written
7 description. In other words, they tie together in that sense. If a person of
8 ordinary skill is looking at it, they would know what it discloses and what
9 you're in possession of because you're in possession of this thing that can be
10 routinely tested in other contexts.

11 So here there's a reaction scheme in the '675 Patent. And if you
12 wanted to do the full scope of these antibodies, the term antibody at this
13 lysine 248 position, understanding that it is the lysine 248 environment of
14 the Fc domain of IgG, then you can do that. And that's our position, that
15 that's the reason why you have written description. Again, if we go to it, the
16 level of ordinary skill in the art is high. Nobody disagrees on that.

17 JUDGE FREDMAN: It's always high in 1600.

18 MR. GIUNTA: Patent Owner Slide 29, yeah. So, the level of
19 ordinary skill in the art is high. There's no disagreement on that. And you
20 can tell from Dr. Tumey's analysis that he is very much willing to consider
21 things predictable with a whole bunch of experimentation.

22 Okay. Without any further questions, I'll --

23 JUDGE REN: I do have a question, your Slide.

24 MR. GIUNTA: Okay. Yes.

25 JUDGE REN: To be fair, are you saying that the prior art has to
26 teach or suggest the synthesis that requires to render obvious the recited

1 compound?

2 MR. GIUNTA: So yes, I'm talking about motivation and
3 reasonable expectation of success. And so, when I talk about motivation, I
4 talk about sort of the structural pieces here. And when I'm talking about
5 reasonable expectation of success, at least you would need an operative
6 method of making what it is that you want to put together. And I believe
7 that you would also -- so either it's disclosed somewhere or enough pieces of
8 it are disclosed with enough specificity that a person of ordinary skill in the
9 art would consider it to be disclosed.

10 JUDGE REN: And you were just saying that Dr. Tumey says the
11 skill is very high. So, you're saying with these high skills required, with the
12 routine experimentation, the PhD that we have here wouldn't be able to
13 synthesize what we have recited in the claims, despite these teachings from
14 the prior art?

15 MR. GIUNTA: That's right. The chemistry is missing. So, the
16 chemistry here in the Yamada reference, that won't work to make this
17 compound because there's no cleavable group that associates with this. And
18 Dr. Tumey admitted. For the Matsuda reference, there's been no argument,
19 one, from Dr. Tumey that the synthesis would work. There's simply nothing
20 in the record on it. And for the PepTalk references, the chemistry is the
21 same as the Yamada reference.

22 JUDGE FREDMAN: So, there's this quote, "a disclosure of
23 millions of compounds does not render obvious a claim to three
24 compounds." It's kind of appropriate here where we have three compounds.
25 We have a disclosure that's probably more than millions. And I think Baird
26 controls, to me.

1 MR. GIUNTA: Okay. If there are no other questions, I'll stop
2 here.

3 JUDGE REN: And now we have Petitioner's rebuttal.

4 MR. MOCK: Okay. I'm ready to go when you are.

5 JUDGE FREDMAN: So let me ask, start with that -- my same
6 question about Teva, which I'm not sure if Counsel realized was on his side.
7 Teva is a case where they found that there was written description for these
8 anti-CGRP antibodies because they were essentially limited. Essentially,
9 they were kind of like a tool. It doesn't really work with -- I don't want to
10 use an analogy to something mechanical because it's never the same with
11 these bio cases. But here, essentially, we have these three chemical entities,
12 whether -- you can argue, if you want to, about the obviousness of them, but
13 that's not my interest right now.

14 But for written description, the question is they're using the tool
15 with an antibody. And you're arguing the antibody matters, I think is really
16 what you're saying.

17 MR. MOCK: Right.

18 JUDGE FREDMAN: And the question that we sort of have to
19 resolve is, does the antibody matter or is it simply it's a tool? And so, the
20 fact that it will work with some antibodies, but probably not all, it's a
21 determinable fact that's actually quite relatively easy to determine in
22 fairness; does that matter?

23 MR. MOCK: Yes. I think this is distinguishable. Because here,
24 not only the antibody matters but the reagents matter too. Part of this
25 equation is the SSAI, the SSFI. And to operate across the full scope of the
26 claim, the full scope of different antibodies, different isotypes that would be

1 encompassed, they're asking --

2 JUDGE FREDMAN: You're saying the surrounding sequences of
3 lysine 248 is what you mean?

4 MR. MOCK: Correct. Because that is what dictates whether or
5 not the SSFI, SSAI is going to bind to. You start modifying that sequence,
6 then you are going to necessarily end up in a spot where the disclosed SSFI
7 is not going to bind. It may not bring the reactive groups in proximity to
8 lysine in a condition precedent that is needed to make this modification.

9 JUDGE FREDMAN: Well, the question there for description is
10 kind of -- I wonder if that matters, that's the question. I'm trying to wrestle
11 with that. I'm going to use a mechanical example, and I apologize. But if
12 I'm taking a socket wrench and I have a 3-millimeter, whatever it is -- I'm
13 not that tool competent, I apologize - and it is a 5-millimeter actually on my
14 snowblower, it's not going to work, right? I need the right tool. But it's just
15 a matter of sort of testing each one. I've described both things. I have the
16 thing I'm attaching it to and the thing I'm attaching with. I have to check to
17 see if they work.

18 MR. MOCK: Sure. But in this context, in that example, in the
19 Teva example, socket wrenches were known.

20 JUDGE FREDMAN: It's much more simple. I understand that.

21 MR. MOCK: Everybody knows about socket wrenches in Teva,
22 like methods for humanization. Those types of modifications were known.
23 Here, I don't know if today there are the necessary agents that have been
24 created to modify an IgM, to modify an IgA, to monitor an IgE or IgG. And
25 so, it's not --

26 JUDGE FREDMAN: Contemporaneously, this is a little bit hard.

1 This isn't brought up, so I'm not -- we won't address it. With AlphaFold,
2 people do this all the time.

3 MR. MOCK: I think the contemporary nature of it matters,
4 though, in this case. Because in situations where, for instance, antibody
5 humanization was routinely practiced, that had been known for decades. If
6 this is something they want to say, sure, we had possession of it, but the
7 technology hasn't even been invented yet, that seems to me to be a little bit
8 strange.

9 JUDGE FREDMAN: When you try and say as of now, there's a
10 recent paper about they took every single lysine out of the ribozyme, literally
11 -- I'm sorry, ribosome, and they got it to work without lysine. Not lysine,
12 sorry, leucine -- I said lysine -- without leucine. And it's put all the leucines
13 (INDISCERNIBLE) and occasionally reconstructed it. And they were able
14 to do that using modern technology. It's quite sophisticated. Of course,
15 AlphaFold, that's a little harder argument. This is kind of right on the edge.

16 MR. MOCK: Sure. I think what's important here, though, is that
17 in order for them to be firmly in a position where they can say this works,
18 you have to import a limitation from the specification. You have to take this
19 construction that Mr. Giunta offered of, well, lysine 248 actually means
20 lysine 248 plus some, and that's not recited in the claims.

21 JUDGE FREDMAN: You could say, though, it means lysine 248
22 in the context that permits binding. We can basically do that as a simple
23 test. It's a very easy thing to test.

24 MR. MOCK: That that is inconsistent, though, with the expressed
25 definition of antibody, and that's also picking and choosing regions out of
26 the specification. For instance, I note that in column 248, starting at line 17

1 of the '675 Patent, they say that the antibody, according to the present
2 invention, may include SEQ ID NO: 1 or may include derivatives thereof.
3 That paragraph goes on say it may include other sequences where lysine is
4 not there.

5 Well, in that case, which one of these are we picking? You can't
6 just say, well, we're only going to select the one interpretation that that
7 works, especially when that is inconsistent with the definition of antibody
8 that says antibody is all immunoglobulins and a bunch of proteins that are of
9 similar structure. In this case, I also note that Mr. Giunta said that they have
10 never briefed this, the claim construction issue.

11 We have, though, that was presented in our original petition. We
12 offered it. We said that the construction of antibody should include IgG plus
13 all of the other immunoglobulins as well as similar structures. The Board
14 noted that definition in Paper 27, their preliminary guidance. Patent Owner
15 had ample opportunity to rebut that construction and/or offer an alternative
16 construction. They did not do that. Doing that here seems like a little bit of
17 a last-ditch effort. So that is an issue that has been of record. I think
18 changing the goalpost now is not exactly equitable.

19 With respect to Mr. Giunta's position that, well, it would work with
20 this sequence, and so even in IgMs or something else you could just plug in
21 this sequence and then you got it, well, that's also a bit inconsistent with the
22 claim. It borderline does not make sense. Because if you just plug this
23 randomly into an IgM, where are you plugging it in? You're going to find
24 the sequence so that lysine ends up at 248 again? Within an IgM, according
25 to the EU numbering system, that might not even be within the Fc domain.
26 And then you're talking about modifying this in a way that -- where's it

1 going to be, the CH-3 domain, the CH-1 domain?

2 These are all issues that are not teased out in the '675 Patent itself.

3 And so, for them to just say -- covering all of this unknown, despite the fact
4 that we would have to come up with potentially new sequences or make
5 these modifications to antibodies to make this work, hand waving that away
6 as routine optimization, routine experimentation, I think, is a little bit bold
7 when the technology is not for any of those modifications.

8 It's not even suggested in this patent. Rather, it says we have
9 disclosed these SSFI that bind to this particular sequence. And the claims
10 should be understood as broader than that, encompassing antibodies and
11 immunoglobulins that do not have those sequences. So, there's a bit of a
12 disconnect there in my mind, especially when, as I noted earlier, there's this
13 position that when it comes to enabling the '675 Patent there's going to be
14 routine experimentation.

15 All that is fine. A person of ordinary skill, this high level of skill
16 they point would know how to take the technology and run with it, make the
17 necessary changes. But when they're referring to Yamada and Matsuda, the
18 PepTalk references, a person of ordinary skill in the art is going to throw
19 their hands up and say, I only know how to do exactly what they have said, I
20 can't make these tweaks.

21 I think there's also a couple inaccuracies with respect to the
22 characterization of those references that I'd like to highlight for the board
23 quickly. Mr. Giunta put up a slide saying that lysine 248 was just one of
24 many options in Yamada, that it's one of many options in the PepTalk
25 references, but they don't really drill down on it too much. That
26 characterization is actually belied by the '675 Patent itself. The '675 Patent

1 references Yamada several times because it's prior art. For instance, at
2 columns 69, lines 48 through 51; 70, lines 12 through 15; 72, 16 through 19;
3 and 71, 36 through 39.

4 So repeatedly, the '675 Patent says that the aim of Yamada was to
5 site selectively modulate lysine 246 or 248 in an Fc domain of IgG. That
6 seems pretty clear. I don't think there can be a different interpretation of that
7 same thing with respect to characterizing the PepTalk references as not
8 clearly laying out lysine 248 or a preference for that. Lysine 248 is the only
9 amino acid position that is mentioned in those references.

10 Slide 16 of the presentation, Exhibit 1007, is titled site-specific
11 functionalization of trastuzumab at lysine 248. All of it is pretty clear that
12 it's geared towards 248. And they note, with respect to this technology, the
13 first generation AJICAP technology, as Patent Owner refers to it, in the
14 conclusion slide on Slide 33 that it provides the benefits of straightforward
15 CMC, enhanced therapeutic windows to stochastic ADCs, wide linker
16 compatibility, which they know specifically, and reactive group
17 compatibility, including files alkenes and azides.

18 So again, while they say that like we're just picking azide out of a
19 hat, that there were 21 options within Yamada, Yamada is combined with
20 the PepTalk references. And the PepTalk references say azide is one of
21 three options. This is a technology that works with it. They also say it's
22 high yield, short conjugation, reactions, all of these benefits.

23 And they note that this is in the context of a conference, a
24 conference where Ajinomoto was going to present this technology to
25 hopeful partners. People would pick it up and run with it. And they want to
26 say that somehow that there's a single slide that gives a preview of a second

1 generation technology that everyone in the audience, all those skilled people,
2 are just going to say, oh, 248 is garbage, that means we can't use this, we're
3 going to wait until the second generation comes out. Second generation,
4 mind you, also --

5 JUDGE FREDMAN: So, you're acknowledging the 248 is
6 enough?

7 MR. MOCK: Well, no, I'm just saying that there are some
8 pervasive mischaracterizations.

9 JUDGE FREDMAN: The way you just say to that, you're like,
10 well, anyone would know you could do it at 248.

11 MR. MOCK: That is not the only thing that's exposed here. The
12 PepTalk references we have lysine 248, (INDISCERNIBLE) use MAM, the
13 same example that is used --

14 JUDGE FREDMAN: Is there any other sequences around it?

15 MR. MOCK: It binds to those same sequences.

16 JUDGE FREDMAN: Right. But the implication that you're sort
17 of raising is that it works on anything where lysine is a 248.

18 MR. MOCK: No. I don't think the implication is that it works on
19 anything. Because the PepTalk references actually suggest that this
20 technology is for modifying IgG1, 2, and 4. That's a case now that they are
21 making is that it's not the case, that this could potentially work more
22 broadly. But with respect to the PepTalk references, again, I will highlight
23 that Dr. Zhou said when they disclose -- when the PepTalk references
24 disclose modifying lysine 248 in an IgG1.

25 He said that anything beyond that is purely aspirational. They
26 have not disclosed the chemistry to do anything beyond that. It's got to be

1 just that. With Yamada, it's got to be that chemistry. That's the only
2 chemistry that we have. But with the '675, there's this gap here. There is a
3 gap in how to modify any other isotype. And that's somehow routine
4 optimization? I just think it's a bit of misaligned characterization there.

5 There couple other things to quickly point out. Patent Owner says
6 time and again that we offered no motivation for selecting azide or
7 norbornene, for example. That is also not exactly accurate. With respect to
8 the record for the click chemistry groups, as I just noted azide is one of three
9 options disclosed within PepTalk references. It says that it will work, that it
10 works good with this technology.

11 JUDGE FREDMAN: We have to make lots of other choices too,
12 right?

13 MR. MOCK: Do what?

14 JUDGE FREDMAN: We have lots of other choices too, right?

15 MR. MOCK: In the PepTalk references it's only three. They
16 provide thiol, azide, and -- I forget the other ones. So, we're not talking
17 about a sea of possibilities. There's three, going back to the three chemical
18 compounds again. I suppose that's a running thing. Also, Dr. Tumey noted
19 in his declaration 1059 at paragraph 32, the azide was extremely well
20 established, commonly used in ADCs, and sites 1050 which showed azide
21 chemistry in an ADC.

22 With respect to the use of norbornene, it is one of a handful of
23 examples in Yamada and Matsuda. But also, in Exhibit 1059, paragraph 39,
24 Dr. Tumey cites three different papers, one of which refers to norbornene
25 click chemistry as known to proceed in a rapid, reliable, and selective
26 manner under mild conditions. That's Exhibit 1053. Exhibit 1054 says that

1 norbornene has attractive properties that have led to its generally applicable
2 method in bioconjugation. That's 1054. And 1055 says that it has an
3 excellent balance between reactivity with tetrazines and overall chemical
4 stability.

5 And I'll note that both 1054 and 1055 disclosed successful use of
6 norbornene click chemistry into in preparing ADCs. So, we're not talking
7 about uncharted territory here for either azide or norbornene. Both of these,
8 as Dr. Tumey stated and supported, were well-known reagents. They were
9 firmly established. They were good reagents that people were using for this
10 product. There's no reason to think that a person of ordinary skill would not
11 have been motivated to select those.

12 I see I'm running out of time. I touched on the linkers before. If
13 you have any other questions and will allow me time to answer those, I'd
14 love to.

15 JUDGE REN: Nothing from me. Thank you.

16 JUDGE FREDMAN: Thank you, sir.

17 JUDGE REN: Patent Owner's rebuttal.

18 MR. GIUNTA: So, I'm bringing up Paper number 2, which is the
19 petition. And one of the reasons why we were sort of surprised here in the
20 hearing and with the things went this way with regard to lysine 248 is
21 because Petitioner actually offered a construction of slightly different claim
22 term, but essentially the same claim term, which is at 248 position of heavy
23 chain amino acid sequence. And that definition -- sorry, that construction
24 says it's determined by the EU numbering system. And specification also
25 suggests that this position is commonly a lysine residue of an Fc domain of
26 the antibody.

1 And because the EU numbering system is widely accepted and this
2 position was in the Fc domain of IgG, a POSA would understand how to
3 determine which position within an antibody heavy chain is at 248 position
4 heavy chain amino acid sequence or a corresponding position for a fragment.
5 Accordingly, it should be interpreted as an amino acid residue within the
6 heavy chain, possibly within the Fc region at position 248 or corresponding
7 position in the case of a fragment as determined by the EU numbering
8 system. That's their --

9 JUDGE FREDMAN: I think they're not really -- maybe I'm
10 misunderstanding what they're saying. And I won't represent it wrongly, I
11 hope. But they're not really arguing that we don't know what 248 is.
12 They're saying is we don't know what's around 248 that permits the reaction
13 to the linker to bind, to create the three-dimensional structure that would
14 permit a linker to come in and bind. That's the argument I think they're
15 making.

16 MR. GIUNTA: Understood. But what's built in here is what we
17 were discussing earlier is that this is with reference to the Fc domain.

18 JUDGE FREDMAN: Right, we understand. I think that's fair,
19 yes.

20 MR. GIUNTA: Right. And so, if it's with reference to the Fc
21 domain, then it does add in that sequence. And so, it would add in that motif
22 that we were pointing to earlier, which is that surrounding area that includes
23 lysine 248.

24 JUDGE FREDMAN: But that isn't required, the claim doesn't
25 require that motif, right?

26 MR. GIUNTA: The entirety of the motif? It's not claimed that

1 way. So, in other words, do we claim it by sequence? The answer is no.
2 Did we claim it by lysine 248 with the intent that that's the region that we
3 were going for? The answer is yes. That's the point. And this construction
4 which they've offered is consistent with that. And it's clear that we are
5 indeed in possession of that, indeed in possession of an operative method of
6 making that. I'm going to move on, unless anyone has more questions.

7 With regard to the issues of for written description purposes,
8 they're saying that the '675 Patent needs chemistry, needs modification to
9 apply to these other groups. We're not really saying that in the same way
10 that they're saying that you would rerun an entire synthetic process or find
11 some other way to create a synthetic process for making the claimed
12 compounds based on the prior art.

13 And one other thing that I will note is that when it comes to the
14 prior art references and how common the norbornene group is or is not, I'll
15 note that the PepTalk reference doesn't have norbornene in it at all. If there
16 are no questions, I'll stop here.

17 JUDGE FREDMAN: Okay.

18 JUDGE REN: Nothing from the panel. Thank you.

19 MR. GIUNTA: Thank you, Your Honors.

20 JUDGE REN: The case is known to the panel for determination
21 and preparation of the final written decision.

22 (Whereupon, the above-entitled matter went off the record at 11:07
23 a.m.)

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Patent 11,896,657

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